# ATLAS of Oral Disease

**Nagato Natsume** **Guang-yan Yu**

# Preface

There are wide variety of oral diseases. Oral diseases treated with oral and maxillofacial surgery have a broad range of symptoms, which requires the doctors' advanced knowledge, treatment techniques and experiences for accurate diagnosis and adequate treatment. This textbook, written by distinguished doctors in the field, provides the latest information necessary for such diagnosis and treatment.

For the diagnosis, we have to evaluate the possible diseases corresponding to the observation with a cool-headed manner and careful decision.

We believe that doctors should take care of patients as if the patients were members of their own family. It is one of the important aspects of these characteristic diseases that require the doctors to attend to the patients with tender care.

On behalf of the authors, we hope this textbook is beneficial for the doctors in dentistry or stomatology, and also for the patients with various oral diseases all over the world.

We express our gratitude for all persons involved in publishing this textbook. Particularly, Prof. S.M. Balaji, who advised in proofreading and editorial process, is acknowledged by editors. We are also grateful to Dr. Xia Hong, Dr. Kumiko Fujiwara and our secretaries, Ms. Rie Osakabe , and Ms. Xiao-jing Li for their supports. We thank them for all their efforts.

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# Contents

# 1

# *Jaw Deformity*

# 1-1. Mandibular protrusion (and/or maxillary deficiency)

Mandibular protrusion is a growth related condition. It results from malpositions or malformations of the jaws. Occurrence of mandibular prognathism has a high familial and racial tendency. The incidence of mandibular prognathism is higher in Asia than Europe. Excessive mandibular growth could arise because of mandibular posture and oral habits. However, the majority of Class III problems are related to inherited jaw proportions.

**Clinical manifestation**

Patients with mandibular protrusion usually present with half cusp or full Class III occlusal relationship and the lower arch is larger than the upper one, especially in the anteroposterior direction. The length of the mandible is increased. The skeletal discrepancy includes mandibular excess and/or maxillary deficiency.

**Diagnosis**

Clinical judgment should be checked with the facial photographs and lateral cephalometric film. The mandible can not move back to the edge to edge position. Patients with mandibular protrusion may present with maxillary deficiency, a concave profile, anterior cross bite and/or posterior crossbite, increased gonial angle and lower facial height. Cephalometric analysis is needed to precisely describe the extent of the mandibular protrusion. It can accurately evaluate the patients' underlying skeletal disproportions.In patients with mandibular protrusion, SNB, gonial angle, total facial height and especially, lower facial height is increased. NA is decreased in patients with maxillary deficiency.

**Treatment**

Mild or moderate mandibular protrusion can be treated orthodontically. In the growing phase, for patients with mandibular protrusion, chin cup is the most commonly used method to inhibit the mandible from growing excessively forward. Chin cup therapy changes the direction of mandibular growth, rotating the chin downward and backward and tipping the lower incisors lingually. Asian children more than others can benefit from chin cup treatment because of their generally shorter face height.

In the growing phase in patients with maxillary deficiency, the skeletal deformity can either be transverse or vertical. The preferred treatment is to move the maxilla into a more anterior and inferior position. Following this or in conjunction with palatal expansion, a facemask with anchorage from the forehead and chin is used to exert a forward force on the maxilla via elastics attached to a maxillary appliance with hooks located in the canine area for attachment to the facemask.

Severe mandibular protrusion usually requires combined orthodontic treatment and orthognathic surgery to obtain the most stable result with optimal function and esthetics. The bilateral sagittal split ramus osteotomy is commonly used for mandibular setback and control of the occlusion. Genioplasty can alter the position of the chin in three planes of space.

The maxillary deficiency is treated mainly with Le Fort I maxillary downfracture osteotomy. This procedure can move the maxilla forward. Patients with total midface deficiency may be effectively managed with a Le Fort II or Le Fort III osteotomy. Anterior distraction of the maxilla has recently been introduced for cleft patients with severe midface deficiency. The maxilla can be segmented for repositioning of dento-osseous segments. In patients with transverse maxillary deficiency, segmentation between the central incisors can be used for maxillary expansion.

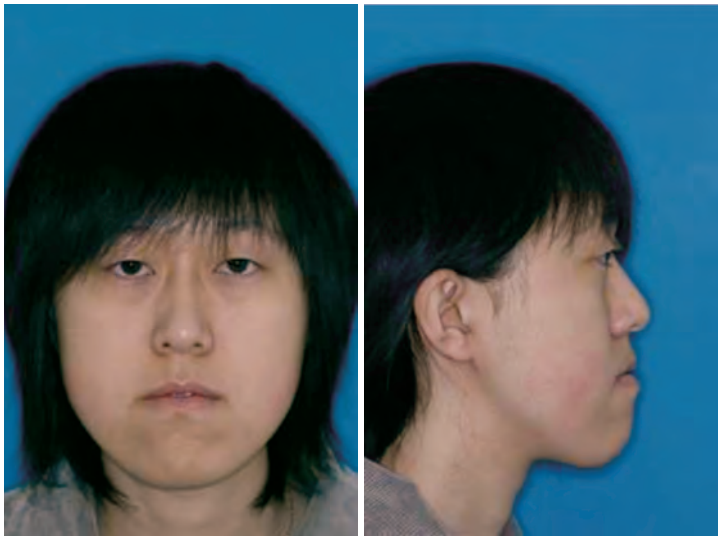

Fig. 1-1-1 Pre-treatment: Patient with mandibular protrusion

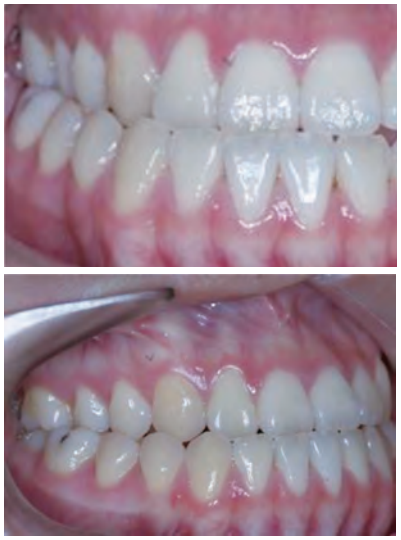

Fig. 1-1-2 Patient with Class III malocclusion and crossbite

Fig. 1-1-3 Post-treatment: After combined treatment of orthodontics and orthognathic surgery (Le Fort I osteotomy and SSRO)

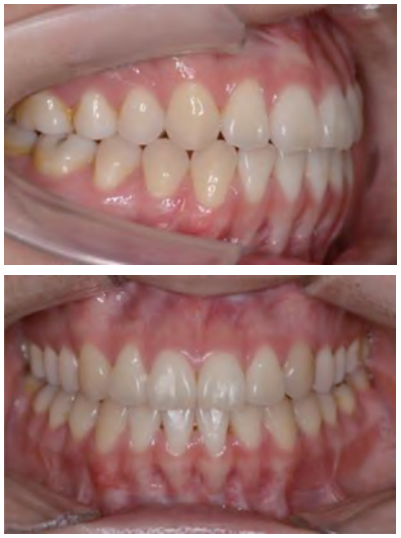

Fig. 1-1-4 The occlusion after treatment

(Yi-lin Jia)

## *1-2. Maxillary protrusion (and/or mandibular deficiency)*

Patients with maxillary protrusion often present with increased overjet, prominent upper lip and lip incompetence. Mandibular deficiency is due to insufficient forward growth of the mandible. The patients usually present with Class II malocclusion.

The etiology of the deformity can be congenital or environmental. Congenital influences include inherited patterns, defects in embryologic development and trauma. Children with deformities involving mandible are much more likely to have a congenital syndrome. Extreme mandibular deficiency at birth is seen in Pierre Robin syndrome. The reduced volume of the oral cavity can lead to respiratory difficulty. Patients with Treacher Collins syndrome also present with mandibular deficiency. The environmental influences include ankylosis of TMJ, condylar fracture and functional problems.

**Clinical manifestation**

Patients with maxillary protrusion can have combined mandibular deficiency and the occlusal relationship is usually half cusp or full Class II. The maxilla often has excessive forward and downward growth and the mandible rotates downward and backward. The combination contributes to skeletal Class II malocclusion. The patients usually present with a convex profile and gummy smile. Patients have lip incompetence and the upper lip is beyond the E-line.

**Diagnosis**

A careful examination of the profile is needed for diagnostic purposes. Lip posture and incisor prominence should be evaluated by viewing the profile with the patient's lips relaxed. In patients with maxillary protrusion, the upper lip is usually significantly forward from E-line. Cephalometric analysis is also needed to precisely describe the nature of the maxillary protrusion. In patients with maxillary protrusion, SNA and ANB is increased. At the same time, SN-Pog and SNB is decreased. In some patients, the mandible demonstrates clockwise rotation, with increased SN-GoGn angle and lower facial height.

**Treatment**

The goal of treatment is to restrict growth of the maxilla while the mandible grows into a more prominent and normal relationship with it. In the growing phase in patients with maxillary protrusion, using extraoral force, in the form of headgear appliance, is the most effective method to inhibit the maxilla from growing forward and at the same time, the mandible grows to catch up. In patients with mandibular deficiency, functional appliance can be used to help the mandible grow.

Severe maxillary protrusion in adults also requires combined orthodontic treatment and orthognathic surgery to obtain optimal results. Maxillary protrusion treated up to the width of a premolar is usually accomplished by removal of a premolar tooth on each side, followed by segmentation of the maxilla.

In patients with mandibular deficiency, bilateral sagittal split ramus osteotomy is usually performed to obtain mandibular advancement. Mandibular distraction has been employed for the patients with severe mandibular deficiency (such as Treacher Collins syndrome).

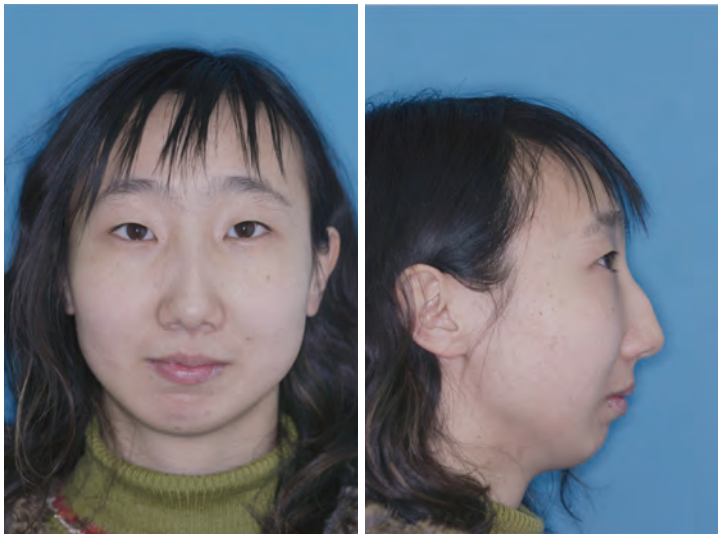

Fig. 1-2-1 Pre-treatment: Patient with mandibular deficiency

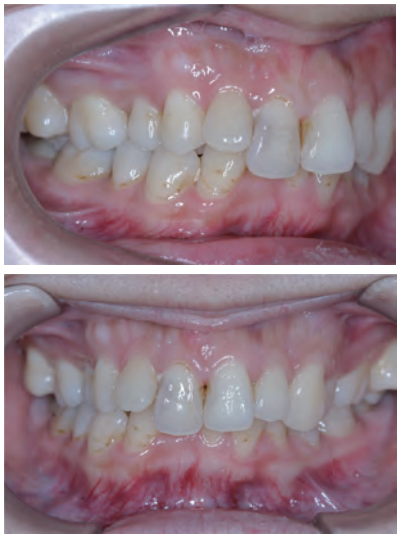

Fig. 1-2-2 Patient with Class II malocclusion and increased overbite

Fig. 1-2-3 Post-treatment: After combined treatment of orthodontics and orthognathic surgery (Le Fort I osteotomy and SSRO)

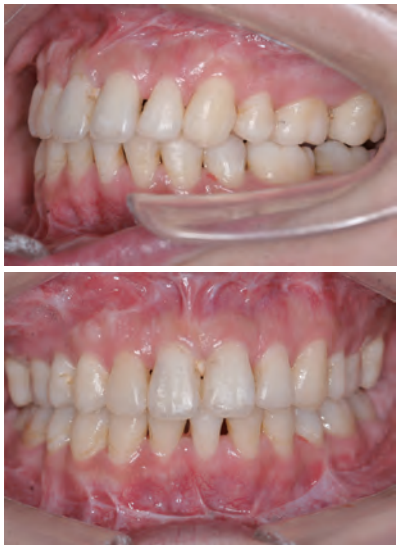

Fig. 1-2-4 The occlusion after treatment

(Yi-lin Jia)

# 1-3. Condylar hyperplasia

Condylar hyperplasia of the mandible is a state of overdevelopment that leads to facial asymmetry, mandibular deviation, malocclusion, and articular dysfunction. The condition was first described by Adams in 1836. Since then, there have been numerous reports in the literatures and it is now considered to be one of the more common conditions for which patients seek surgical attention. The cause of condylar hyperplasia has yet to be elucidated; trauma, infection (particularly in the TMJ), heredity, and intrauterine influences have been suggested as possible etiologic factors. It usually occurs in early adolescence or in mid-teens, with increasing deformity until growth is complete, usually by the end of the second decade.

Clinical features of condylar hyperplasia include an enlarged mandibular condyle, elongated condylar neck, outward bowing and downward growth of the mandibular body (Fig. 1-3-1), causing fullness of the affected side and flattening of the contralateral side of the face. If the deformity occurred before growth is complete the occlusal plane is usually slanted because of dental compensation, whereas posterior open bite is usually apparent if the deformity occurred after completion of growth.

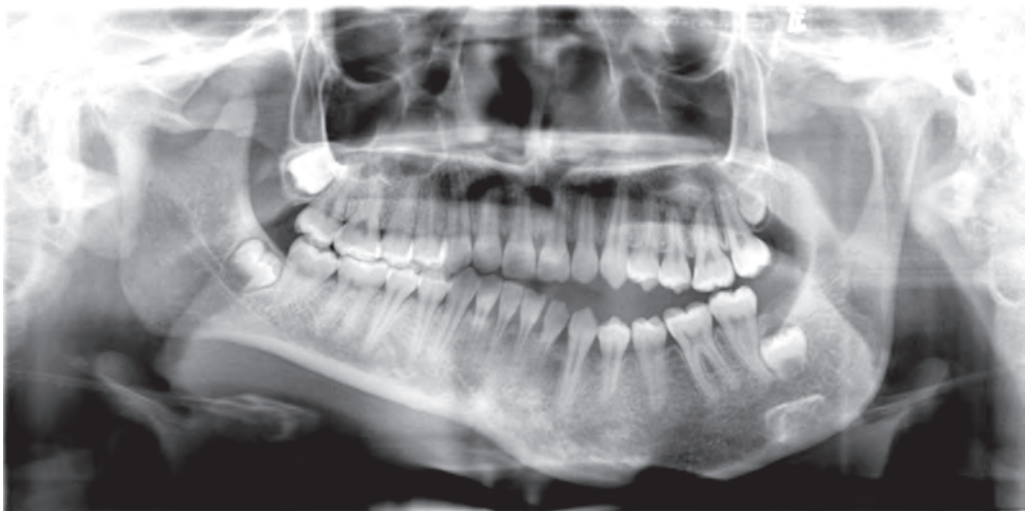

Fig. 1-3-1A Panoramic radiograph showing an enlarged mandibular condyle, elongated condylar neck, outward bowing and downward growth of the mandibular body in the left side.

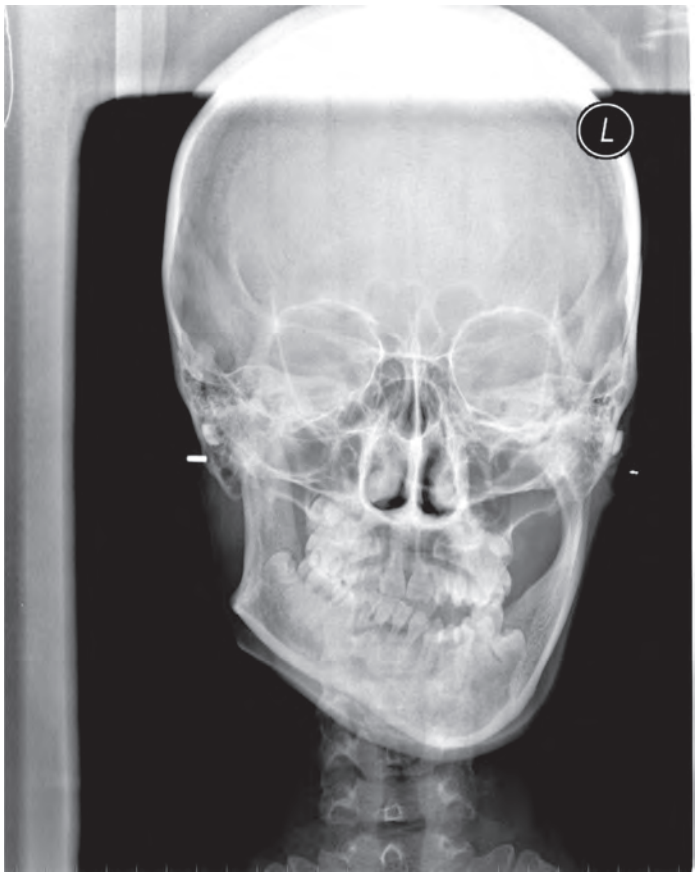


Fig. 1-3-1B Radiograph of the posterior-anterior projection showing facial asymmetry with fullness of the affected side.

The basic consideration in the management of facial asymmetry secondary to condylar hyperplasia is to control the growth process to allow more balanced facial development. High condylectomy or condylar shave in actively growing cases can be performed with other related mandibular surgery. Orthodontic treatment is essential afterward in patients treated by early condylar resection. Surgical methods are used for correcting asymmetry, mandibular sagittal split osteotomy, subcondylar ramus osteotomy, Le Fort I wedge osteotomy to re-level the tilted occlusal plane, and contouring of the lower mandibular margin can be done depending on the degree of deformity.

(Kai-yuan Fu)

# 2

# *Infection*

# 2-1. Dental caries and non-caries tooth tissue loss

**a. Dental caries**

Dental caries is the most common reason for tooth defect, toothache and even tooth loss. Dental caries is a multifactorial disease involving the host, the microflora and the substrate. When cariogenic oral flora and fermentable carbohydrates are present on the susceptible tooth for sufficiently long time, calcified tooth tissue is demineralized and dissolved, and caries occurs.

**Clinical Manifestation**

Dental caries mostly occurs in occlusal fissures and proximal tooth surfaces. In case of hyposalivation, caries progression is accelerated and cavity may appear in caries-unsusceptible sites, such as cusps & smooth surfaces on buccal and lingual areas.

In early stage, caries appears as a white spot caused by demineralization of tooth enamel. The white-spot lesion could be remineralized in case of removal of acids and if sufficient minerals are provided. Once the demineralization process continues destruction and cavitations of enamel and dentin take place.

The consistency and color of decayed tooth tissues vary depending on caries progression. When caries develops quickly, the decay generally is soft and of a light color. Hard and dark decay usually indicates that progression is slow.

**Diagnosis**

According to caries progression rate, caries lesions can be classified as acute caries, chronic caries and arrested caries.

Acute caries progresses rapidly, is soft tactile and has a light color. It often occurs in children and teenagers.

Active caries occurring in patients with pharmacotherapy, radiotherapy or systematic disorders, such as Sjögren syndrome, is termed as rampant caries (Fig. 2-1-1). The carious lesions frequently involve unsusceptible surfaces of several teeth.

Slowly progressing caries is referred to as chronic caries. It appears dark brown in color and is hard & tactile.

When caries risk factors are removed, the progress of caries will arrest and remineralization may occur. It could be defined as arrested caries which is hard tactile, dark brown in color and has a shiny surface.

In addition to visual inspection and exploration, radiograph is valuable in

diagnosing interproximal caries. The affected tissue is seen as a radiolucency due to demineralization of calcified tooth tissue.

Diagnosis of incipient lesions in occlusal fissures or proximal surfaces is difficult. Numerous approaches other than traditional diagnostic methods are used for early detection of caries, such as DIAGNOdent based on pulsed red light (Fig. 2-1-2), DIFOTI based on visible light, ECM based on electrical current, etc.

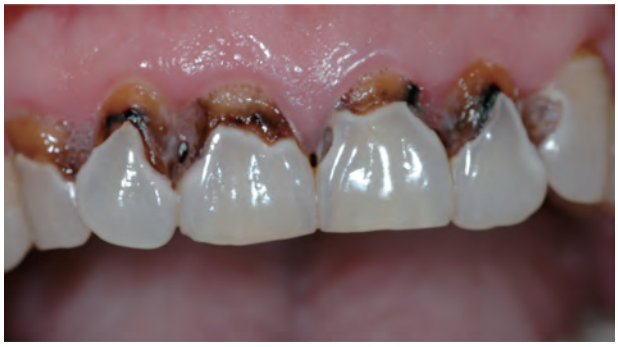

Fig. 2-1-1 Rampant caries

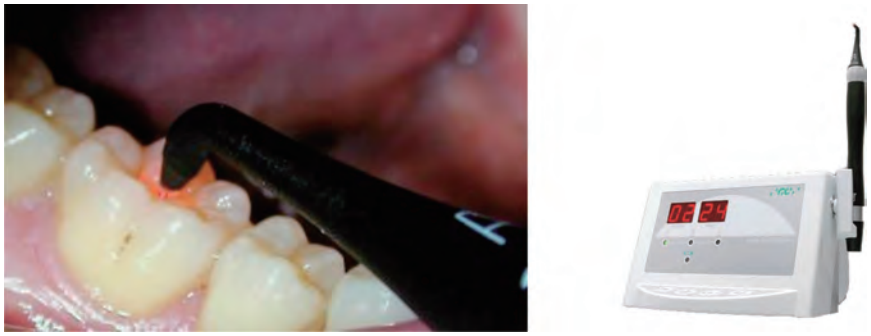

Fig. 2-1-2 DIAGNOdent for early caries detection

**Treatment and Prevention**

Nowadays, the gained knowledge on caries indicates that a lifelong management of dental caries is necessary. Management of dental caries involves not only restoring the cavity but also preventing the occurrence by multiple approaches. Prevention of caries includes improving oral hygiene, reducing sugar intake and adopting fluoride agents, etc.

Minimal intervention of carious lesions is a core concept of modern caries management. Carious lesions should be remineralized without operative intervention unless the lesion extends into dentin. When restoring the decay, a conservative cavity preparation is suggested, which only requires removing carious tissues (Fig. 2-1-3). Using micropreparation burs and adhesive filling materials minimizes unnecessary removal of healthy tooth tissues.

Caries detector dyes assist the dentist to distinguish the infected and uninfected dentin, thus the uninfected softer dentin could be left behind for remineralization. Carisolv, a chemo-mechanical technique, is effective and minimally invasive.

Techniques other than conventional bur preparations are used for cavity preparation such as laser and air-abrasion technology.

In populations where caries is highly prevalent, preventive filling materials like GICs or Giomers releasing fluoride in combination with other preventive approaches are effective to manage caries (Fig. 2-1-4).

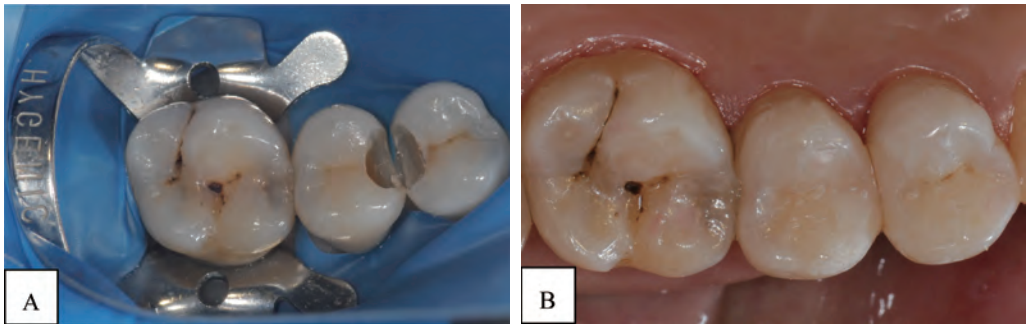


Fig. 2-1-3 Conservative cavity preparation and adhesive restoration
(A) Conservative cavity preparation. (B) Completed adhesive restorations

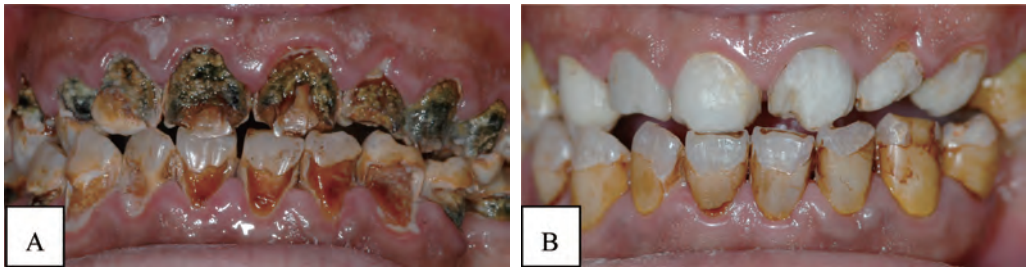


Fig. 2-1-4 Caries control with GIC sealing
(A) Preoperative view of carious lesions.
(B) After half a year with GIC sealing. (Courtesy of Dr TIAN Fu-cong)

**b. Non-carious tooth tissue loss**

Non-carious tooth tissue loss is usually used to describe a wide range of dental defects other than dental caries. These diseases mainly include abrasion, dental erosion and wedge-shaped defects.

**1) Abrasion**

Hard tissue of teeth may get worn away due to chewing, tooth-tooth contact or friction of exogenous materials forced over tooth surface. The loss of teeth structure from opposing tooth contact is termed attrition. Abrasion refers to loss of tooth substance caused by physical and mechanical factors other than tooth contact.

**Clinical Manifestation**

The abrasive lesions appear in a variety of forms: dish-shaped, pitted, flattened or as irregular defects. The defect is glossy and with a distinct margin (Fig.2-1-5A).

Dentin sensitivity to mechanical irritation could exist when the defect involves enamel-dentin junction. As the defect progresses, reversible or even irreversible pulpitis may occur (Fig. 2-1-5B).

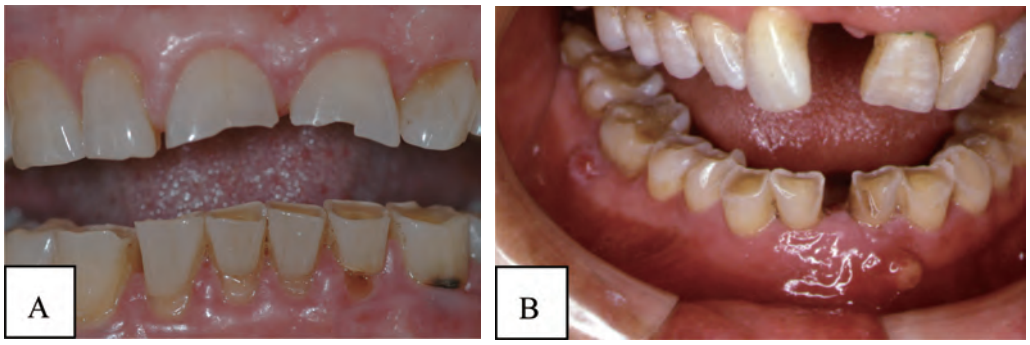


Fig. 2-1-5 Tooth abrasion
(A) Tooth abrasion. (B) Apical periodontitis with sinus tract caused by tooth abrasion

**Diagnosis**

Tooth abrasion is determined mainly by visual inspection. Tooth wear index is useful to define the severity of tooth abrasion (Table 2-1-1).

Table 2-1-1 Smith and Knight tooth wear index

| Score | Surface | Criteria |
|---|---|---|
| 0 | B/L/O/I | No loss of enamel surface characteristics |
| | C | No loss of contour |
| 1 | B/L/O/I | Loss of enamel surface characteristics |
| | C | Minimal loss of contour |
| 2 | B/L/O | Loss of enamel exposing dentine for less than one third of surface |
| | I | Loss of enamel just exposing dentine |
| | C | Defect less than 1 mm deep |
| 3 | B/L/O | Loss of enamel exposing dentine for more than one third of surface |
| | I | Loss of enamel and substantial loss of dentine |
| | C | Defect less than 1–2 mm deep |
| 4 | B/L/O | Complete enamel loss–pulp exposure–secondary dentine exposure |
| | I | Pulp exposure or exposure of secondary dentine |
| | C | Defect more than 2 mm deep–pulp exposure–secondary dentine exposure |

**Treatment and Prevention**

A treatment plan for tooth abrasion includes not only restoring the defect and alleviating the symptoms but also removing or modifying etiological factors. Monitoring and preventing further tooth loss are desirable.

With development of adhesive dentistry, composite resin and ceramic materials have been used to restore the abrasive defects.

When several teeth are involved, treatment interventions should be considered cautiously. A series of techniques can be adopted depending on patient's complaints and circumstances. The most complicated case may simultaneously require occlusion adjustment, surgical crown lengthening, orthodontics or even treatment of temporomandibular joint disease.

**2) Dental erosion**

Dental erosion is defined as dissolution of tooth substance by chemicals other than dental plaque. Among exogenous and intrinsic erosion agents, soft drinks popular in adolescents account for the increased prevalence of dental erosion.

**Clinical Manifestation**

In early stage of dental erosion, enamel presents with a smooth glazed or dull appearance. Along gingival margin, intact enamel margin may be detected (Fig. 2-1-6A). In more advanced stage, tooth morphology is further changed. Shallow concavity on enamel is developed, and tooth cusp is rounded. Restorations are elevated due to the loss of adjacent tooth tissue (Fig. 2-1-6B). The whole morphology of facial or occlusal surface may be changed. With the progression of erosion, pulp could be involved.

**Diagnosis**

The clinical features are critical to diagnose dental erosion. When dental erosion occurs on facial surfaces, it should be distinguished from wedge-shaped defect. The differential diagnosis of erosion on occusal surfaces should include attrition and abrasion. In most cases, attrition, abrasion and erosion may simultaneously exist.

**Treatment and Prevention**

It is important to diagnose dental erosion in early stage and prescribe preventive measures for patients. Reducing the erosive agents is fundamental. Rinsing the mouth after food intake and using remineralization agents routinely are also useful to retard the progression of lesions.

The involved dentin should be restored as early as possible to protect the remaining dentin from further erosion (Fig. 2-1-6C, D). Endodontic treatment is recommended when pulpitis or apical periodontitis occur in severe cases.

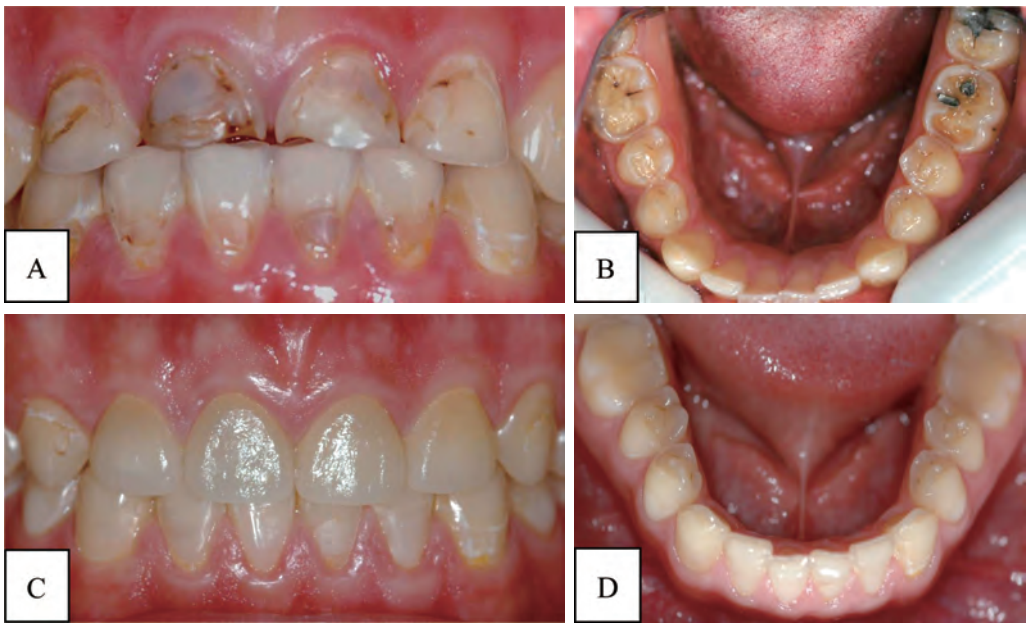


Fig.2-1-6 Dental erosion
A. “Enamel margin” along gingival margin. B. Amalgam restoration “island”.
C. Completed ceramic crown and adhesive composite restorations. D. Postoperative view of lower teeth.

**3) Wedge-shaped cervical defect**

The combined role of abrasion, erosion and stress are supposed to cause a wedged-shaped defect in cervical area of tooth.

**Clinical Manifestation**

The cervical lesion appears as shallow wedge-shaped, disk-shaped or irregular defects with sharp margins. The exposed dentin is mostly shining, hard and tactile. (Fig. 2-1-7A)

It may cause sensitivity to mechanical irritation when the defect is near enamel-dentin junction. When defects progress close to pulp, reversible or even irreversible pulpitis may occur.

**Diagnosis**

Wedge-shaped defects can be diagnosed easily according to their cervical location. Occlusion analysis of the involving teeth should be performed.

**Treatment and Prevention**

Proper teeth brushing technique should be recommended.

The cervical defect should be filled with adhesive tooth-colored materials to restore esthetic and morphological properties (Fig. 2-1-7B). Occlusion adjustment is supposed to benefit the longevity of restorations.

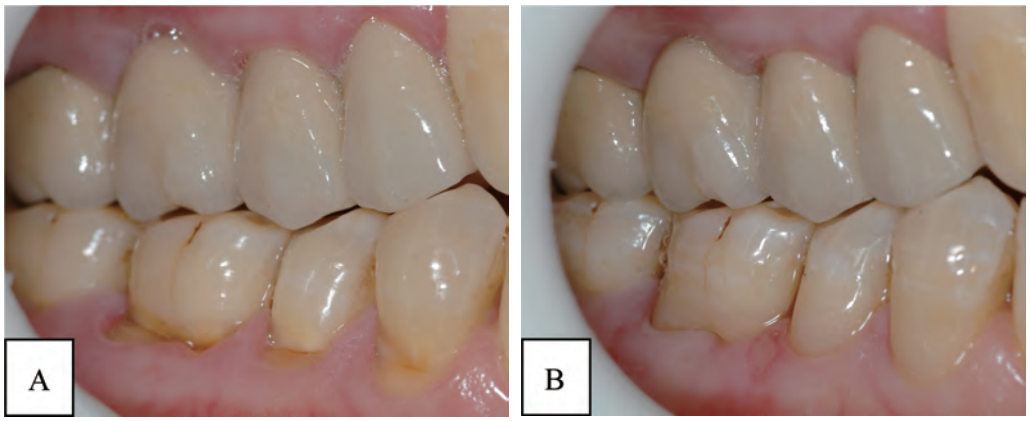


Fig. 2-1-7 Wedge-shaped defect
A, Wedge-shaped defect. B, Completed composite restorations

(Xiao-yan Wang, Xue-jun Gao)

## 2-2. *Periodontic infections*

The most common form of periodontal disease is that which is associated with local irritation. This begins as marginal gingivitis which usually progresses, if untreated or treated improperly, to severe chronic periodontitis. This type of periodontitis, sometimes referred to as marginal periodontitis, is most common in adults, although it is found occasionally in children, especially when oral hygiene is lacking, or in certain cases of malocclusion. In adults, periodontal disease of this type accounts for more than 90 per cent of the cases of periodontal disturbances and is responsible for greater tooth mortality than dental caries[1)].

**a. Pericoronitis (Fig. 2-2-1, Fig. 2-2-2)**

An inflammatory lesion known as pericoronitis can develop around impacted or partially erupted teeth when food debris and bacteria are present beneath the gingival flap overlying the crown. If the debris and bacteria become entrapped deep within the gingival flap, an abscess develops. Abscess development is most frequently seen in association with the mandibular third molars, and the predominant symptoms are extreme pain in the area, a foul taste, and inability to close the jaws. The affected area is erythematous and edematous, and the patient often has lymphadenopathy, fever, leukocytosis, and malaise[2)].

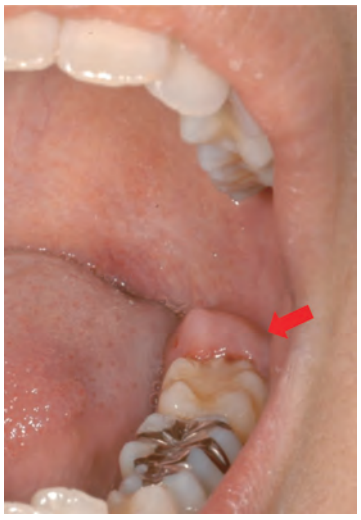

Fig. 2-2-1
Pericoronitis. Painful erythematous enlargement of the soft tissues overlying the crown of the partially erupted left mandibular third molar

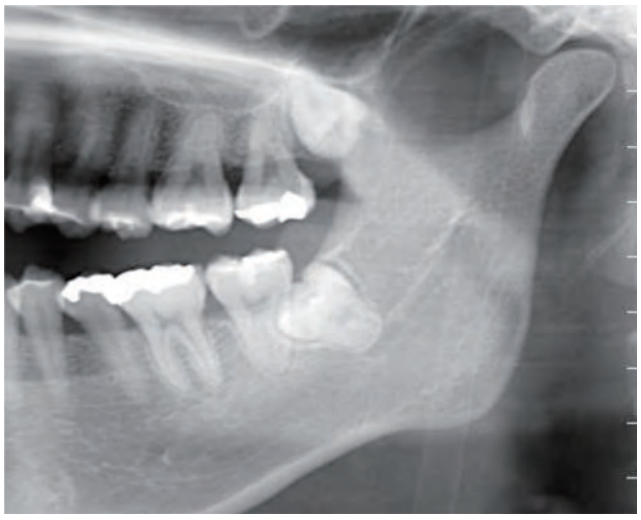

Fig. 2-2-2
Pericoronitis. Left mandibular X-ray of the same patient depicted in Fig. 2-1-1

**Symptoms**

Throbbing pain.

Extreme sensitivity to palpation of the affected gingival flap.

Sensitivity and mobility of adjacent teeth.

Foul taste.

Lymphadenopathy.

Occasionally: fever, leukocytosis, and malaise.

**Diagnosis**

Symptoms and x-ray scanning.

**Treatment**

Systemic antibiotics.

Extraction of teeth.

If tooth retention is desirable, the overlying gingival flap is removed surgically, followed by elimination of all food debris and bacterial colonies by thorough curettage.

**Standard treatment**

Reducing inflammation.

Extraction of infected teeth.

**b. Periapical periodontitis (Fig. 2-2-3)**

Once infection has become established in the dental pulp, spread of the process can be in only one direction-through the root canals and into the periapical region. Here a number of different tissue reactions may occur, depending upon a variety of circumstances. It is important to realize that these periapical lesions do not represent individual and distant entities, but rather that there is a subtle transformation from one lesion into another type in most cases. Furthermore, it should be appreciated that a certain degree of reversibility is possible in some lesions. The interrelations existing between the types of periapical infections must be clearly understood[3].

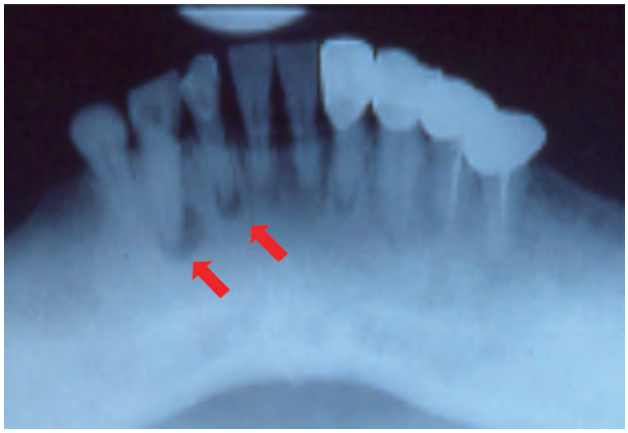

Fig. 2-2-3 Periapical periodontitis.
Periapical radiolucency associated with the apices of the mandibular teeth

**Symptoms**

Tenderness of periapical gingival flap.
Mobility of teeth.
Percussion tenderness of teeth.

**Diagnosis**

Symptoms and x-ray scanning.
Differential diagnoses: Periapical granuloma and Periapical.

**Treatment**

Root canal treatment of teeth.
Extraction of teeth.

**Standard treatment**

Root canal treatment of teeth.
Extraction of teeth.

**References**

1) William GS, Maynard KH and Barnet ML: A Textbook of Oral Pathology: W. B. Saunders Company, Philadelphia, 1974, p733-734.
2) Brad WN, Douglas DD, Carl MA, Jerry EB: Oral & Maxillofacial Pathology: W. B. Saunders Company, Philadelphia, 1995, p135.
3) William GS, Maynard KH and Barnet ML: A Textbook of Oral Pathology: W. B. Saunders Company, Philadelphia, 1974, p440-441.

(Masatsugu Yoshida, Mitsuyoshi Matsuda)

# 2-3. Infection of jaw

**a. Periostitis (Fig. 2-3-1, Fig. 2-3-2)**

The patient may complain of pain due to odontogenic infection before intermittent, usually nontender, swelling at the inferior border or other peripheries of the mandible develops. If chronic infection becomes established just beneath the periosteum and is not treated, the swelling will persist and soon become hard as new bone is laid down. After the infection has been eliminated, hard elevation will usually slowly disappear as the bone is re-contoured by the functional forces[1].

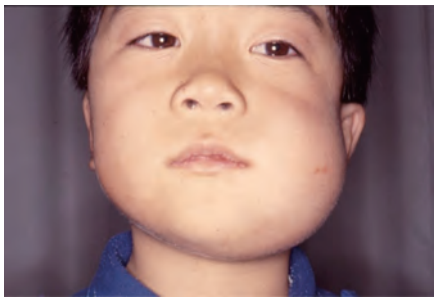

Fig. 2-3-1
Periostitis: Facial swelling due to infection originating in the mandibular deciduous molar

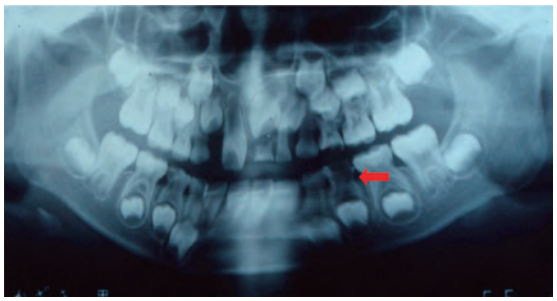

Fig. 2-3-2
Periostitis: Radiolucency associated with the mandibular deciduous molar

**Symptoms**

Swelling, pain, redness and fever of the affected jaw.
Induration and tenderness of the affected jaw.
Mobility and percussion tenderness of the affected teeth.

**Diagnosis**

Symptoms and x-ray scanning.

**Treatment**

Antibiotic therapy.
Drainage.
Treatment of the teeth causing the infection or extraction of the teeth.

**Standard treatment**

Antibiotic therapy.
Drainage.

**b. Osteomyelitis (Fig. 2-3-3, Fig. 2-3-4)**

Osteomyelitis, an inflammation of bone and bone marrow, may develop in the jaw as a result of odontogenic infection as well as a variety of other situations. The disease may be either acute, subacute or chronic and presents a different clinical course depending upon its nature[2].

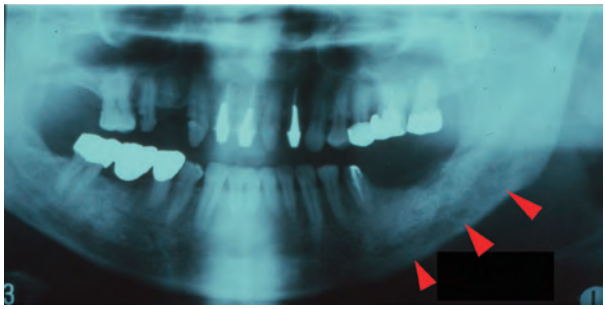

Fig. 2-3-3
Osteomyelitis. Ill-defined area of radiopacity in the left body of the mandible

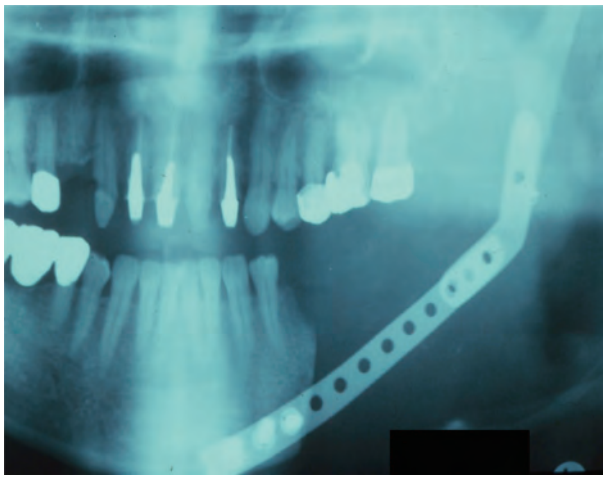

Fig. 2-3-4
After reconstructive surgery for chronic osteomyelitis. -metal plate was used for occlusion construction.

**Symptoms**

Acute Osteomyelitis

Patients with acute osteomyelitis have signs and symptoms of an acute inflammatory process that typically has been less than 1 month in duration.

Fever.

Leukocytosis.

Lymphadenopathy.

Soft tissue swelling of the affected area.

Tooth mobility.

Neuroparalysis of trigeminal nerve

Chronic Osteomyelitis

If acute osteomyelitis is not resolved expeditiously, the entrenchment of chronic osteomyelitis occurs, or the process may arise primarily without a previous acute episode.

Swelling.

Pain.

Purulent discharge.

Sequestrum formation.

Tooth loss.

Pathologic fracture.

Patients may experience acute exacerbations or periods of decreased pain associated with chronic smoldering progression.

**Diagnosis**

Symptoms.

X-ray scanning.

Computerized tomography.

Magnetic resonance imaging.

Scintigraphy($^{67}$Ga, $^{99m}$Tc).

Bone biopsy

**Treatment**

Antibiotic therapy.

Anti-inflammatory therapy.

Surgery (sequestrectomy).

Hyperbaric oxygen therapy.

**Standard treatment**

Antibiotic therapy.

**References**

1) William GS, Maynard KH and Barnet ML: A Textbook of Oral Pathology: W. B. Saunders Company, Philadelphia, 1974, p456-457.

2) William GS, Maynard KH and Barnet ML: A Textbook of Oral Pathology: W. B. Saunders Company, Philadelphia, 1974, p453.

(Masatsugu Yoshida, Mitsuyoshi Matsuda)

# 2-4. *Infection of soft tissue*

**a. Cellulitis of the floor of the mouth (Fig. 2-4-1, Fig. 2-4-2)**

Cellulitis is a diffuse inflammation of soft tissues which is not circumscribed or confined to one area, but which, in contradistinction to the abscess, tends to spread through tissue spaces and along facial planes. This type of reaction occurs as a result of infection by microorganisms that produce significant amounts of hyaluronidase and fibrinolysins which act to break down or dissolve, respectively, hyaluronic acid, the universal intercellular cement substance, and fibrin. Streptococci are particularly potent producers of hyaluronidase and are therefore a common causative organism in cases of cellulitis. The less common hyaluronidase-producing staphylococci are also pathogenic and frequently give rise to cellulitis[1)].

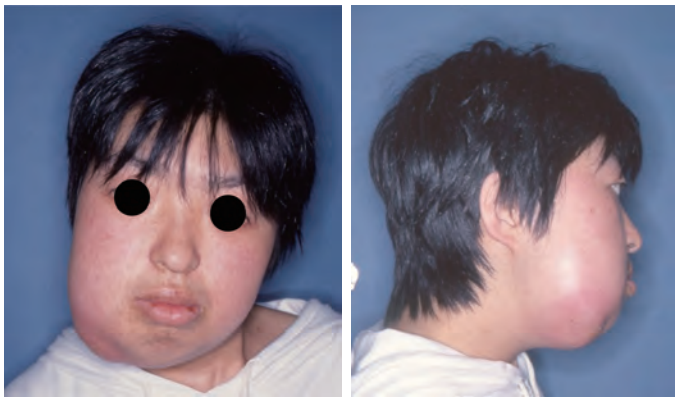

Fig. 2-4-1
Cellulitis of the floor of the mouth.
Metal plate was used for occlusion construction

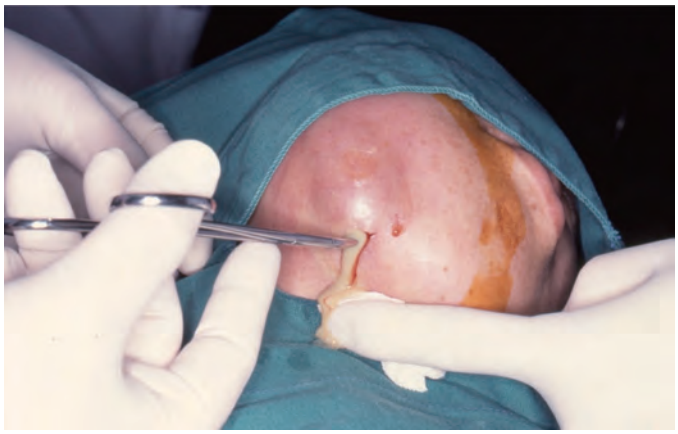

Fig. 2-4-2
Drainage of the cellulitis of the floor of the mouth. After incising the right submandibular skin, pus discharge seen

**Symptoms**

Swelling of the floor of mouth, tongue, and submandibular region.

Involvement of the sublingual space results in elevation, posterior enlargement, and protrusion of the tongue.

Submandibular space spread causes enlargement and tenderness of the neck above the level of the hyoid bone.

High fever.

Chills.

Leukocytosis.

Elevated sedimentation rate.

**Diagnosis**

Symptoms.

X-ray scanning.

Computerized tomography.

**Treatment**

Antibiotic therapy.

Surgical drainage.

**Standard treatment**

Antibiotic therapy.

Surgical drainage.

**b. Lymphadenitis**

This is the second most common pathological cervical mass and the most common painful enlargement found in the neck. The primary infection may be in the oral cavity, the nasal cavities, the tonsils, or the pharynx. Frequently minor mucosal erosions or shallow ulcers permit the entrance of sufficient bacteria to produce a regional lymphadenitis. Depending on the location of the tooth, a periapical abscess, periodontal abscess, or pericoronitis-type infection may cause painful swollen nodes in the submental, submandibular, or subdigastric area. Rapid progress of the inflammation may result in the node returning to normal, being nonpalpable. In more chronic cases the node will become fibrosed or persist as an asymptomatic lymphoid hyperplasia. In either circumstance, the node is enlarged, firm, and usually freely movable[2)].

**Symptoms**

Acute lymphadenitis.

Tender or quite painful on palpation. Node will be round, firm, discrete.

**Diagnosis**

Symptoms as differential diagnosis metastatic node.

Computerized tomography.

**Treatment**

Antibiotic therapy.

Treatment of primary illness.

**Standard treatment**

Antibiotic therapy.

**c. Maxillary sinusitis (Fig. 2-4-3, Fig. 2-4-4)**

Maxillary sinusitis, an acute or chronic inflammation of the maxillary sinus, is often due to direct extension of dental infection, but originates also from infectious diseases such as common cold, influenza and exanthematous disease. Perhaps this arises from local spread of infection in the adjoining frontal or paranasal sinuses, or from traumatic injury of the sinuses with a superimposed infection. The occurrence of maxillary sinusitis as a result of the extension of dental infection depends to a great extent upon the relation and proximity of the teeth to the sinus. When sinusitis is secondary to dental infection, the microorganisms associated with the sinusitis are the same as those associated with the dental infection[3].

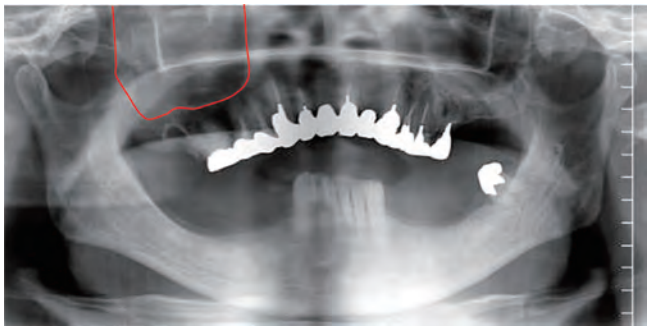

Fig. 2-4-3
Sinusitis. X-ray of panoramic view.
Cloudy right maxillary antrum

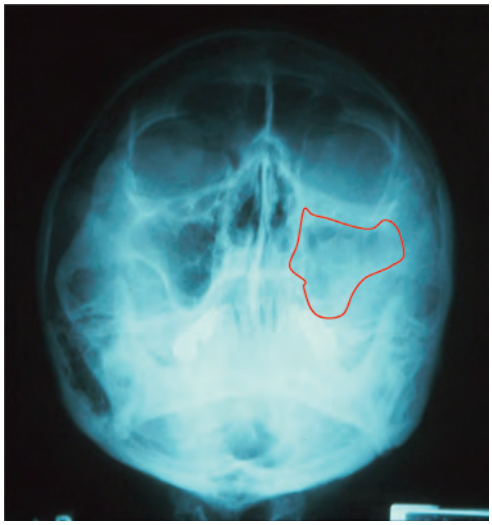

Fig. 2-4-4
Sinusitis. X-ray of Waters' view.
Cloudy left maxillary antrum is shown.

**Symptoms**

Acute sinusitis

Headache, fever, and facial pain over the affected sinus.

Anterior nasal or posterior pharyngeal discharge.

Increased pain when the head is held upright and less discomfort when the patient is supine.

**Diagnosis**

Symptoms.

Plain radiographs, such as the Waters, Caldwell-Luc, lateral, and submental vertex views.

Nasal endoscopy.

Computed tomography.

**Treatment**

Antibiotic therapy.

Radical surgery of the maxillary sinus (radical stripping of the diseased sinus mucosa) .

Nasal endoscopy (endoscopic sinus surgery).

Root canal treatment of the teeth causing the sinusitis.

Extraction of the teeth causing the sinusitis.

**Standard treatment**

Antibiotic therapy.

Radical surgery of the maxillary sinus.

Nasal endoscopy.

Root canal treatment of the teeth causing the sinusitis.

Extraction of the teeth causing the sinusitis.

**References**

1) William GS, Maynard KH and Barnet ML: A Textbook of Oral Pathology: W. B. Saunders Company, Philadelphia, 1974, p464.

2) Norman KW, Paul WG: Differential Diagnosis of Oral Lesions: The C. V. Mosby Company, 1980, p272.

3) William GS, Maynard KH and Barnet ML: A Textbook of Oral Pathology: W. B. Saunders Company, Philadelphia, 1974, p470.

(Masatsugu Yoshida, Mitsuyoshi Matsuda)

# 2-5. Specific inflammation

**a. Actinomycosis of Jaw**

This disease is caused by *Actinomyces israelii* -one of normal bacterial flora in the mouth. Sometimes, it causes mixed infection with other purulent bacterium in the mouth. Actinomycosis of jaw occurs from oral cavity to jaws, neck and face. Though the causes are thought to be pericoronitis of wisdom tooth, infection after tooth extraction, caries, periodontal disease, apical periodontits and so on, it is still unclear. It occurs in adolescence and adulthood. Actinomycosis causes chronic inflammation and it does not produce a high fever.

**Symptoms**

A diffused swelling grows on the soft tissues around the mandibular angle or cheek, with abscess formation accompanied with marginal granulation. Once inflammation extends to masticatory muscles, they become fibrous and show "board-like induration" (Fig. 2-5-1, -2). Trismus also appears. Multiple abscesses are formed and sulfur granules called drusen can be observed in them (Fig. 2-5-3). Abscesses extend to the bone marrow.

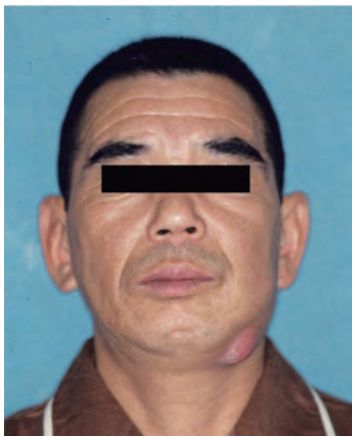

Fig. 2-5-1
A patient with actinomycosis abscess

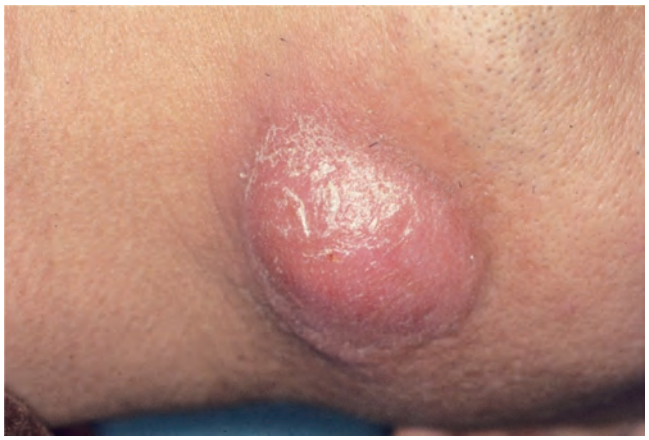

Fig. 2-5-2
An abscess with "board-like induration"

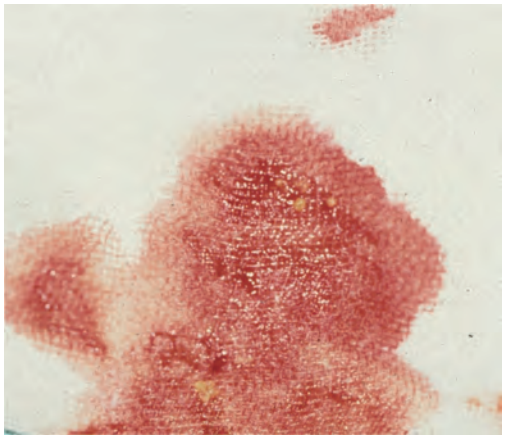

Fig.2-5-3
Sulfur granules called drusen

**Diagnosis**

Final diagnosis is made by detecting masses of *A. israelii* or isolation culture.

**Treatment**

The basic treatment is high dose administration of penicillins. As *A. israelii* is obligate anaerobe, active incision and drainage of the abscess is effective.

**b. Tuberculosis**

Tuberculosis is mainly caused by Mycobacterium tuberculosis infection. This disease is transmitted through the air by cough, sneeze and saliva of the patient.

**Symptoms**

1) Primary tuberculosis

Aspirated M. tuberculosis spreads lymphogenously and/or hematogenously into a human body and lies latent in the cells. But they show no symptoms. A host with insufficient immune response acquires tuberculosis mainly on the upper lung field or the apex of lung.

2) Reactivation of tuberculosis

In a host with sufficient immune response, once immunity of the host is disturbed, M. tuberculosis will be active. The factors disturbing immune response are aging, malnutrition, AIDS, diabetes mellitus, malignant tumor and using drugs like steroids or immunosuppressants.

3) Pharyngeal tuberculosis

As tuberculosis progresses, M. tuberculosis infects the tongue, gingiva and palate, causing ulcers in these regions. The ulcer has a sharp edge and is perforatable. There are caseous (cheese like) granules in the floor of the ulcer. Typical ulcer is shallow without peripheral induration but painful. Sometimes it is accompanied with severe pharyngodynia.

4) Lymphadenitis tuberculosis

It is called scrofula and is spread lymphogenously and/or hematogenously from lung or oral cavity. The lymph node swelling occurs with rapid caseous necrosis without pain (Fig. 2-5-4, -5). Sometimes it appears beadlike. Differential diagnosis is required between reactive lymph node swelling by bacterial infection, tumor metastasis, sarcoidosis, cat scratching disease, subacute necrotizing lymphadenitis and autoimmune lymphadenitis.

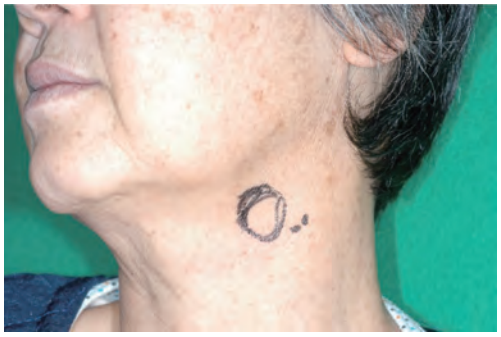

Fig. 2-5-4
Lymphadenitis tuberculosis

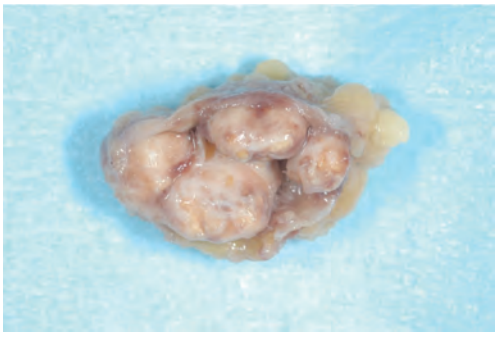

Fig. 2-5-5
Lymph node with caseous necrosis tuberculosis

**Diagnosis**

Final diagnosis is made by smear sample or isolation culture from the focus. Recently PCR is adopted for quick examination.

**Treatment**

The combination chemotherapy with 4 drugs, Isoniazid (INH), Rifampicin (RFP), Pyrazinamide (PZA), and Ethambutol (EB) or Streptmycin (SM) are adopted. The medication period is generally 6-9 months.

**c. Syphilis**

Syphilis is caused by *Toreponema pallidum* infection and is a systemic and chronic disease. It is classified as congenital syphilis and acquired syphilis. Congenital syphilis is feto-maternal infection via umbilical cord. Most of acquired syphilis are sexually transmitted disease (STD), and few are posttransfusion infection. The oral cavity often becomes a route of infection and has various symptoms.

**Symptoms**

1) Congenital syphilis

i. Neonatal syphilis

Pemphigus like enathema occurs 2-3 months after birth. This on the lip sometimes leaves a scar called 'Parrot's grove'.

ii. Late congenital syphilis

'Hutchinson's triad' occurs after 7-8 years of age. The triad consists of Hutchinson's tooth, parenchymatous keratits and inner ear hearing loss

2) Acquired syphilis

The symptoms appear 1-13 weeks after infection. It is rare to find a patient in 3rd or 4th stage owing to efficient use of antibiotics in developed countries. In the first several weeks of the 1st stage, no antibody is formed and the examination proves negative.

i. First stage

The painless induration (initial sclerosis) occurs in the region of infection (pubic region, lip, oral cavity) from 3 weeks to 3 months after infection. It becomes a 'hard chancre' with pus. It disappears soon, but rarely ulcer formation occurs. The serological test can detect the antibody 6 weeks after infection. The infectivity in the 1st and 2nd stage is strong.

ii. Second stage

The swelling of systemic lymph nodes, fever, fatigue, arthralgia occurs from 3 months to 3 years after infection. The typical systemic eruption called 'rose spot' sometimes occurs. The milk spot on lip and/or tongue, syphilitic angular stomatitis, pharyngeal syphilis, granulomatous cheilitis and butterfly phenomenon occurs. These symptoms disappear within 1 month without treatment.

iii. Latent stage

The early part of latent stage starts when the symptoms of 2nd stage disappear. In these 2-3 years, the symptoms of 2nd stage may recur. The latter

part continues even to 10 years as unapparent infection. There is no infectivity in this period

iv. Third stage

Gumma occurs on the skin, muscle and bone after 3-10 years after infection. Perforation of the soft palate, nasal septum, saddle nose and herpetic infection will occur in the oral region.

v. Fourth stage

Multiple tumor formation in many organs occurs more than 10 years after infection. As these tumors affect the brain, vertebral column and nerves, the general paralysis and tabes dorsalis may lead to death.

**Diagnosis**

Diagnosis is mainly made by the serological test after the 2nd stage. AIDS examination is recommended, simultaneously.

**Treatment**

The administration of penicillins is effective. The administration period is 2-4 weeks in the 1st stage, 4-8 weeks in the 2nd stage, 8-12 weeks in the 3rd and 4th stage.

(Yoshihide Mori, Takahiro Yamashiro, Hiroyuki Nakano, Tomoki Sumida)

## *2-6. Others*

**HIV infection including AIDS**

Human immunodeficiency virus (HIV) causes chronic and progressive cell-mediated immunodeficiency by infection. This acquired immunodeficiency is called 'Acquired Immune Deficiency Syndrome' (AIDS). HIV virus belongs to retrovirus family and it has plus-strand RNA with an envelope. It is classified as Type 1 (HIV-1) and Type 2 (HIV-2). HIV-1 infection occurs throughout the world and HIV-2 infection is limited to West Africa and several European and Asian countries.

HIV is a very weak virus in a usual environment, and there is seldom opportunity for infection to develop in a normal social life. The source of infection is blood, seminal fluid, vaginal secretion and breast milk which contain enough virus concentration. The route of infection is mucosa or wound and no infection occurs from woundless skin. Additionally, the infection occurs by sexually transmitted disease (STD), feto-maternal infection and blood infection. Standard precautions should be used for handling HIV patients.

**Symptoms**

1) Acute infection period

Early symptoms of infection include infectious mononucleosis like symptoms, influenza like symptoms, and persistent general lymph node swelling (PGL) occurs because of acute seroconversion. These symptoms occur 2-4 weeks after infection, improve within several days-10 weeks and enter asymptomatic stage. It is difficult to detect infection, because the concentration of antibodies is less for several weeks to 1 month after infection.

2) Asymptomatic period

The symptoms improve after the acute infection period and no symptoms are seen for 5-10 years. In this period, HIV actively grows, on the other hand, CD4 positive T-cell (CD4T-cell) as immunologically competent cells are also produced for a number of viruses. Then, the concentration of virus is repressed. But number of CD4T-cells slowly decreases in this period.

3) Attack period

Common cold like AIDS related symptoms occur. These symptoms include general malaise, acute body weight loss, chronic diarrhea, severe fatigue, herpes zoster, hyper ventilation, vertigo, eruption, stomatitis (Fig. 2-6-1, -2), fever, pharyngitis, cough, etc.

When the number of CD4T-cell in the blood is decreased and falls to less than 200/mm$^3$ (normal 800-1200/mm$^3$), the immune response is decreased and various opportunistic infection will occur. When one of the AIDS marker diseases (23, Table 2-6-1, Fig. 2-6-3, -4) occurs, the patient is diagnosed to have AIDS.

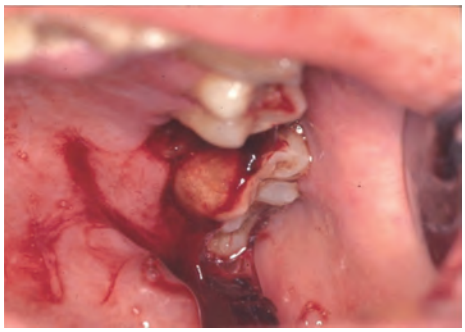

Fig. 2-6-1
Gingival bleeding in an AIDS patient

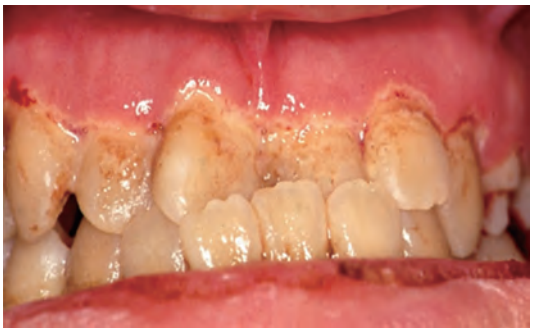

Fig. 2-6-2
Acute necrotizing ulcerative gingivitis in an AIDS patient

Table 2-6-1 AIDS marker disease

A. mycosis
1. candidiasis
2. cryptococcosis
3. coccdioidomycosis
4. histoplasmosis
5. pneumocystis pneumonia

B. protozoiasis
6. toxoplasmosis
7. cryptosporidiosis
8. isosporiasis

C. bacterial infection
9. purulent bacterial infection
10. salmonellosis
11. active tuberculosis
12. nontuberculous mycobacterial infection

D. viral infection
13. cytomegalovirus disease
14. herpes virus infection
15. progressive multifocal leukoencephalopathy

E. tumor
16. Kaposi's sarcoma
17. primary encephalic lymphoma
18. Non-Hodgkin lymphoma
19. aggressive cervical cancer

F. others
20. recurrent pneumonia
21. lymphoid interstitial pneumonia
22. HIV encephalopathy
23. HIV marantic syndrome

reference: http://www.mhlw.go.jp/bunya/kenkou/kekkaku-kansenshou11/01-05-07.html

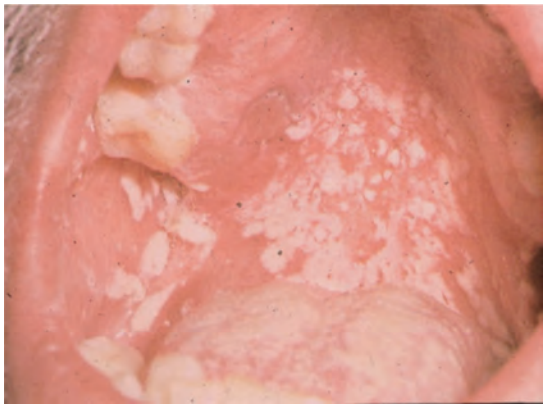

Fig. 2-6-3
Candidiasis in an AIDS patient

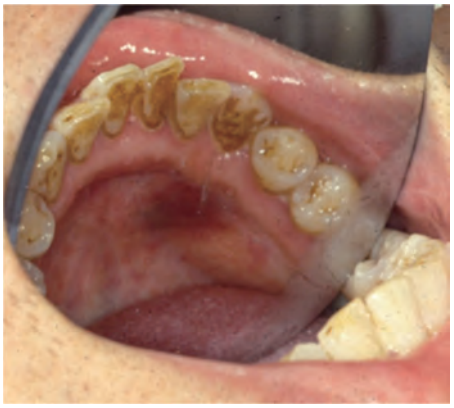

Fig. 2-6-4
Kaposi's sarcoma in an AIDS patient

**Diagnosis**

Diagnosis is made by screening examination (ELISA or PA antibody examination) from blood. The examination should be carried out more than 3 months after the opportunity of infection. The nucleic acid amplification test (NAT) is adopted as an accurate examination. When these test turn positive, Western Blot antibody examination and PCR examination are necessary to get final diagnosis. As conventional screening sometimes gives pseudopositive, to get final diagnosis is essential.

**Treatment**

As treatment method is improved day by day, to refer the latest guidelines is important. The guideline of US Department of Health and Human Service (DHHS)[1)] is most referred in the world. Various anti-HIV drugs are developed. The basic treatment is Highly Active Anti-Retroviral Therapy (HAART). As it is difficult to eliminate HIV virus completely, treatment must be continued throughout life.

**References**

1) US DHHS Guidelines: http://aidsinfo.nih.gov/guidelines

(Yoshihide Mori, Hiromitsu Morita, Ryosuke Inoue, Toshiko Futatsuki)

# 3

# *Trauma*

# 3-1. Tooth trauma

Tooth trauma or dental injury mainly involves maxillary central incisors, lateral incisors and mandibular incisors. The essential reason is a sudden excessive force applied on affected teeth.

**Clinical Manifestation and Diagnosis**

1. Tooth concussion

The concussed tooth usually shows no mobility and a normal periodontal ligament width radiographically. The affected tooth is occasionally sensitive to percussion. A recently concussed tooth may not respond to pulp vitality testing.

2. Tooth displacement

Tooth displacement is subcategorized into lateral displacement, intrusive displacement and extrusive displacement with reference to its original position.

Typically the affected tooth presents sulcular bleeding with or without mobility. The pulp may not respond to vitality testing at the time of injury. In radiographs, the ligament space is widened or absent.

3. Tooth avulsion

When a tooth is avulsed, the socket is swollen, painful, and bloody. Diagnosis of tooth avulsion is straight forward with aids of radiograph (Fig. 3-1-1, -2).

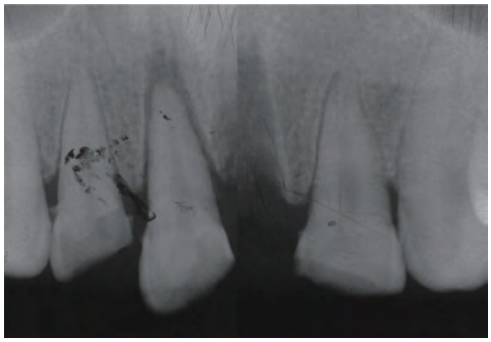

Fig. 3-1-1
Radiograph of tooth displacement and avulsion

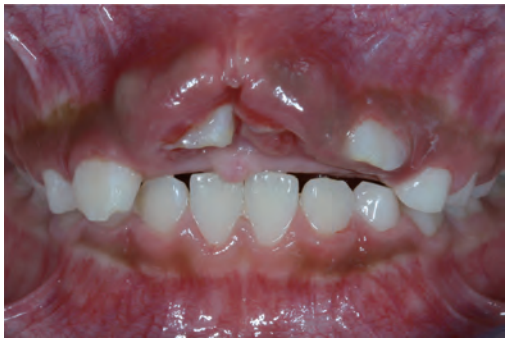

Fig. 3-1-2
Intrusive tooth displacement
(Courtesy of Dr ZHENG Shu-guo)

4. Tooth fracture

Tooth fracture line may appear in crown or root only, or extend from crown to root.

Crown fracture exhibits either infraction in enamel or fracture across both enamel and dentin with or without pulp exposure (Fig.3-1-3, Fig.3-1-4). The exposed dentin may be sensitive to exploration. Exposed pulp frequently shows a

pink color and there may be slight bleeding from the exposed site. The thermal sensitivity of tooth with a fractured crown depends on the extent of fracture.

Root fracture is classified as coronal third, middle third and apical third depending on the location. When the fracture line is close to the coronal, higher degree of mobility and percussion sensitivity is recorded. Multiple directions of radiograph or a cone-beam CT is useful in examining an oblique fracture (Fig. 3-1-6).

Crown-root fracture is similar to root fracture depending on the fracture location in the root (Fig. 3-1-5).

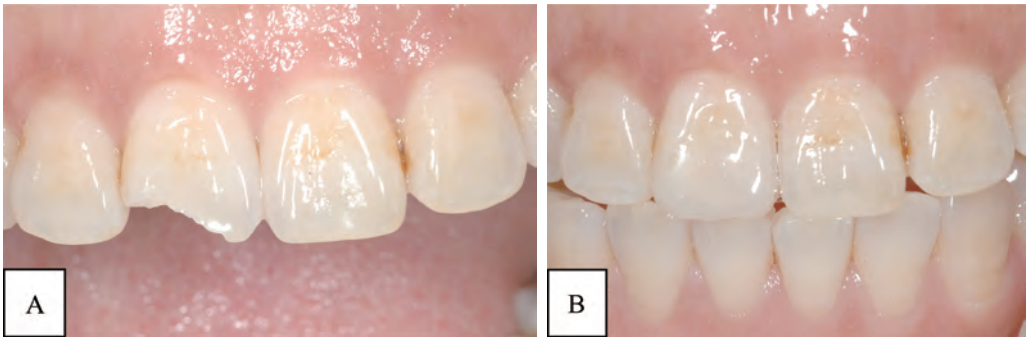


Fig. 3-1-3
A. Crown fracture without pulp exposed. B. Direct adhesive composite restoration

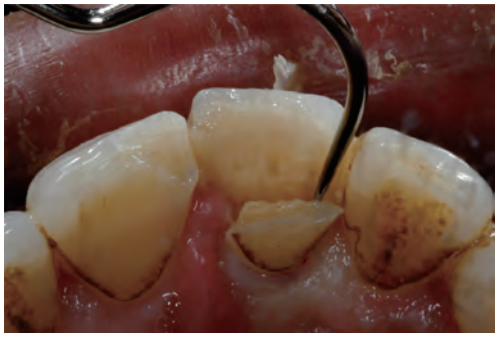

Fig. 3-1-4 Crown fracture with pulp exposure

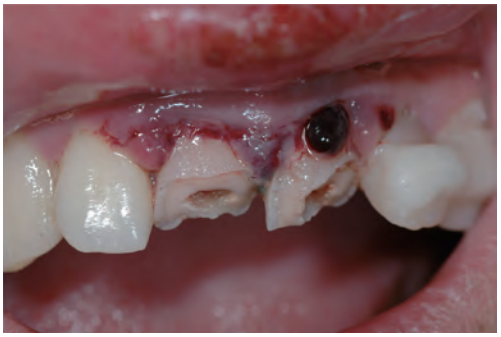

Fig. 3-1-5 Crown-root fracture

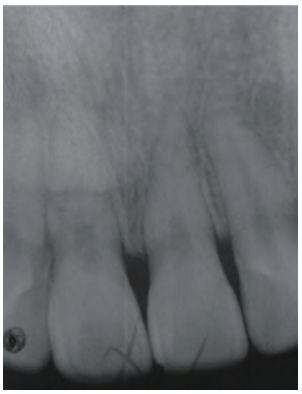

Fig. 3-1-6 Radiograph of root fracture

**Treatments**

Treatment of tooth trauma varies depending on the severity of injury of tooth.

**Field treatment**

For first aid, clean the injured tooth and surrounding regions gently with warm water and then go to a dentist immediately. Any pieces of the broken tooth should be brought along.

When a permanent tooth is completely knocked out, it must be picked up immediately by holding the natural crown. The tooth should be replanted back or placed in milk or saliva and never be scrubbed. If possible, the patient and the tooth should be taken to the dentist within 30 minutes after tooth loss.

**Emergency management**

The avulsed tooth should be rinsed thoroughly, then replanted into the socket and fixed with a semi-rigid splint for 7~10 days.

In case of displacement, the tooth should be repositioned to its original position using minimal force as soon as possible. Splint fixation technique to keep the tooth stable should be adopted for 1 week to 4 weeks (Fig. 3-1-8). If in case a displaced primary tooth may affect the secondary permanent tooth, extraction of the primary tooth is the best choice.

For tooth with enamel infractions, sealing the enamel surface with adhesives or surface coatings may be useful to alleviate sensitivity to the cold.

For crown fracture without pulp exposure, the rough edges may be simply polished or the missing section may be restored with composite resin. Coronal fragment of the broken tooth may be reattached using dental adhesives (Fig. 3-1-7).

For crown fracture with fresh pulp exposure, it is recommended to maintain a vital pulp for immature teeth and young teeth by adopting direct pulp capping or pulpotomy. For nonvital immature tooth, apexification is recommended.

For tooth with root fracture, a fixation is necessary in case of noticeable mobility and displacement of crown fragment. Semi-rigid fixation is preferred and should be for no more than 4 weeks.

For tooth with crown-root fracture, the crown should be removed and the restorability of remaining root should be assessed. If it is restorable, endondontic treatment should be performed.

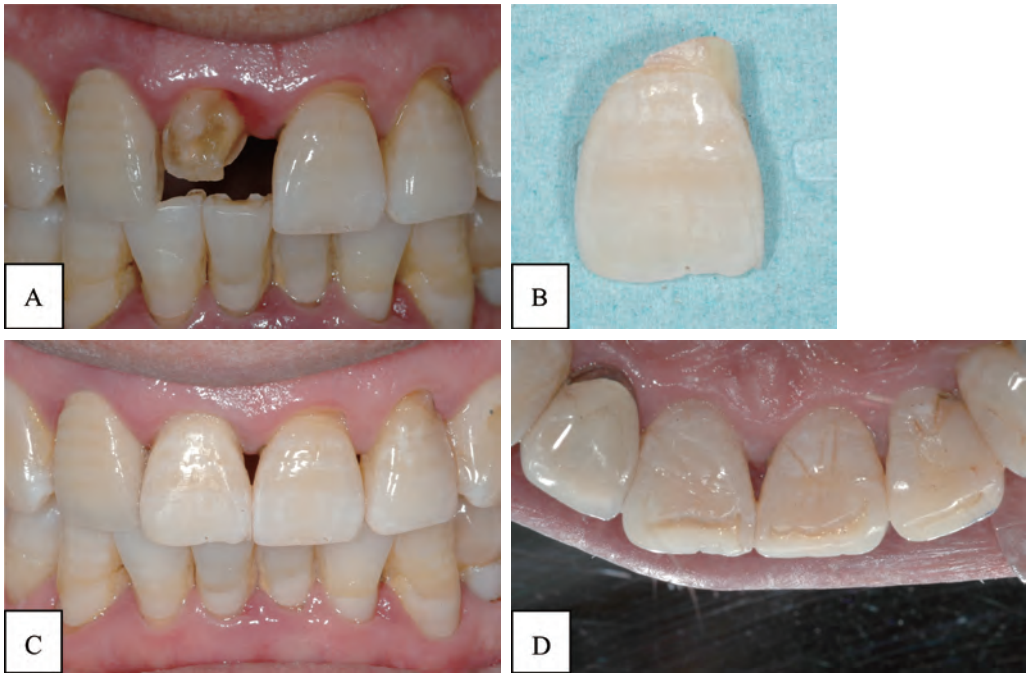


Fig. 3-1-7 Reattachment of tooth fracture:
A. Crown fracture of the upper right central incisor.
B. The coronal tooth fragment.
C. Reattach the fragment with dental adhesive.
D. Palatal view of the restored tooth.
(Courtesy of Dr LI Guang-sheng)

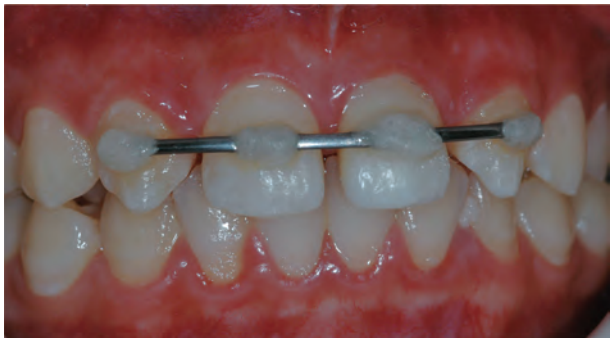

Fig. 3-1-8 A split fixation technique using wire and adhesive resin

**Follow-up**

Immature tooth should be initially recalled at least every 4 weeks. Once the root development is observed radiographically, a follow-up of every 3 months is preferred until the root is completely developed. The mature tooth can be regularly recalled every 6 months.

When pulp necrosis is determined, RCT is suggested.

When root resorption occurs, calcium hydroxide is used to stop the continuous root resorption and to form an apical barrier.

In case of nonhealing of the coronal third root fracture after endondontic treatment other treatments like orthodontic extrusion, periodontal crown lengthening or extraction may be adopted.

An avulsed tooth should be followed up as early as 7 days after replantation. The splint should be removed at this visit and endondontic therapy is suggested for mature tooth. For asymptomatic immature tooth, longer observation of root development without root canal therapy is an option.

**References**

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2) Wang Jia-de, Gao Xue-jun, Ed (2006). Cariology, endodontology and operative dentistry. Beijing: PKU Medical Press.

(Xue-jun Gao, Xiao-yan Wang)

## *3-2. Trauma to the soft tissues*

**a. Abrasions**

**Symptoms and diagnosis**

Abrasions result from friction between an object and the surface of the soft tissue, which often occur on the prominent sites in maxillofacial region, such as the tip of the nose, lips, cheeks and chins. This wound is usually superficial, denudes the epithelium, occasionally involves deeper layers, and leaves a raw, bleeding reticular layer of the dermis exposed. This type of wound may be painful owing to exposed nerve endings in the reticular dermal layer. (Fig. 3-2-1)

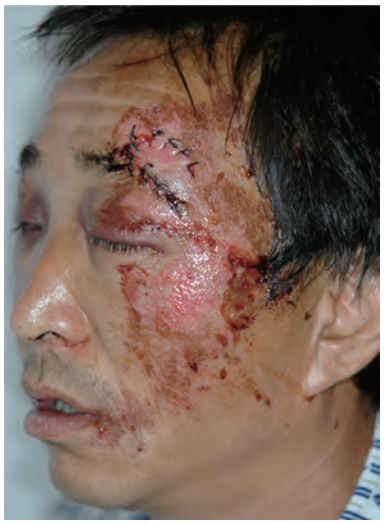

Figure 3-2-1 Facial abrasion wound

**Treatment**

The wound should be gently scrubbed clean with a mild soap solution and irrigated with saline under local anesthesia. All particles of foreign bodies must be removed as soon as possible to prevent fixation within the tissue and formation of a traumatic tattoo. After the wound is cleansed the abrasion is covered with a thin layer of topical antibiotics ointment to minimize desiccation and dressed with cotton gauze.

Reepithelialization without significant scarring is complete in 7 to 10 days if the epidermal pegs have not been completely removed. If the wound extends deeply into the dermal layer, notable scarring from granulation tissue formation will result. Excision of the remaining dermal tissue or excision of secondary scar tissue, with primary closure of the skin wound with 4-0 chromic sutures in the dermal layer and 6-0 nylon sutures at the surface, is indicated.

(Xin Peng)

**b. Contusions**

**Symptom and diagnosis**

Contusions are usually produced by blunt trauma that causes edema and hematoma formation in the subcutaneous tissues without a break in the soft tissue surface. The associated soft tissue swelling and ecchymosis can be extensive. The importance of contusions from a diagnostic point of view is that when they occur, a search for osseous fractures should be made.

**Treatment**

Contusions generally do not require treatment since the hemorrhage is usually self-limiting. For early stages of contusions, the application of ice or pressure dressing may help constrict blood vessels and therefore decreases the amount of hematoma. Small hematomas usually resolve without treatment, hypopigmentation or hyperpigmentation of the involved tissue can occur, but is rarely permanent. Large hematomas should be drained to prevent permanent pigmentary changes and secondary subcutaneous atrophy. During the resorption of hematomas, the patient can expect areas of ecchymosis as “black-and-blue mark”, which will turn a variety of colors i.e. blue, green and yellow in the next several days.

(Xin Peng)

**c. Lacerations**

**Symptom and diagnosis**

Lacerations are perhaps the most common type of soft tissue injury with tearing in the epithelial and subepithelial tissues and caused most commonly by a sharp object such as a knife or a piece of glass. Lacerations can have sharp, contused, ragged, or stellate margins. Laceration wounds may be divided into three types: simple lacerations, stellate lacerations and flaplike lacerations. Some lacerations involve the external surface only, but others extend deeply into the tissue, disrupting nerves, blood vessels, muscle, and salivary glands or their ducts. (Fig. 3-2-2)

Figure 3-2-2
Facial laceration wound

**Treatment**

After adequate anesthesia is provided, the surgical management of lacerations involves four major steps: cleansing, debridement, hemostasis and closure. Contaminated wounds should be cleansed and closed primarily, even if a delay of up to 5 to 7 days after trauma is necessary. Closure is performed using a layered technique. If the margins are beveled or ragged they should be conservatively excised to provide perpendicular skin edges to prevent excessive scar formation. Displaced tissue should be returned to the original anatomic position and orientation. Rarely is there an indication for changing the direction of the wound margins by Z plasty at the time of primary wound repair. Flap-like lacerations occur when a component of the soft tissue has been elevated secondary to trauma. Eliminating dead space by layered closure and pressure dressing is especially important in these “trapdoor” injuries.

(Xin Peng)

**d. Avulsions**

**Symptom and diagnosis**

Avulsive injuries are characterized by the loss of segments of soft tissue. Avulsive wounds are usually related to high-velocity agent in which portions of soft tissues are completely removed. The raw surfaces are often irregular with bleeding, bone exposure and severe pain. (Fig. 3-2-3)

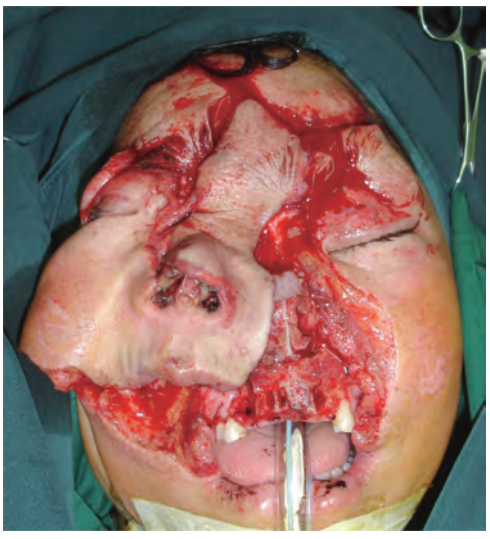

Figure 3-2-3
Facial avulsion injury

**Treatment**

If small areas of tissue are missing, simple local undermining of the skin may provide for primary closure without tension on the wound margins. If there has been a notable loss of tissue and the wound cannot be closed free from tension with local undermining, the raw surface should be covered with a skin graft, local flaps, free flaps or apposition of the skin margin to the mucosal membrane. Under no circumstances should a wound on the face be allowed to heal by secondary granulation tissue because of excessive scar formation.

(Xin Peng)

**e. Bites**

**Symptoms and diagnosis**

Dog Bites are the most commonly reported animal bites in humans primarily children and the midface is frequently involved. The wounds are often with irregular margins, punctures, scratches and loss of soft tissues. Animal and human bites are most often polymicrobial, containing aerobic and anaerobic organisms. Bite wounds have a higher chance of infection. (Fig. 3-2-4)

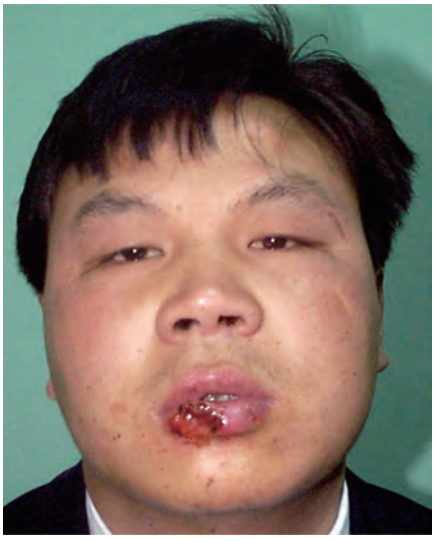

Figure 3-2-4
Dog bite wound of lower lip

**Treatment**

Bite wounds should be evaluated under local anesthesia. Wound irrigation and debridement are very important in reducing infection. Historically, animal bite wounds were often open primarily, although some investigators supported closure. In most laceration types of injuries, it is safe to close the wounds primarily after proper wound preparation without increased risk of development of infection. Puncture types of wounds should not be closed primarily because it is difficult to adequately clean and prepare the wound. Bite wounds with extensive crush injury and wounds requiring a considerable amount of debridement are best treated with delayed primary closure.

Antibiotic therapy is important in the prevention and treatment of infections. Animal bites should be considered prone to tetanus and treated accordingly. Rabies prophylaxis should be given for bite wounds that occurred from an unprovoked domestic dog or cat that exhibits bizarre behavior.

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(Xin Peng)

**f. Traumatic facial nerve injury**

Trauma is the most common cause of facial paralysis except for Bell's palsy. The incidence is increased recently along with the rising trend of maxillofacial trauma, surgical injury, and iatrogenic injury. Devriese indicated the incidence rate of trauma was 18.83% in 4149 patients of facial paralysis. May reported 17% (1575 patients). The result by Labella was 32% (147 patients); facial paralysis caused by iatrogenic factors and tumors are included. Maxillofacial trauma and iatrogenic injury are the main causes among all traumatic factors. Conley reported the rate of

facial paralysis after parotid surgery was 30% and the rate of transient facial palsy was 20%.

**Etiology, pathology and pathogenesis**

There are many reasons of trauma to the peripheral branches of facial nerve which would cause nerve injuries of different degrees and ranges. Seddon indicated a three scale classification for peripheral nerve injury in 1943 which included neuropraxia, axonotmesis and neurotmesis. The five- scale classification proposed by Sunderland is commonly used clinically.

Degree Ⅰ: Neuropraxia. Transient dysfunction occurs in the site of injury. The continuity of the neuronal cell, axon and final effectors is intact. There is no wallerian degeneration in the distal segment. The reaction to electrical stimulation is normal or a little weak. Normal facial movement may return in 3~4 weeks.

Degree Ⅱ: Axonotmesis. Degeneration of axon occurs in the site of injury and there is wallerian degeneration in the distal segment. The endoneural tubes are intact. There is transient nerve conduction disorder which would recover in 1~2 months.

Degree Ⅲ: Neurotmesis. There is not only axon interruption and wallerian degeneration in distal segment, but also loss of endoneural tubes. The perineurium is still continuous. The injury may be localized or affect adjacent nerve tissues along the facial nerve, especially the axon loss in the proximal segment. As the continuity of endoneural tubes is lost, there will be incorrect regeneration of axon. The recovery is always incomplete accompanied by synkinesis.

Degree Ⅳ: The axons are totally disrupted. The epineurium is partially damaged which could maintain the continuity of nerve. Traumatic neuroma and incorrect regeneration of axon are common since the perineurium and endoneural tubes are all disrupted. This kind of injury would seldom recover completely.

Degree Ⅴ: It is the most severe injury which means complete transection of nerve with a scar filled gap. The nerve function is lost without surgical intervention.

There are many reasons for facial nerve injury. Summed up in the following respects:

1. Mechanical injury: Most traumatic facial nerve injuries are mechanical such as acute or chronic crush, contusion, traction, compression, laceration, sharp cutting

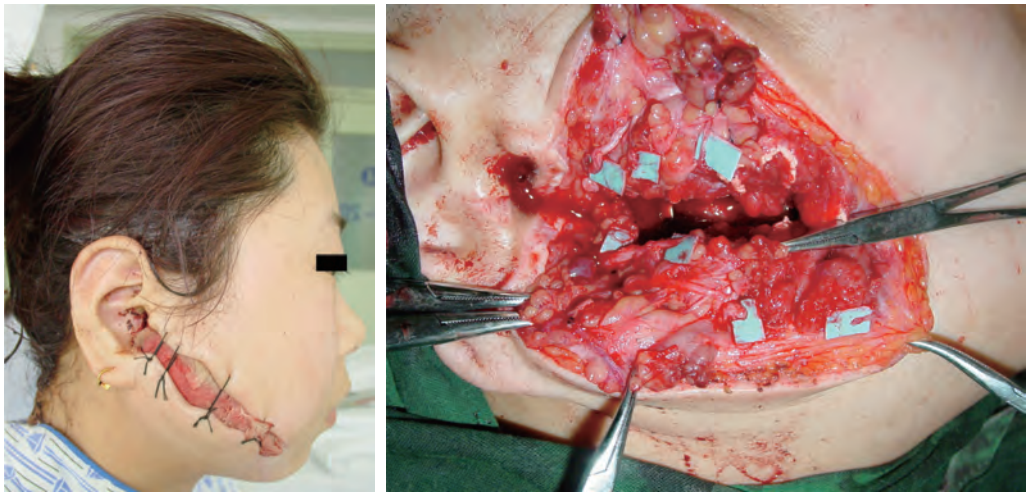
injury and friction by blunt objects.

2. Physical injury: Frozen injury, heat injury, electric injury, radiation damage, ultrasound injury and laser damage.
3. Chemical injury: Nerve injury caused by toxic substances, including long-term exposure to toxic substances, and injection of neurotoxic substances in the facial nerve area, such as alcohol, penicillin and calcium bromide.
4. Iatrogenic injury: It is a composite injury, almost including all of the injuries mentioned above. In oral and maxillofacial surgery or treatment, most injuries occur in the peripheral branches distal to the stylomastoid foramen. Several common iatrogenic factors are listed as follows : cutting off the nerve by mistake during operation; penetration and laceration to the nerve trunk while suturing the wound; crushing injury to the facial nerve by clamp or ligation during hemostasis; traction injury during removal of parotid tumors in deep lobe; electric damage caused by improper use of electric scalpel; damage caused by cryotherapy; penetration and laceration to the nerve trunk by injection, and the chemical injury caused by alcohol brought in by the needle; electric damage by too much electric current of the facial nerve stimulator.

All of these factors will result in ischemia of facial nerve which is the main cause of traumatic facial nerve palsy.

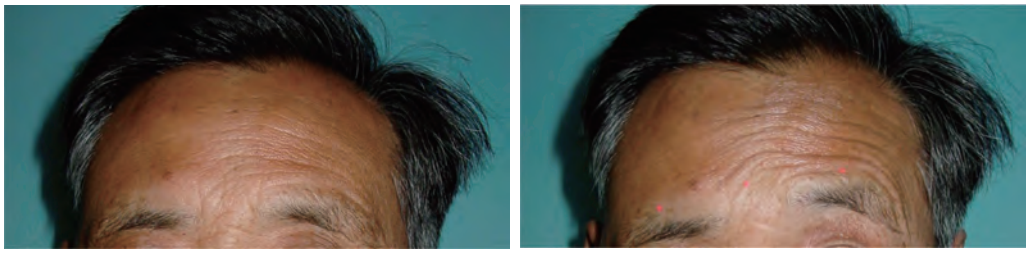
**Diagnosis**

1. Clinical manifestations
   (1) Obvious traumatic factors are present (Fig. 3-2-5A).
   (2) Trauma in the region of peripheral portion of facial nerve without abnormal tear secretion and taste lost in anterior two thirds of tongue (Fig. 3-2- 5B).
   (3) The typical facial paralysis symptoms include (Fig. 3-2-6): decrease or absence of forehead wrinkles and nasao-labial fold; drooping of corner of mouth; in severe cases, obvious facial asymmetry, palpebral fissure enlargement, lachrymation, hyperemia of palpebral and conjunctival, and even ablepsia induced by infection. Slight or no movement of forehead; inability to close eye completely with maximal effort; unable to wrinkle up the nose; air leakage when puffing the cheeks; Asymmetry of corner of month while pursing lips; sequelae such as synkinesis and hyperactivity may occur during recovery period.

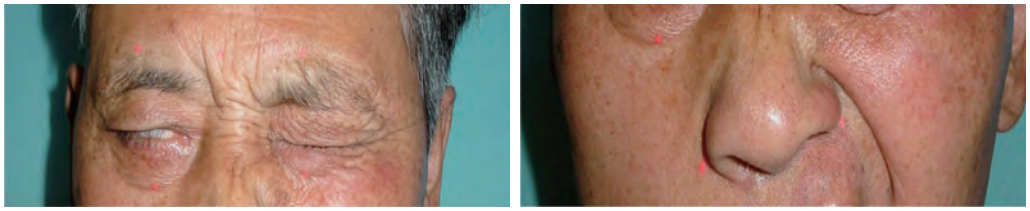


A. Trauma to the lower face. B. The stumps of injured facial nerve.

Fig. 3-2-5 Traumatic facial nerve injury.



A. Absence of forehead wrinkles. B. No movement of forehead.



C. Incapability of palpebral fissure closure D. Absence of naso-labial fold.

E. Drooping of corner of mouth F. Inability to whistle

Fig. 3-2-6 The typical facial paralysis symptoms

2. Special examination

A diagnosis could be made based on the clinical symptoms and medical history. Estimating the severity and predicting prognosis are more important. Traditionally the degree of facial movements is the criteria. The electrophysiology test of nerve and muscle is developing rapidly after electrometer was invented by Galvani.

(1) Grading systems of facial nerve function: There are numerous methods to assess a patient's facial function. Subjective grading systems include five-point gross scales, regional systems and specific criteria scales. The House-Brackmann grading scale, introduced in 1983 and endorsed by the Facial Nerve Disorders Committee of the American Academy of Otolaryngology in 1984, provides a standard method for reporting facial nerve function. Burres-Fisch system and facial nerve function index (FNFI) proposed by Fields are Objective methods. Cai proposed the quantitative facial nerve estimate system (QFES) by integrating the two objective systems.

(2) House-Brackmann grading scales: It is the most widely accepted subjective grading system until now and used worldwide (Table 3-2-1).

Table 3-2-1 House-Brackmann Facial Nerve Grading System

| Grade | Description | Characteristics | |
|---|---|---|---|
| I | Normal | Normal facial function in all areas | |
| II | Mild dysfunction | Gross | Slight weakness noticeable on close inspection; may have very slight synkinesis |
| | | At rest | Normal symmetry and tone |
| | | Motion | Forehead: Moderate to good function |
| | | | Eye: Complete closure with minimum effort |
| | | | Mouth: Slight asymmetry |
| III | Moderate dysfunction | Gross | Obvious but not disfiguring difference between two sides; noticeable but not severe synkinesis |
| | | | Contracture and/or hemifacial spasm |
| | | At rest | Normal symmetry and tone |
| | | Motion | Forehead: Slight to moderate movement |
| | | | Eye: Complete closure with effort |
| | | | Mouth: Slightly weak with maximum effort |
| IV | Moderately severe dysfunction | Gross | Obvious weakness and/or disfiguring asymmetry |
| | | At rest | Normal symmetry and tone |
| | | Motion | Forehead: None |
| | | | Eye: Incomplete closure |
| V | Severe dysfunction | | Mouth: Asymmetric with maximum effort |
| | | Gross | Only barely perceptible motion |
| | | At rest | Asymmetry |
| | | Motion | Forehead: None |
| | | | Eye: Incomplete closure |
| VI | Total paralysis | | Mouth: Slight movement |
| | | | No movement |

(3) Quantitative facial nerve estimate system (QFES): In order to avoid the limitation of subjective systems, Burres proposed facial linear measurement index (B-FLMI) based on studies of facial biomechanics of seven standard facial expressions in subjects with normal facial nerve function. This index is calculated by a series of seven steps equations using the percent displacement of various facial anatomic landmarks during movement compared with repose. Although it is more subjective, the calculation of the linear measurement index is an arduous, time-consuming process.

The metric point (Fig. 3-2-7):

So: Superior orbit, directly above pupil and the highest point of the brow arch.

Io: inferior orbit, directly below pupil.

Lc: bony lateral canthus.

Mc: media canthus.

F: middle point of bilateral point So.

L: junction of nasolabial fold.

M: corner of mouth.

Mid: midline at center of mouth.

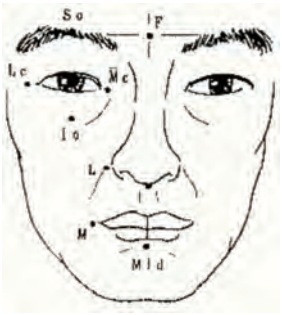



Fig. 3-2-7
The metric point of the quantitative facial nerve estimate system

Following metric indices were evaluated at rest and relative facial motions:

Forehead raise: SoIo ① ;

Eyes closed tight: SoIo ② ;

Eyebrows knit tight: SoF ③ ;

Nose wrinkle: McL ④ ;

Smile: LcM ⑤ and MMid ⑥ ;

Pout: LcM ⑦ and MMid ⑧ ;

Mouth open to maximal: MMid ⑨ ;

Eyes closed normally and tightly: distance of the palpebral fissure ⑩ .

(1) d1: the metric distance of the uninvolved side at rest

d2: the metric distance of the uninvolved side at motion

D1: the metric distance of the involved side at rest

D2: the metric distance of the involved side at motion

(2) Count formulae:

PD = ｜ d1-d2 ｜ / ｜ D1-D2 ｜

PD: percent of movement distance

(3) FNI1-FNI10 indicate the PD values in different motions ①～⑩ .

(4) Total facial nerve index:

TFNI= (The sum of FNI) / (All merit numbers)

(5) Total percent of FNI (TPr):
TPr= (TFNI after facial palsy) / (Normal TFNI)
(6) Regional facial nerve index (RFNI):
RFNI = the sum of the PD of one region/the motion times in merit

3. Electrodiagnosis.

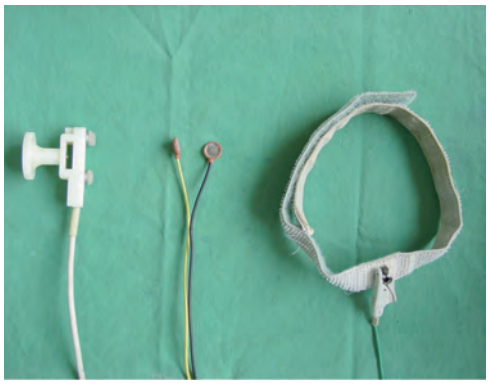
Neuromuscular excitability test was the first technique applied to evaluate the facial nerve function. Nerve excitability test (NET), maximal stimulation test (MST), intensity-time curve and Chronaxic test, electroneurography (ENoG) or evoked electromyography (EEMG), electromyography (EMG), motor conduction latency time (MCLT) and motor conduction latency velocity (MCLV) have emerged since then. They provide different objective indexes for evaluating facial nerve injury.

(1) Nerve excitability test (NET): The minimal current which could cause the observed contracture of muscles by stimulating the facial nerve trunk with a square wave pulse of 0.1-1.0 ms is recorded. The response on the involved side is compared to that on the normal side.
(2) Intensity-time curve and Chronaxic test: Intensity-time curve is drawn from the relationship between intensity of electric current and time of stimulation in order to evaluate the nerve and muscle function. Ordinate is the intensity and abscissa is the time of pulse. Most experts choose 8~10 different times of pulse to stimulate the muscle to record the currents which could cause the minimal contracture of the muscle. The nerve function is estimated by the curve drawn from these records. Chronaxic test is correlated to the form and location of the curve with few exceptions. The change of quantity can be observed.
(3) Maximal stimulation test (MST): The facial nerve is stimulated by increasing electric current to 5mA or until the patient feels unpleasant. The value of current in the involved side is compared to that in the normal side to evaluate the facial nerve degeneration.
(4) Electromyography (EMG): EMG is an effective method to measure the facial nerve function when nerve degeneration is too severe to get the MST and EEMG results. The wave forms include rest potential (RP), fibrillation potential (FP), spontaneous motor unit potential, positive sharp wave (PSW), poly-phase neural regeneration Potential (PP).
(5) Electroneurography (ENoG, Fig. 3-2-8): ENoG is an electrophysiology method which records the compound muscle action potential (CAP) in the facial expression muscles innervated by facial nerve by stimulating the trunk of facial nerve. The action potential is recorded from muscles and the principle based on the contraction of muscle to electric stimulated nerve which is the same as MST.

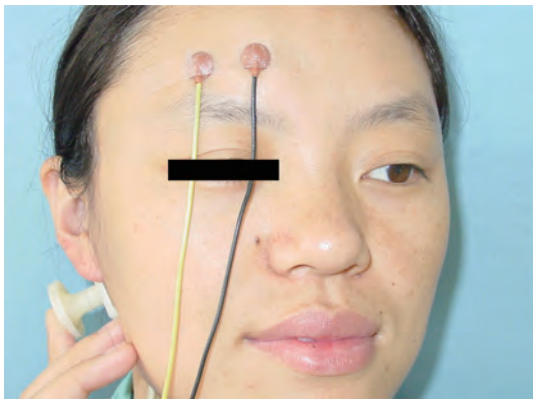
ENoG is accepted by more scholars because the result is more valid than NET and MST to evaluate the degree of facial nerve damage. The ENoG evaluates facial nerve function and prognosis when performed 3~14 days after onset of facial palsy. Incomplete recovery is indicated if the result is 0 to 20%. Normal function recovery is expected if the result is higher than 60%. No improvement of ENoG in 6~12 months after injury indicates poor prognosis.

(6) Motor conduction latency time (MCLT) and motor conduction latency velocity (MCLV): The facial nerve trunk is stimulated by 0.1~1.0ms pulse square wave current to induce the action potential in the muscles innervated by facial nerve. MCLT is the time interval from stimulation to the start point of induced potential. MCLV is the rate of comparing the nerve length between stimulating point to the recording point to MCLT. Delay or vanish of MCLT is an objective index for facial nerve lesion. Delay of MCLT means reduction of nerve conduction speed which is correlated to the nerve axon degeneration. The maximal MCLT is 4ms which is proved by both domestic and foreign scholars.

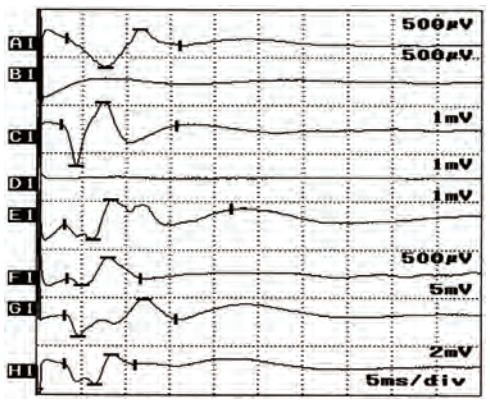
A. Instruments of ENoG (made in Japan)



B. Electrodes of measurements.



C. Methods of measurements.




D. Results of measurements.

Fig. 3-2-8 Electroneurography (ENoG) measurements.

**Treatment**

Surgical treatment and non-surgical treatment including medical and physical therapy are the two main categories of management of traumatic facial paralysis patients. In addition to traditional neurotrophic and corticosteroid drugs, the neural growth factor (NGF) has been rapidly developed and widely used over the past 10 years. Functional training is an effective way of physical therapy. Acupuncture and Chinese herbal medicine are also optional methods in China. Although these non-surgical treatments are applied to temporary facial paralysis and acute phase of traumatic facial paralysis, there is still lack of studies on the indications and effectiveness.

1. The spontaneous recovery of nerve function

Martin and Helsper reported the spontaneous return of function in patients whose facial nerves were sacrificed in parotidectomy in 1950s. The possible reasons include regeneration of facial nerve, cross innervations from contralateral facial nerve, interaction of trigeminal nerve and glossopharyngeal nerve, other unclear nervous pathways or a combination of these possibilities.

2. Non-surgical treatments

(1) Medical therapy

① Corticosteroid drugs: Corticosteroid should be applied in 3 days after trauma or surgery to reduce the exudation and edema. 10 mg of dexamethasone is administered intravenous per day generally.

② Neurotrophic drugs: Vitamin $B_{12}$ and $B_2$ are given through muscle injection for 30 days or through iontophoresis locally.

③ Neural growth factor (NGF): There are reports of clinical application by systemic or local administration, but the effect is still uncertain.

(2) Physical therapy

① Functional training of muscles of expression: It is effective in all periods of facial paralysis and the most important time of training is 2 weeks to 3 months after injury. The muscles of expression are divided into four functional groups: forehead, periocular region, nasal, perioral region. Additional force is given in the contraction direction of muscles to force synergic movement to control lateral muscles.

② Iontophoresis therapy:

A. Vitamins. Vitamin $B_{12}$ 500 μg and Vitamin $B_1$ 100 mg is given by direct current in positive electrode for 20 minutes a day for 10 days. An

interval of one week is recommended between two periods.

B. Iodide ion. It is given in the same way as Vitamins except by negative electrode. Ultrashort wave, microwave, ultrared ray could be used together with iontophoresis for 10 minutes a day.

③ Electrical therapy: It is generally applied in the late stage of facial paralysis. Multi-functional electrical stimulation is given for 30 minutes a day for 10 days for a total of 2 periods with an interval of one week.

Physical therapies should be used with caution in patients with tumor or after tumor surgery because they may induce the proliferation and metastasis of cancer cells.

3. Surgical therapy.

The aim of surgery is not only to acquire balance and symmetry at rest, but also symmetry and harmony during facial expressions. Static rehabilitation techniques such as myofascial suspension and muscle flap transposition are the traditional methods. In recent years, many new techniques are developed including crossover anastomosis of facial nerve to other nearby motor nerves, autologous nerve grafting, vascularized nerve grafting, cross-face nerve grafting, vascularized free muscle transfer, neurovascularized free muscle transfer and fascia grafting. The research data of effect and functional evaluation is limited so that there is no standard for choosing an appropriate technique.

(1) Static rehabilitation. Fascia suspension, dermis suspension, tissue substitute suspension and muscular flap suspension are the main techniques. This method has a nice static recovery in a near term, but the fibrous contracture or slacking in the late stage make it rarely used nowadays. Muscular flap transposition is substituting the function of expression muscles with adjacent muscle transfer. Platysma, frontalis and sternocleidomastoid transposition are proved of no clinical application value. Temporalis or masseter muscle transposition is effective to suspend eyelid and lip. The temporalis muscular fascia provides enough length and amount of tissue for static suspension of multiple positions. With biotechnological advancements, a lot of elastic biomaterials can substitute the muscular fascias. This technique is an alleviative treatment which cannot solve the asymmetry during movements.

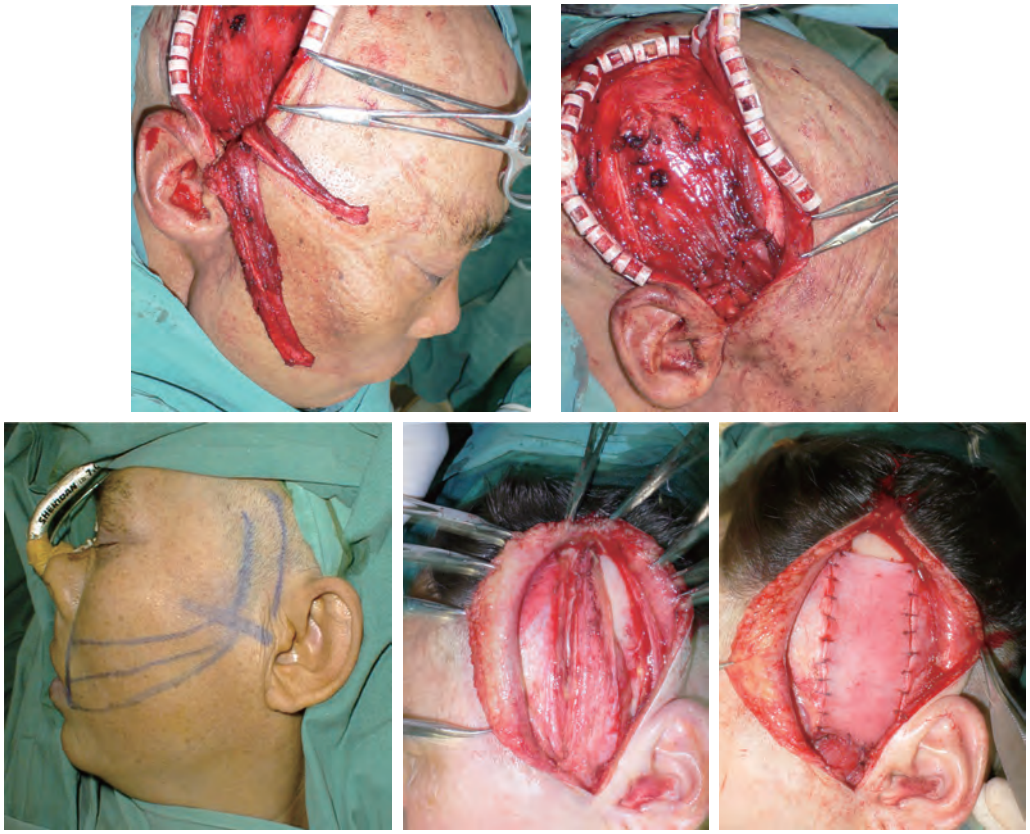


Fig. 3-2-9 Static rehabilitation with temporalis muscular fascia flap or artificial materials.

(2) Adjacent motor nerve crossover. Hypoglossal nerve, accessory nerve, glossopharyngeal nerve or phrenic nerve is used for anastomosis to facial nerve. This technique can be done for cases in early stage before the atrophy and degeneration of muscle especially in cases of instant facial nerve injury with a defect in the main trunk in which proximal end is unavailable and the distal end is normal. After this operation, the facial movement on the paralyzed side would be improved but the facial muscles are not innervated by facial nerve so facial expressions are unbalanced and asymmetrical. This method is sometimes used as a first stage treatment to keep the function of distal end of facial nerve and facial muscles. Cross-face grafting is recommended in a late stage for improvement of facial movement.

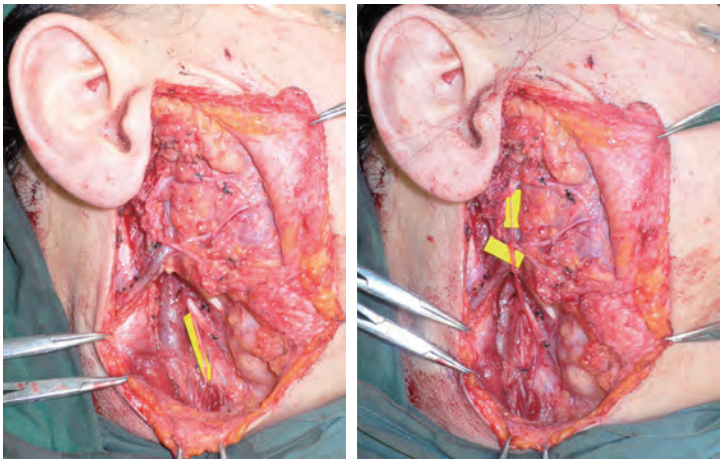


Fig. 3-2-10 Adjacent motor nerve (the hypoglossal nerve) crossover.

(3) Facial nerve repair: Different facial nerve repair techniques have made great progress since 1970s with the development of microsurgery. It is the basic technique for nerve repair which is available when the nerve injury is fresh with mild damage and the nerve can be directly approximated without tension on a solid soft tissue bed. There are three techniques of nerve anastomosis: epineural suturing, perineurial suturing and combination of epineural and perineural suturing. Perineural suturing is the best method theoretically but difficult as a clinical application. Facial nerve anastomosis could get the best functional result among all nerve repair techniques which requires the fresh nerve ends and the clear structure of epineurium and perineurium. If facial nerve is injured by crushing, compression or laceration, the nerve ends should be trimmed for the requirement mentioned above.

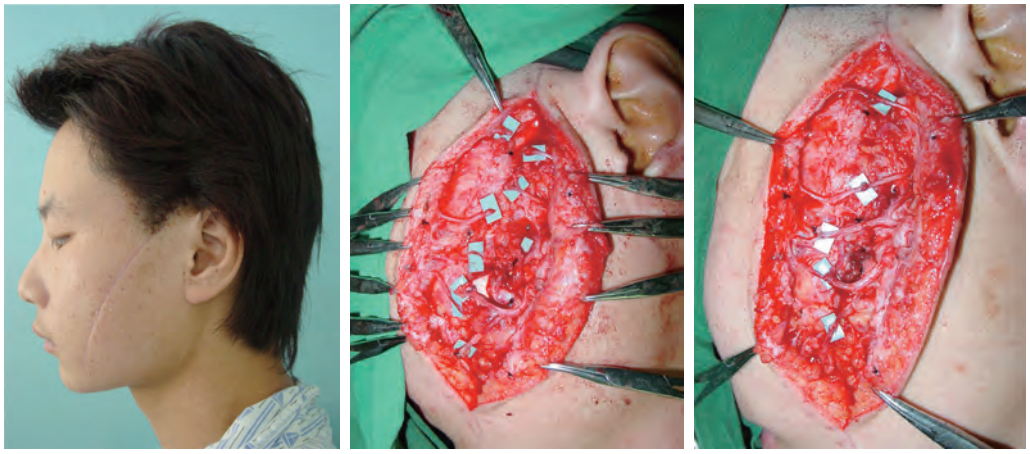


Fig. 3-2-11 The facial nerve anastomosis.

① Autologous nerve grafting. A section of autologous sensory nerve is grafted for rehabilitation for the continuity of injured facial nerve when the nerve defect is too large to be repaired directly. The donor nerve can be harvested from great auricular nerve, sural nerve, lateral femoral cutaneous nerve and the sensory nerve of forearm. Great auricular nerve which is located near the facial nerve is the first option because it can be harvested in the same operative region. This nerve has several branches and is thick enough to be split into several branches. Sural nerve is another choice which provides adequate nerve tissue especially for cross-face grafting.

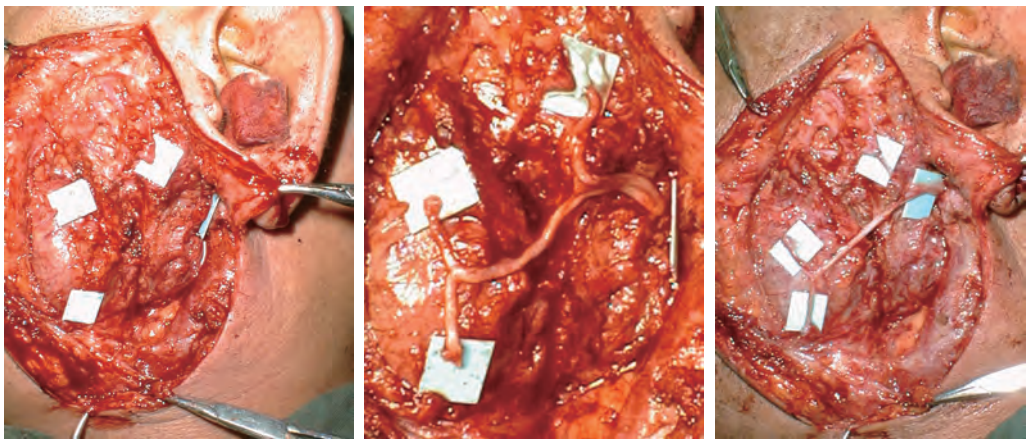


Fig. 3-2-12 Autologous nerve grafting with the great auricular nerve.

② Cross-face grafting is another way of autologous nerve grafting for facial paralysis in which one end of donor nerve is sutured to the facial nerve in the normal side and the other end to the distal end of the injured side through a subcutaneous tunnel. In this case, the facial muscles in the injured side can be innervated by the control lateral facial nucleus. It is indicated when the proximal end of injured nerve is unavailable but the facial muscles have no obvious degeneration with a reliable soft tissue bed. This technique would preserve the function of facial muscles. If the atrophic muscles have no ability of regeneration, this technique is useless so that a combination of neurovascularized free muscle transfer and cross-face grafting could be considered for functional reanimation.

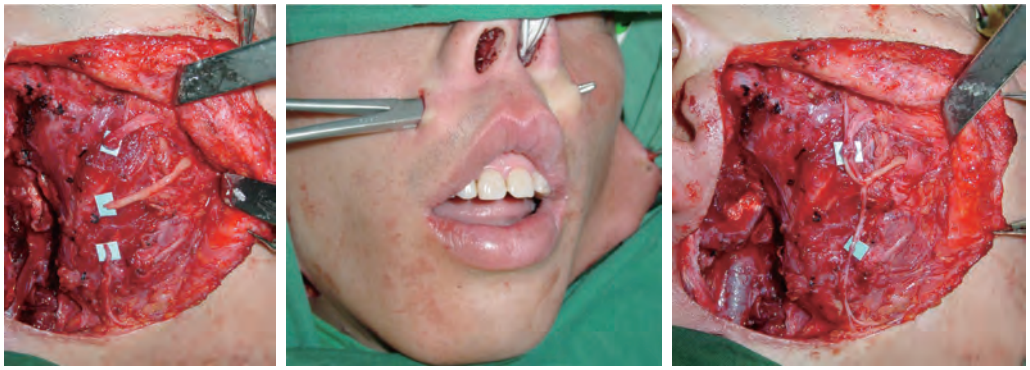


Fig. 3-2-13 Cross-face grafting with the sural nerve.

③ Neurotization: It is a nerve repair method in which the end of donor nerve is implanted to the expression muscles directly. It is available if the distal end of injured nerve is too thin to be sutured but the final functional recovery would be incomplete. The operation should be performed in 6 months after nerve injury before the muscles degenerate. Nerve would not reinnervate if the muscle is atrophic and fibrotic or the muscle has not lost innervation yet. Strict indications are necessary for this technique.

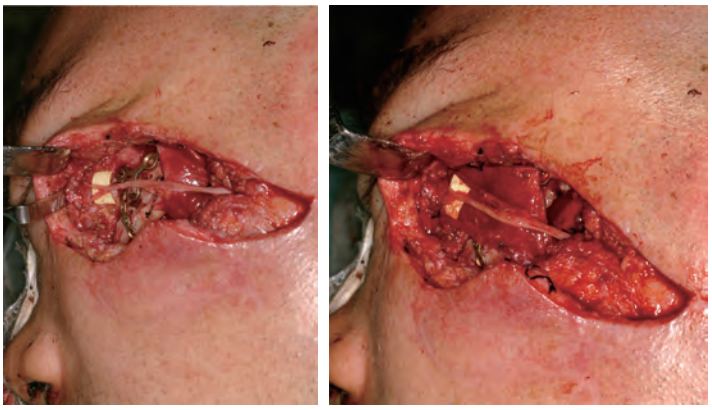


Fig. 3-2-14 Neurotization.

④ Vascularized nerve grafting. It is an adaption of cross-face grafting if there is a lot of scar tissue in the injured side and the blood supply is poor. Sural nerve is grafted with small saphenous vein which is sutured to the artery in the normal side and vein in the other side in order to nourish the nerve.

(4) Regional muscle transfer:

① Free muscle transfer: In 1971, Thompson proposed the free transplantation of skeletal muscle from extensor pollicis brevis or extensor digitorum brevis to improve the symmetry of face. Hakelius supported Thompson's work in 1974. The denervated muscle could survive for a period which is long enough for the revascularization and reinnervation. This technique is effective for late stage of facial paralysis when the nerves and muscles are atrophic and fibrotic. The procedure is simple with a little trauma to the donor site and no obvious change of facial contour so that it is easily accepted by patients.

② Neurovascularized free muscle transfer: Tamai and Harri performed neurovascularized free muscle transfer in animal models and patients in 1970s. Since 1980s, pectoralis minor muscle, serratus anterior muscle, rectus femoris muscle, latissimus dorsi muscle, rectus abdominis muscle, extensor pollicis brevis and extensor digitorum brevis all have been used as donor muscle in this method. This is the only functional rehabilitation operation that is available for late stage of facial paralysis with muscle atrophy. Latissimus dorsi muscle is often harvested with thoracodorsal nerve, artery and vein. The advantage is that the facial movements in the injured side could be innervated by the normal side to restore some function. The disadvantages include two time-consuming major operations, scar in donor sites and slow recovery of facial movement.

(5) Non-nerve tissue grafting. As mentioned above, a section of sensory nerve should be harvested for the autologous nerve grafting. This may cause loss of sense and neuromatic stump pain in the donor site. There is a limitation in the length and diameter of the donor nerve which is different from the requirement of nerve defect. Immunologic rejection of allogeneic nerve grafting is still a problem to be solved. Recently, there are many researches on non-nerve tissue which could be a substitution for nerve defect repair. There are two main categories. One is biomaterials, such as autologous vein, degenerated skeletal muscle, synovial sheath of tendon and human amniotic basement membrane. The other is non-biological materials, such as silicon tube and PGA tube.

**Prognostic factors**

The recovery progress of peripheral facial nerve injury is affected by many factors whether it is treated or not. The main factors are type and degree of injury,

the location of injury and the age of patients. Other factors are the interval of injury and treatment, the accuracy of operation, the length of defect and accompanying generalized disorders.

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(Zhi-gang Cai)

# 4

# *Cysts*

**Cysts of Oral and Maxillofacial Region**

A cyst is a pathologic cavity occurring in the hard or soft tissues. It is usually lined by epithelium, fibrous tissue or occasionally by neoplastic tissue and may contain fluid, semifluid or gas. Cyst formation undergoes two phases: cyst initiation and enlargement. The stimulus for cyst formation is not quite clear except the inflammatory odontogenic cyst which is caused by infection of the involved teeth. In others, there may be a predisposition to form cysts from developing epithelia, i.e. from dental lamina and its remnants, enamel organ, extensions of basal cells from the overlying oral epithelium, reduced enamel epithelium, cell rests of Malassez, etc. Once cyst is formed, it continues to grow and enlarge and results in resorption of the surrounding bone and displacement of the surrounding soft tissues.

The classification of cysts is presented in Table 4-1.

Table 4-1 Intraosseous and soft tissue cysts

| Intraosseous cysts | Soft tissue cysts |
|---|---|
| Epithelial cysts | 1. Odontogenic |
| 1. Odontogenic epithelial origin | 2. Non-odontogenic |
| a. Radicular cyst | a. Anterior median lingual cyst |
| b. Keraticyst | b. Nasolabial cyst |
| c. Dentigerous cyst | 3. Retention cysts |
| d. Lateral periodontal cyst | a. Sebaceoous cyst |
| 2. Non-odontogenic epithelial origin | b. Mucocele and Ranula |
| a. Globulomaxillary cyst | 4. Developmental cysts |
| b. Nasopalatine duct cyst | a. Dermoid and epidermoid cysts |
| c. Median palatal cyst | b. Lymphoepithelial cyst |
| 3. Non-epithelial cysts | c. Thyroglossal duct cyst |
| a. Solitary bone cyst | d. Branchial cleft cyst |
| b. Aneurysmal bone cyst | e. Cystic hygroma |
| c. Stafne's bone cavity | |

# *4-1. Odontogenic cysts*

**a. Radicular cysts**

Radicular cyst is an inflammatory cyst resulting from infection coming from the pulp into its periapical tissues. When radicular cyst develops apically it is termed as a periapical (periodontal) radicular cyst; when it develops on the side of the tooth root it is termed as a lateral (periodontal) radicular cyst. The latter may confuse with developmental lateral periodontal cyst which has a vital pulp.

**Clinical features**

Radicular cyst is the most common cyst of odontogenic origin. More males are affected than females. The affected age peak is in the third and fourth decades. Majority of the cyst occur in the anterior maxilla because the maxillary incisors are most prone to caries and trauma that cause pulp infection. In the mandible, the cyst more commonly involves the infected mandibular posterior teeth.

The cyst itself is usually symptomless and is often discovered when periapical radiographs are taken because of non-vital pulp or apicitis teeth. Pain is a chief complaint in the presence of infection. It grows slowly and gradually causes swelling of the involved jaw. Initially, the swelling is bony hard. When the covering bone becomes thin it feels spring-like. In the maxilla, buccal and palatal expansion can be seen. In the mandible, lingual expansion is rare. The mucosa overlying the expansion is of at first normal color, when the cyst enlarges to certain degree, the color will have a dark bluish tinge. Intraoral fistula may form with discharging pus or brownish fluid in the presence of infection. Pathologic fracture may be present in very large lesions. The involved tooth/teeth is/are non-vital, discolored, sometimes with huge restorations or a failed root canal therapy and may be sensitive to percussion, highly mobile or displaced. The contents of the cyst is straw colored or brownish and has cholesterol crystals (Fig. 4-1-1). When the cyst has a long-standing infection, the contents become thick and look like caseous material or is just pus.

**Radiological features**

Radicular cyst is a round or ovoid shaped radiolucency and is outlined by a narrow radio-opaque margin (a white line). This outlined white line may be absent in case of infected cysts or very large cysts. Root resorption is rare. (Fig. 4-1-2)

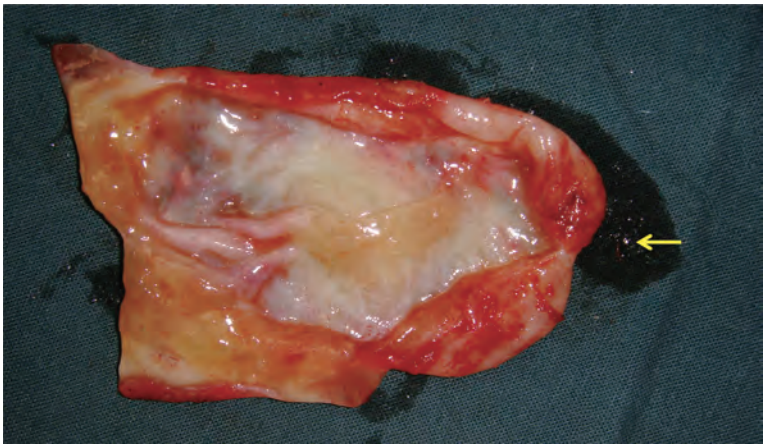


Fig. 4-1-1 Radicular cyst with cholesterol crystals.

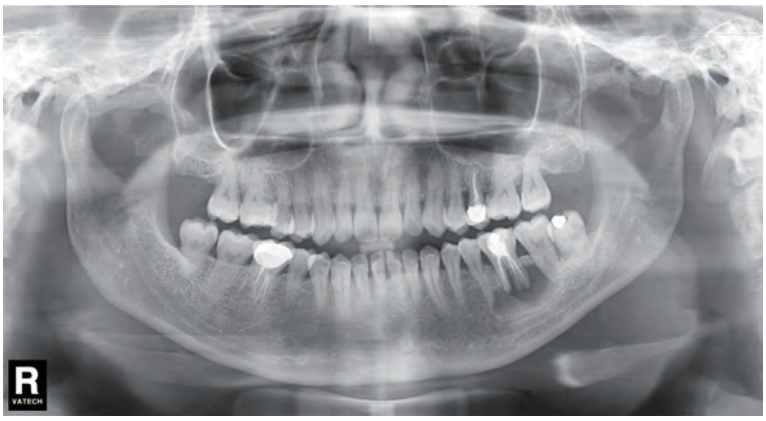


Fig. 4-1-2 Panoramic radiograph of radicular cyst. The lesion exhibits an ovoid shaped radiolucency with outlined white line.

**Pathology**

The cyst is lined by stratified squamous epithelium. The fibrous capsule is composed of collagen and loose connective tissue. Inflammatory cell infiltration may present in the fibrous capsule.

**Treatment**

Enucleation with primary closure is standard surgical procedure for most cysts. Very small cyst can be removed through the tooth socket; very large cyst may be preliminarily treated by marsupialization and when the cyst become smaller enucleation can be employed. The involved teeth can either be extracted or retained depending on conditions of sufficient bone support and restorative possibilities. The bone cavity remained after enucleation is not suggested to fill with any restorative materials.

**b. Follicular cyst (dentigerous cyst)**

Dentigerous cyst is also called follicular cyst, caused by the enlargement of the follicular space of the whole or part of the crown of an impacted or unerupted tooth, and is attached to the neck of the tooth.

**Clinical features**

The dentigerous cyst is also a commonly seen cyst, appearing mostly in the first, second, and third decades, with no significant sex predilection. It occurs more frequently in the mandible than the maxilla and the lower third molars are most frequently involved.

The typical feature is clinically a tooth missing from the normal series; sometimes, other adjacent teeth may also fail to erupt. Like the other odondotogenic cysts, dentigerous cyst has no special symptoms at beginning. When it becomes large, expansion of the involved jaw is visible and when the covering bone is thin enough, it feels as ping-pong ball crackling. If the cyst keeps growing, the covering bone may gradually disappear and pathologic fracture may follow.

The contents of the cyst are yellowish fluid in which cholesterol crystals may exist.

**Radiological features**

It is generally an unilocular radiolucency associated with crowns of unerupted impacted teeth (Fig. 4-1-3), having a well defined sclerotic margin which may disappear when infection sets in. The unerupted tooth may be pushed away from its direction of eruption, e.g. the lower third molar to the inferior border or into the ascending ramus.

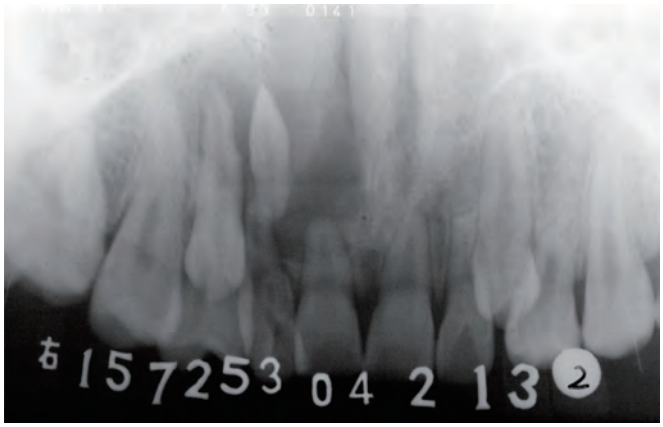



Fig. 4-1-3 Radiograph of dentigerous cyst

**Pathology**

The cystic lining consists of 2 to 3 cell layers of flat or cuboidal cells and is attached to the tooth at the cementoenamel junction. The epithelial lining is not keratinized. Hyaline bodies may be seen within the epithelium. Clefts from cholesterol crystals may be observed in the connective tissues of the capsule.

**Treatment**

For adults, the cyst is generally enucleated with extraction of the involved tooth; for children, the involved tooth may be preserved by separating the lining from the neck of the tooth. The tooth may erupt into occlusion or may be guided into occlusion by orthodontic forces. If the cyst is very large, marsupialization is indicated. (Fig. 4-1-4A,B)

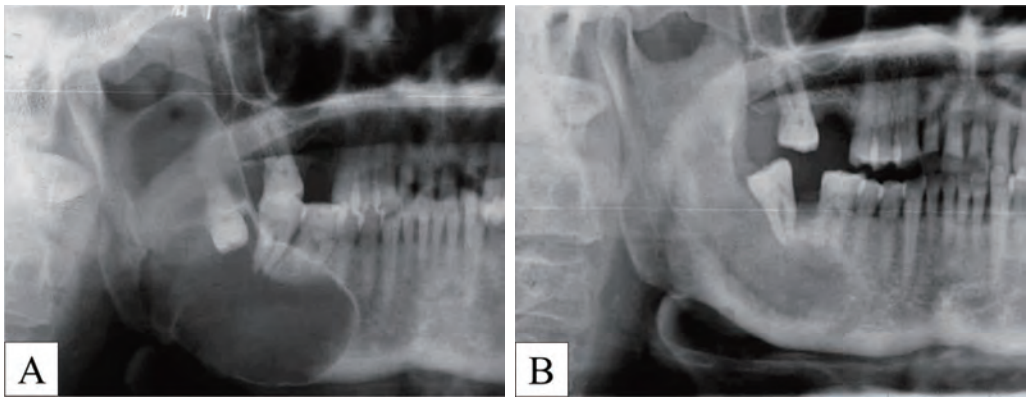



Fig. 4-1-4 (A) Radiograph of large mandibular dentigerous cyst.
(B) Six months after marsupialization.

## *4-2. Non-odontogenic cyst*

**a. Nasopalatine duct cyst**

It is also termed as incisive canal cyst, arising from embryonic epithelial remnants within the nasopalatine canal.

**Clinical and radiological features**

It is the most common type of facial fissure cysts, seen in adults, with a slight predilection for the males. It may be located along the incisive canal, but is seen more commonly in the lower portion of the maxilla between the apices of the central incisor.

Enlarged cysts may cause displacement of the involved teeth and patients may complain of swelling, pain and “salty taste” discharge.

A typical heart-shaped radiolucency may be seen between two maxillary central incisors.

**Pathology**

The epithelial lining is different at different levels. At lower level, it may be stratified squamous; at higher level, it may be pseudostratified columnar ciliated epithelium. Mucous glands, goblet cells and cilia may be present.

**Treatment**

Enucleation with primary closure is common procedure. The neurovascular bundle may be preserved.

**b. Globulomaxillary cyst**

This cyst arises from epithelium inclusions at the site of fusion of the globular process of the medial process and the maxillary process.

**Clinical and radiological features**

It is between the maxillary lateral incisor and cuspid teeth and is seen in adults, in either sex. The lateral and maxillary cuspid teeth are tilted coronally with root divergence.

A typical pear-shaped radiolucency can be seen between the maxillary lateral

incisor and cuspid teeth with the apex pointing toward the alveolar crest. The roots show divergence.

**Pathology**

The epithelial lining is of pseudostratified columnar ciliated epithelium. The wall is thick.

**Treatment**

Enucleation with primary closure is common procedure.

**c. Nasoalveolar cyst (median palatine cyst)**

It arises from epithelial inclusion during the fusion of the palatal processes of the maxilla.

**Clinical and radiological features**

It is seen in adults with no sex predilection. It is located in the hard palate, between the incisive fossa and the posterior border of the hard palate.

It is usually symptomless until it becomes large enough to cause swelling of the hard palate.

An ovoid radiolucency in the mid-palatal region can be seen in a maxillary occlusal view or CT.

**Pathology**

The lining may be stratified squamous epithelium, pseudostratified columnar ciliated epithelium or cuboidal epithelium.

**Treatment**

Enucleation with primary closure is common procedure.

## *4-3. Cystic lesion*

**Static bone cyst (solitary bone cyst)**

It is also termed as traumatic of haemorrhagic bone cyst. It can also be seen elsewhere in the skeleton besides the jaws. Its etiology is undefined. Possible theories were proposed: trauma and haemorrhage with failure of organization, spontaneous atrophy of the tissue in a central benign giant-cell lesion, abnormal calcium metabolism, chronic low-grade infection, necrosis of fatty marrow secondary to ischaemia, aberration in the development and growth of the local serous tissue.

**Clinical features**

Compared to the other jaw cysts, it is quite rare. It occurs particularly in children and adolescents. Males are affected more often than females, which is due to the fact that boys are exposed to trauma more than girls. Majority of the cyst are seen in the subapical area of the cuspid and molar region.

It is usually symptomless and found incidentally during a radiographic examination. The associated teeth are vital. Expansion of the cyst may first involve the lingual aspect. The content of the cyst is yellowish fluid containing plasma proteins. Some cysts may be empty, perhaps containing gas such as nitrogen, oxygen or carbon dioxide.

**Radiographic features**

The cyst is unilocular. It may grow into the interdental bone between the teeth, but do not cause root resorption. Tooth displacement may be seen. The outline of the cyst is not so clear as the other cysts.

**Pathology**

No visible lining is present. A thin fibrous wall may be seen. The adjacent bone has osteoclastic resorption on its inner surface.

**Treatment**

Gentle curettage is the choice of treatment.

# 4-4. Soft tissue cysts

**a. Dermoid and epidermoid cysts**

The dermoid and epidermoid cysts are lined by epithelium. The former contains skin appendages, e.g. hair, sebaceous glands or teeth; the latter does not. They arise from epithelial rests, being comprised of a combination of ectoderm, mesoderm and endodermal elements.

**Clinical features**

It is usually seen in adolescents with no sex predilection. It occurs more often in the floor of the mouth than in the other region. Swelling is the main symptom and sign. When the cyst is located above the geniohyoid muscle, the tongue will be elevated (Fig. 4-4-1), causing difficulty in mastication and speech. When it is inferior to the geniohyoid muscle, a submental swelling is present, looking like double chins. Palpation shows a dough-like feel. The content of the cyst is white thick sebaceous material (Fig. 4-4-2).

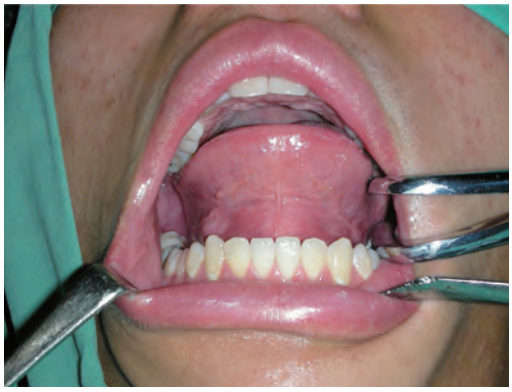


Fig. 4-4-1 Dermoid cyst in the floor of the mouth.

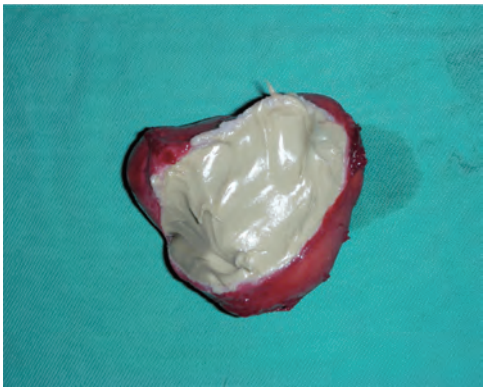


Fig. 4-4-2 Content of dermoid cyst.

**Pathology**

They are lined by keratinizing stratified squamous epithelium. The wall of dermoid cyst has dermal appendages, such as sebaceous glands, sweat glands, hair follicles, etc.

**Treatment**

Surgical excision is the choice of treatment. Intraoral approach is indicated for cysts present in the floor of the mouth above the mylohyoid muscle (Fig. 4-4-3A, B, C) and extraoral approach is designed for large cysts inferior to the muscle.

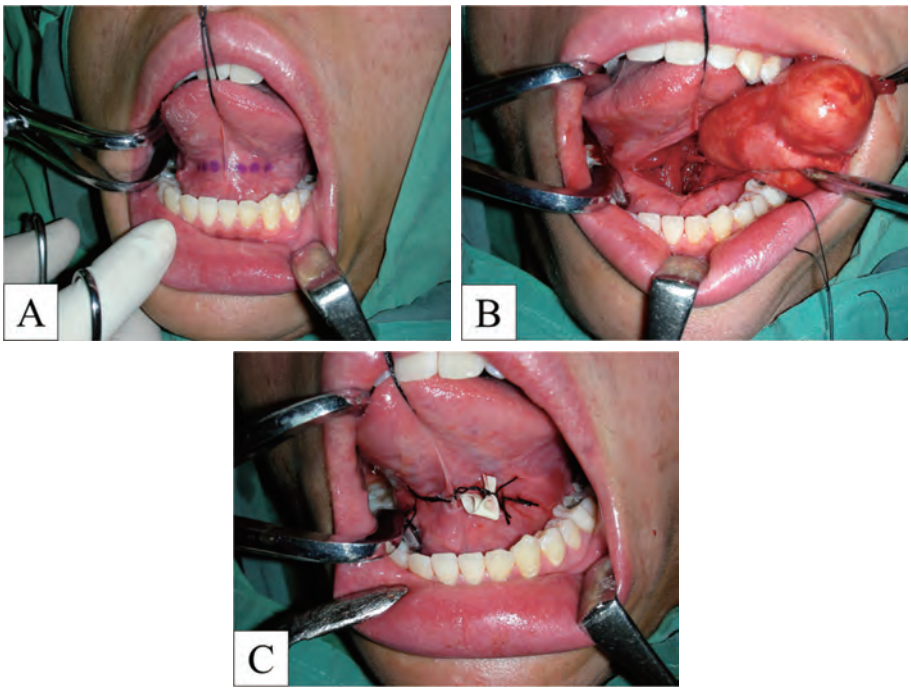



Fig. 4-4-3 Surgical excision of dermoid cyst in the floor of the mouth.

**b. Thyroglossal duct cyst**

The thyroid gland rudiment develops around the fourth embryonic week at the base of the tongue which later becomes the foramen cecum. A hollow stalk known as the thyroglossal duct extends from this foramen cecum through the neck to the thyroid gland. Around the tenth week this duct disappears. If it does not, its residues may develop into cysts at any point along its course.

**Clinical features**

This cyst often occurs in 1 to 10 years old without sex predilection. It may appear at any point in the midline along the course of the embryonic thyroglossal duct. Common site of occurrence is the area round the hyoid bone (Fig. 4-4-4).

Typical swellings are in the midline; some cysts may slightly deviate from the midline. When the cyst is located beneath the hyoid, it may move during swallowing and protrusion of the tongue. Cysts in the base of the tongue will cause

dysphasia or dyspnoea. Around 25 percent of the cyst may develop into sinus tract because of infection. The content of the cyst is yellowish or viscose fluid.

It should be distinguished from ectopic thyroid. $I^{125}$ radioisotope scanning or ultrasonic examination may help in the differential diagnosis.

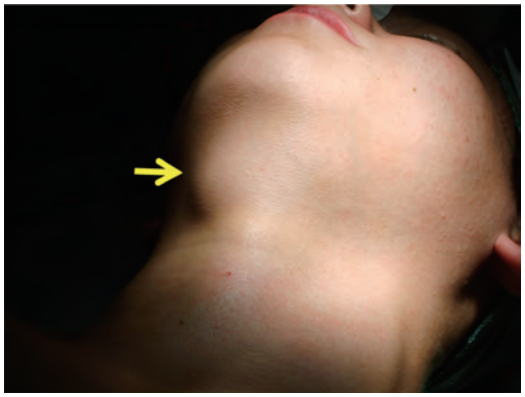


Fig. 4-4-4 Thyroglossal duct cyst located round the hyoid bone

**Pathology**

Thyroglossal duct cysts are lined with squamous or columnar-affiliated epithelium. They can be surrounded by fibrous tissue with inflammatory cell infiltration so that the epithelial island of thyroid tissue and mucous glands may be present.

**Treatment**

Complete surgical excision of the cyst, its tract and a central part of the hyoid bone (about 1 to 2 cm long) is important to decrease possible recurrence (Fig. 4-4-5).

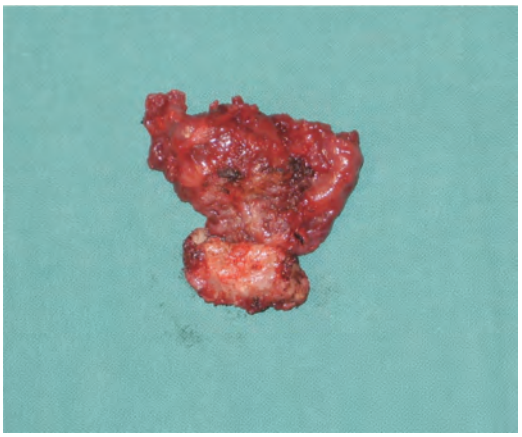


Fig. 4-4-5 Excision of the cyst with a central part of the hyoid bone

**c. Others**

**1. Sebaceous cyst**

A sebaceous cyst is a closed sac or cyst beneath the surface of the skin that has a lining that resembles the uppermost part of a hair follicle and fills with a fatty white, semi-solid material called sebum. Sebum is produced by sebaceous glands of the epidermis.

**Clinical features**

Sebaceous cysts easily occur in the scalp, ears, back, face, and upper arm. They are more common in hairy areas, where in cases of long duration they could result in hair loss on the skin surface immediately above the cyst. They are smooth to touch, vary in size, and are generally round in shape. One typical feature is that part of the overlying skin is closely attached to the cysts, where a black point may be seen on the skin which is the blocked hair follicle opening (Fig. 4-4-6). If the cysts continue to grow, they may become unsightly, painful, infected, or all of the above. Their content is generally a fatty substance that resembles cottage cheese. The nature of the contents of a sebaceous cyst, and of its surrounding capsule, will be determined by whether the cyst has ever been infected or operated. Poor surgical technique or previous infection leads to scarring or purulent fluid.

**Treatment**

Surgical excision of a sebaceous cyst is a commonly adopted procedure. The skin adhered to the cyst should be removed with the cyst and its contents (Fig. 4-4-7A, B).

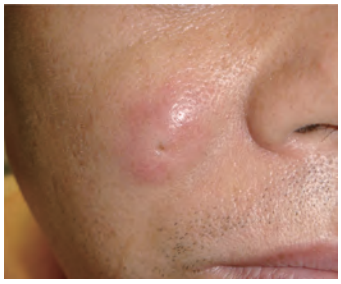


Fig. 4-4-6 Sebaceous cyst with a black point on the skin.

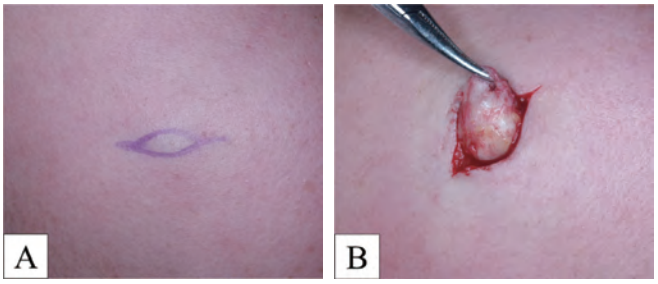



Fig. 4-4-7 Surgical excision of sebaceous cyst.

**2. Branchial cleft cysts**

Branchial cleft cysts are congenital epithelial cysts, which arise on the lateral part of the neck from a failure of obliteration of the branchial cleft in embryonic development. At the fourth week of embryonic life, the development of 4 branchial (or pharyngeal) clefts results in 5 ridges known as the branchial (or pharyngeal) arches, which contribute

to the formation of various structures of the head, the neck, and the thorax. The second arch grows caudally and, ultimately, covers the third and fourth arches. The buried clefts become ectoderm-lined cavities, which normally involute around week 7 of development. If a portion of the cleft fails to involute completely, the entrapped remnant forms an epithelium-lined cyst with or without a sinus tract to the overlying skin.

**Clinical features**

Typical branchial cleft fistulae are present at birth; cysts tend to present later than fistulae. A branchial cyst most commonly presents in the second through fourth decades of life. Males and females are equally affected and there is occasionally a hereditary tendency. An estimated 2-3% of cases are bilateral. Twenty to 40 percent of the patients relate its discovery to an attack of pharyngitis, ear infection, or dental infection, and many report temporary enlargement with or without tenderness during periods of upper respiratory tract infection. Infected cysts may progress to abscess formation with the possibility that rupture or incision and drainage will lead to either permanent sinus formation or to recurrent cyst formation and infection (Fig. 4-4-8). Larger cysts may displace the sternomastoid muscle posterolaterally and the carotid artery and internal jugular vein medially.

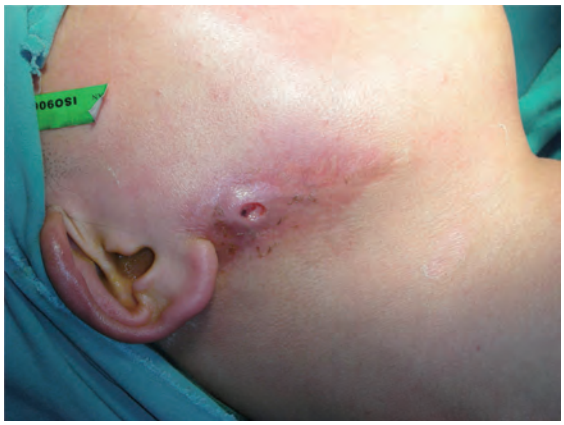


Fig. 4-4-8 Fistula of the branchial cyst.

The first cleft cysts occurred twice as often as sinuses or fistula. The second branchial cleft cysts occur three times more often than second branchial sinuses or fistulae. Ninety-five percent of branchial anomalies are second branchial anomalies. Third and fourth branchial arch anomalies are rare.

The first branchial anomalies are usually located posterior and/or inferior to the angle of the mandible. A fistula or sinus tract may course toward the external

auditory canal and open more laterally near the bone and cartilage junction. The first branchial cysts, sinuses, and fistulas are intimately involved with the parotid gland and facial nerve.

A sinogram may be obtained. If a sinus tract exists, radiopaque dye can be injected to delineate the course and to examine the size of the cyst (Fig. 4-4-9). Ultrasonography helps to delineate the cystic nature of these lesions. A contrast-enhanced CT scan shows a cystic and enhancing mass in the neck (Fig. 4-4-10). It may aid preoperative planning and identify compromise of local structures. MRI allows for finer resolution during preoperative planning. The wall may be enhancing on gadolinium scans.

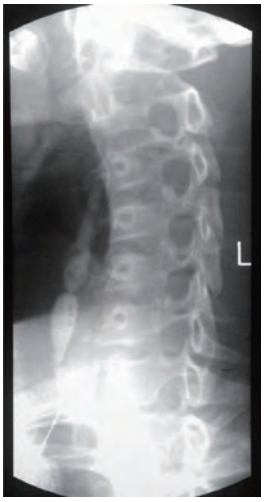



Fig. 4-4-9
Sinogram of the fistula.

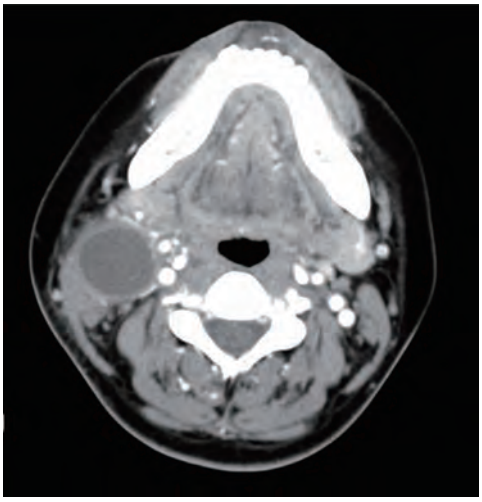


Fig. 4-4-10
CT of branchial cyst

Fine-needle aspiration may be helpful to distinguish branchial cleft cysts from malignant neck masses. Fine-needle aspiration and culture may help guide antibiotic therapy for infected cysts.

**Pathology**

Most branchial cleft cysts are lined with stratified squamous epithelium with keratinous debris within the cyst. In a small number, the cyst is lined with respiratory (ciliated columnar) epithelium. Lymphoid tissue is often present outside the epithelial lining. Germinal center formation may be seen in the lymphoid component, but true lymph node architecture is not seen. In infected or ruptured lesions, inflammatory cells are seen within the cyst cavity or the surrounding stroma.

**Treatment**

Surgical excision is definitive treatment for branchial cleft cysts, is best performed after the patient is at least 3 months old, and should not be attempted during an episode of acute infection or if an abscess is present. When a fistula is present, “blue dye” (methylthioninium chloride) can be gently injected into the fistula to delineate the course, which helps to guide the dissection of the fistula (Fig. 4-4-11). Surgical excision of branchial cleft cysts may damage their nearby vascular or neural structures.

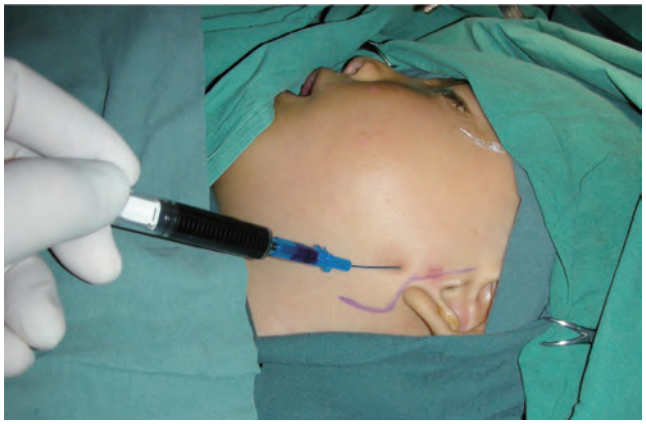


Fig. 4-4-11 Injection of blue dye before surgery.

**3. Cysts of facial fissure**

Cysts of facial fissure are non-odontogenic cysts, arising from epithelial inclusions of entrapments in the lines of closure of the developing facial processes during the embryonic period of life. They are also called non-odotogenic ectodermal epithelial cysts.

(Chuan-bin Guo)

# 5

# *Tumor and Tumor-like lesions*

# 5-1. Odontogenic tumor; benign tumors

Table5-1-1 shows classification of odontogenic tumors provided by World Health Organization (WHO) in 2005.

Table 5-1-1 Classification of odontogenic tumors (WHO, 2005)

| |
|---|
| **Malignant tumors** |
| **Odontogenic carcinomas** |
| Metastasizing(malignant) ameloblastoma |
| Ameloblastic carcinoma - primary type |
| Ameloblastic carcinoma - secondary type (dedifferentiated), intraosseous |
| Ameloblastic carcinoma - secondary type (dedifferentiated), peripheral |
| Primary intraosseous squamous cell carcinoma - solid type |
| Primary intraosseous squamous cell carcinoma derived from keratocystic odontogenic tumor |
| Primary intraosseous squamous cell carcinoma derived from odontogenic cysts |
| Clear cell odontogenic carcinoma |
| Ghost cell odontogenic carcinoma |
| **Odontogenic sarcomas** |
| Ameloblastic fibrosarcoma |
| Ameloblastic fibrodentino-and fibro-odontosarcoma |
| **Benigh tumor** |
| **Odontogenic epithelium with mature, fibrous stroma without odontogenic ectomesenchyme** |
| Ameloblastoma, solid / multicystic type |
| Ameloblastoma, extraosseous / peripheral type |
| Ameloblastoma, desmoplastic type |
| Ameloblastoma, unicystic type |
| Squamous odontogenic tumor |
| Calcifying epithelial odontogenic tumor |
| Adenomatoid odontogenic tumor |
| Keratocystic odontogenic tumor |
| **Odontogenic epithelium with odontogenic ectomesenchyme, with or without hard tissue formation** |
| Ameloblastic fibroma |
| Ameloblastic fibrodentinoma |
| Ameloblastic fibro-odontoma |
| Odontoma |
| Odontoma, complex type |
| Odontoma, compound type |
| Odontoameloblastoma |
| Calcifying cystic odontogenic tumor |
| Dentinogenic ghost cell tumor |
| **Mesenchyme and/or odontogenic ectomesenchyme with or without odontogenic epithelium** |
| Odontogenic fibroma |
| Odontogenic myxoma / myxofibroma |
| Cementoblastoma |
| **Bone-related lesions** |
| Ossifying fibroma |
| Fibrous dysplasia |
| Osseous dysolasia |
| Central giant cell lesion (granuloma) |
| Cherubism |
| Aneurysmal bone cyst |
| Simple bone cyst |
| **Other tumors** |
| Melanotic neuroectodermal tumor of infancy |

**Odontogenic epithelium with mature, fibrous stroma without odontogenic ectomesenchyme**

**a. Ameloblastoma**

The ameloblastoma is a benign but locally aggressive neoplasm derived from odontogenic epithelium. It is the most common type of odontogenic tumors but, even so, only accounts for approximately 1 % of all oral tumors. It most often arises in the mandibular ramus and body, with peak age of onset between 10 and 30 years. The male:female ratio is 3: 2. Symptoms are painless swelling of the jaw bone and tooth movement. Ameloblastomas exhibit a number of histologic appearances that can usually be described as follicular, plexiform, acanthomatous, granular cell and basal cell types. However, there appears to be no consistent correlation between these histologic patterns and their clinical behavior, and therefore, such microscopic subtyping of ameloblastomas has now become essentially an academic exercise bearing little therapeutic and/or prognostic implications.

The classification with respect to behavior, that currently appears to be commonly accepted, separates ameloblastoma into solid or multicystic, unicystic, peripheral and desmoplastic subtypes, with further separation of these variants based on individual clinical, radiographic and microscopic features. There is increasing justification for regarding these variants as distinct entities and it is no longer appropriate to generally discuss ameloblastomas as if all cases were essentially similar. In fact, the new WHO classification of head and neck tumors published in 2005 does not simply classify ameloblastoma as a single entity. Rather, it recognises the existence of variants, by using the plural term: ameloblastomas. Four ameloblastoma variants mentioned above are now recognized and the bioprofiles of these ameloblastomas vary in relation to age, distribution, localization, imaging features, and in particular, prognosis.

**1. Ameloblastoma, solid /multicystic type**

The solid/multicystic ameloblastoma (A-S/M) is the most common variant of ameloblastoma, also known as conventional ameloblastoma or classical intraosseous ameloblastoma. It is a slowly growing, locally invasive, epithelial odontogenic tumor of the jaws with a high rate of recurrence if not removed adequately, but with virtually no tendency to metastasize.

The age range is broad, extending from childhood to late adulthood. Mean ages have been most commonly between 35 to 45 years. Males are slightly more affected than females. The mandibular molar-ramus area is the most favored site (60%), although it may occur anywhere in the mandible or maxilla.

A-S/Ms usually present as variably sized swellings of the jaws. Small tumors are asymptomatic. Large tumors present with swelling of the jaws but pain or paresthesia is unusual. (Fig. 5-1-1) Radiographically, the tumor may exhibit a unilocular or multilocular radiolucent appearance with well defined margins, occasionally scalloped. Resorption of the roots of adjacent teeth is common creating a characteristically sharp surface likened to a "knife cut" (Fig. 5-1-2, -3). Cortical bone may be thin and expansive. Impacted teeth are noted in 50% cases.

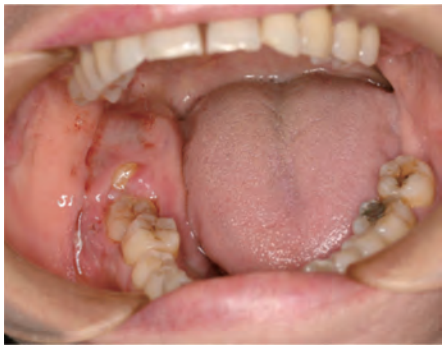


Fig. 5-1-1 Large A-S/M of the right mandibular ramus.Swelling of the retromolar region is seen.

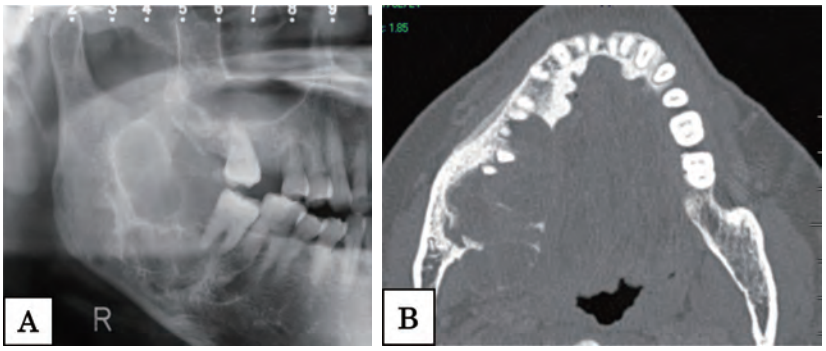



Fig. 5-1-2 Panoramic radiograph of an A-S/M patient (same case shown in Fig.5-1-1).
(A) Multilocular radiolucent region with a sharp margin located in the ramus of the mandible.
(B) CT shows multicystic lesion extending to the lingual side of the mandible.

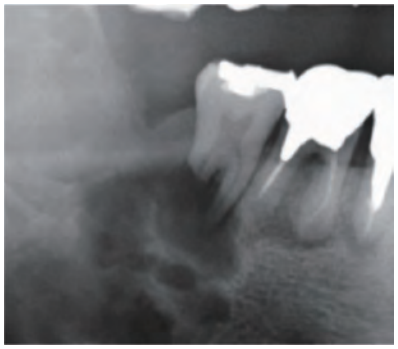


Fig. 5-1-3 Root resorption caused by A-S/M, with "knife-cut" appearance.
The distal root of the second molar is sharply resorbed.

Numerous histological patterns of ameloblastoma have been described, but common to all subtypes is the polarization of cells around the tumor nests in a pattern similar to ameloblasts of the enamel organ. Central to these cells are loosely arranged cells that mimic the stellate reticulum of the enamel organ. There are two basic histopathologic patterns, the follicular and plexiform. The follicular type is composed of islands of tumor cells that mimic the normal dental follicle. The tumor island is composed of a peripheral layer of columnar cells whose nuclei are generally well polarized, resembling ameloblasts or preameloblasts. Its central part is composed of loosely arranged cells resembling stellate reticulum (Fig. 5-1-4, 5). If these cells are spindle-shaped, basaloid, granular or showing squamous differentiation, the terms spindle cell ameloblastoma, basal cell ameloblastoma, granular ameloblastoma and acanthomatous ameloblastoma have been used. The plexiform ameloblastoma is arranged as a network of interconnected strands of cells. Each of these strands is bounded by a layer of columnar cells, and between these layers may be found stellate reticulum-like cells (Fig. 5-1-6). Treatment of A-S/Ms should include excision with an adequate margin of uninvolved tissues. Lesions involving the posterior maxilla, usually show a poorer prognosis. Long-term follow up is essential, since recurrences have been noted more than ten years after the initial treatment.

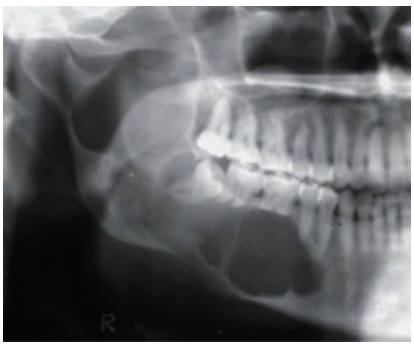


Fig. 5-1-4 Radiograph of a mandibular ameloblastoma (A-S/M)

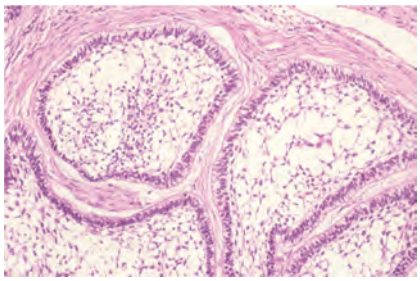


Fig. 5-1-5 The follicular type of A-S/M (H&E, x200). This tumor consists of islands of odontogenic epithelium within a fibrous stroma.

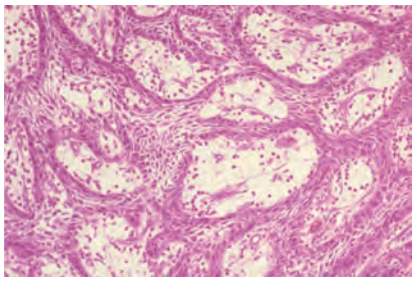


Fig. 5-1-6 The plexiform type of A-S/M (H&E, x200). This tumor contains basal cells arranged in anastomosing strands with a delicate stroma.

**2. Ameloblastoma, unicystic type**

The unicystic ameloblastoma (A-U) represents an ameloblastoma variant, presenting as a cyst. It has been termed variously as mural ameloblastoma, intracystic ameloblastoma, cystogenic ameloblastoma, cystic ameloblastoma and plexiform unicystic ameloblastoma. It accounts for 5-15% of all ameloblastomas. A-U tends to occur at a younger age (mean age about 25 years) than A-S/M (mean age about 35 years). More than 90% of cases involve the mandible, usually the posterior region. The lesion is asymptomatic or presents as a painless swelling. It may be expansile and destroy a portion of the jaw. The lesion presents radiographically as a well corticated unilocular, often pericoronal radiolucency (Fig. 5-1-7) Root resorption may occur. The clinical radiographic diagnosis is frequently a dentigerous (follicular) cyst. Three basic histological variants exist. In the first, a unilocular cystic lesion lined by ameloblastomatous epithelium (i.e. columnar basal cells with hyperchromatic nuclei, nuclear palisading with polarization and cytoplasmic vacuolation with intercellular spacing; (Fig. 5-1-8A). There is no infiltration of neoplastic epithelium. In the second variant the cystic lining is similar to that of the first, but a localized nodule arises from part of this cyst lining and projects into the lumen of the cyst. The intraluminal nodule comprises odontogenic epithelium with a plexiform pattern which closely resembles that seen in the plexiform ameloblastoma (Fig. 5-1-8B). There is no evidence of tumor infiltration of the fibrous cyst wall. This type is sometimes referred to as the plexiform unicystic ameloblastoma. Unlike the first two types, the third type of lesion contains tumor islands invading the fibrous wall (Fig. 5-1-8C). The invading tumor components may show plexiform or follicular pattern of ameloblastoma. Cyst linings partly showing ameloblastomatous features and/or intraluminal tumor nodules may also be present. The response of A-U to enucleation or curettage is more favorable. Conservative surgery seems to be justified in preference to mutilating radical surgery, despite the obvious risk of recurrence probably related to the presence of infiltrative tumor components in the cystic wall. Long-term follow up is mandatory.

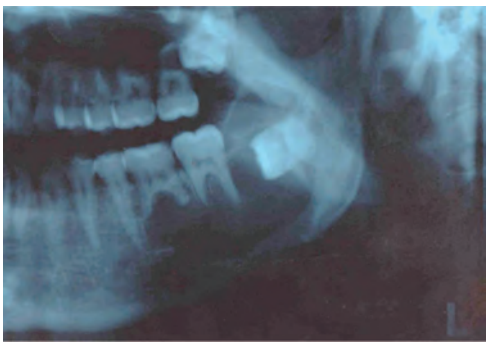


Fig. 5-1-7 Panoramic radiograph of an A-U patient. Monolocular radiolucent lesion with an impacted tooth resembling a dentigerous cyst.

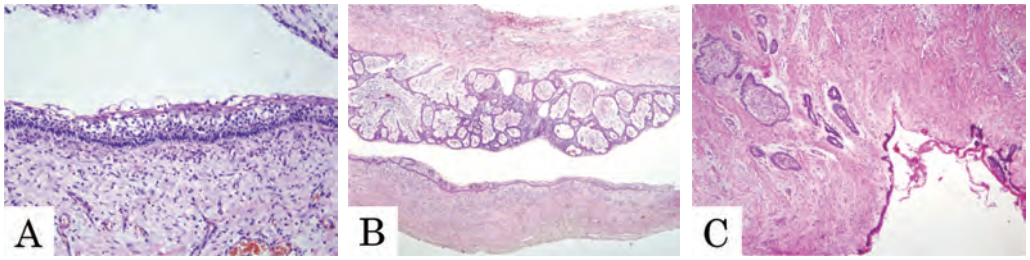



Fig. 5-1-8
(A) The epithelial lining of unicystic ameloblastoma shows typical features of ameloblastoma (HE, X200). Variants of A-U showing predominantly intraluminal plexiform proliferation of the epithelium (B, HE, X40) or invasion of tumor islands into the cyst wall (C, HE, X100).

**3. Ameloblastoma, desmoplastic type**

Desmoplastic ameloblastoma (A-D) is a variant of ameloblastoma, characterized by specific clinical, radiological and histological features. Although A-D is similar to A-S/M regarding age and gender distribution, the maxilla:mandible ratio is 1:1, which is in sharp contrast to A-S/M (1:5.4). Only 6% of A-Ds are found in the mandibular molar region as compared to over 50% of A-S/M cases. A painless swelling of the jaw bone is commonly the chief initial complaint. Radiographically, about 50% of A-Ds show a mottled, mixed radiolucency / radiopacity with diffuse margins, suggesting a fibro-osseous lesion (Fig. 5-1-9A).

Histologically, the stromal component of A-Ds dominates, compressing the odontogenic epithelial components. The epithelial tumour islands are small and irregular in shape. The epithelial cells at the periphery of the islands are cuboidal with inconspicuous nuclear polarity. The islands have a swirled, hypercellular center with spindle- shaped or squamous, epithelial cells (Fig. 5-1-9B). Formation of metaplastic osteoid trabeculae may be present. A fibrous capsule is not present corresponding to the radiographically poorly defined tumour margin. Similar treatment modality to A-S/M was recommended for A-D.

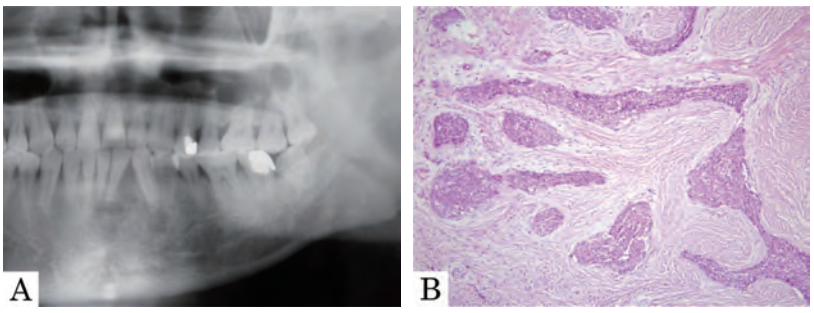



Fig. 5-1-9
(A) Radiograph of a mandibular desmoplastic ameloblastoma (A-D).
(B) The tumor stromal component dominates, compressing the odontogenic epithelial components (HE, X100).

**4. Ameloblastoma, extraosseous /peripheral type**

The extraosseous / peripheral ameloblastoma (A-E/P) is the extraosseous counterpart of the intraosseous solid / multicystic ameloblastoma.

The mean age of patients with A-E/Ps (over 50 years) is significantly higher than that for A-S/M (about 35 years). The male:female ratio is 1.9:1. A-E/Ps is located to the gingival with a mandible:maxilla ratio of 2.4:1. The A-E/P is a painless, firm and exophytic growth with a smooth or papillary surface. Apart from a superficial erosion, there is rarely significant bone involvement.

The A-E/P shows similar patterns of odontogenic epithelium seen in A-S/M. Some lesions are located entirely within the connective tissue of the gingiva, whereas others seem to fuse with the overlying mucosal epithelium (Fig. 5-1-10)

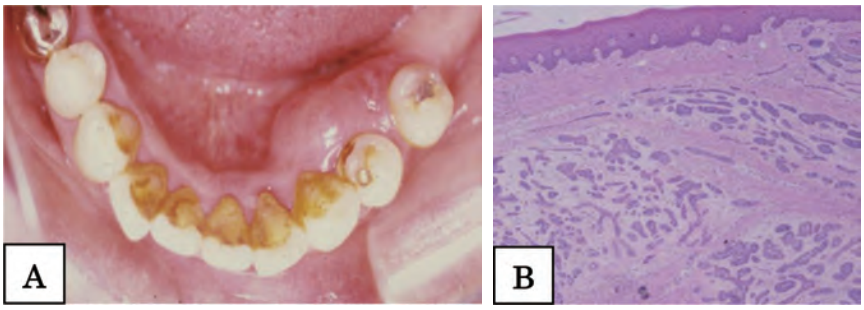



Fig. 5-1-10 An A-E/P of the left mandibular premolar region.
(A) An exophytic smooth-surfaced mass is seen in the lingual gingiva of the mandibular premolar.
(B) Many islands of odontogenic epithelium are seen within a fibrous stroma.

A-E/P does not show invasive behavior and conservative excision is the treatment of choice. Long-term follow-up is recommended.

(Tie-jun Li, Tomohiro Yamada, Tetsuya Yamamoto)

**b. Squamous odontogenic tumor**

**General description**

Squamous odontogenic tumor (SOT) is a locally infiltrative tumor consisting of islands of well-differentiated squamous epithelium in a fibrous stroma.

**Clinical features**

SOT presents as a painless swelling of the gingiva, with mobility of the teeth. It occurs more frequently in the mandible than in the maxilla. It is thought to develop in the periodontal ligament of vital permanent tooth.

**Diagnosis**

Radiologically, most SOTs show unilocular or triangular radiolucency between the tooth roots. Multilocular patterns may be seen in extensive lesions. Histologically, the tumor is composed of islands of well-differentiated squamous epithelium in intense collagenous fiber. Epithelial islands can contain keratinization.

**Treatment**

Conservative surgical treatment is usually sufficient. Recurrences are rare after complete excision.

(Tomohiro Yamada, Tetsuya Yamamoto)

**c. Calcifying epithelial odontogenic tumor (Pindborg tumor)**

**General description**

Calcifying epithelial odontogenic tumor (CEOT) is a locally invasive tumor with the presence of amyloid material that may become calcified.

**Clinical features**

CEOT presents as an asymptomatic, slowly growing mass in the jaw. It accounts for about 1% of all odontogenic tumors with no gender predilection. The tumor arises mostly in the mandiblular molar region; however, extraosseous lesions may occur in the anterior region.

**Diagnosis**

Radiologically, CEOT shows unilocular mixed radiolucent-radiopaque lesions. Histologically, the tumor consists of a fibrous stroma with islands and sheets of polyhedral epithelial cells with abundant eosinophilic cytoplasm. The nuclei are commonly pleomorphic, with giant nuclei; however, mitosis as malignant tumor is rarely seen. Eosinophilic, homogeneous hyaline material is often calcified within or around the sheets of tumor cells. This material is amyloid and positively stained with Congo red and thioflavine T.

**Treatment**

As CEOT is a locally invasive tumor, treatment is usually consistent with ameloblastoma-solid/multicystic type.

(Tomohiro Yamada, Tetsuya Yamamoto)

### d. Adenomatoid odontogenic tumor

**General description**

Adenomatoid odontogenic tumor (AOT) is composed of odontogenic epithelium with an adenomatoid architecture, embedded in a mature connective tissue stroma.

**Clinical features**

AOT accounts for 2-7% of all odontogenic tumors with no gender predilection. More than 2/3rds are diagnosed in patients less than 20 years of age. The tumor occurs mostly in the maxillary anterior region. AOT presents as a slow growing swelling of the jawbone. The tumors are usually no more than 3cm in diameter, and rarely become large.

**Diagnosis**

Radiologically, AOT shows a well-defined unilocular radiolucency around the crown of an unerupted tooth. Radiopaque flecks are often present. Histologically, various sized solid nodules of cuboidal or columnar cells of odontogenic epithelium form nests or lattice- or rosette-like structures with little fibrous stroma. There may be also a tubular or duct-like appearance, or nodules. Nodules may contain amorphous amyloid-like material or calcified materials. (Fig. 5-1-11)

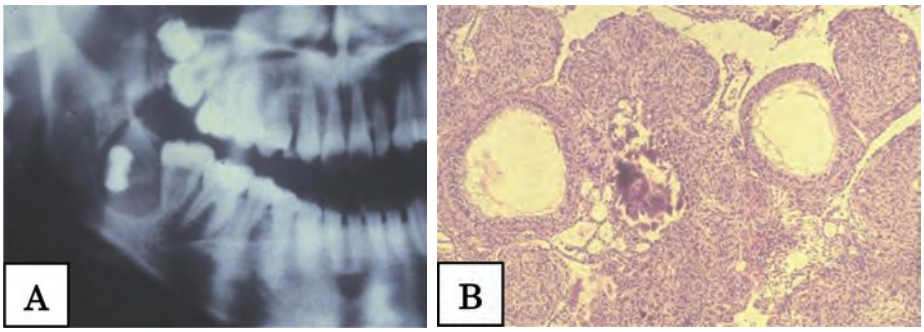



Fig. 5-1-11 Adenomatoid odontogenic tumor.
(A) Well-defined unilocular radiolucent lesion around the crown of the right mandibular third molar.
(B) Solid nodules of cuboidal or columnar cells of odontogenic epithelium with little fibrous stroma are seen.

**Treatment**

AOT is treated by local excision. Recurrence is rare.

(Tomohiro Yamada, Tetsuya Yamamoto)

**e. Keratocystic odontogenic tumor**

Keratocystic odontogenic tumors (KCOTs, previously known as odontogenic keratocysts) are locally aggressive, cystic jaw lesions with a putative high growth potential and a propensity for recurrence.

**Clinical features**

KCOTs present over a wide age range, but peak in the 2nd and 3rd decades and is more common in male. The mandible is the most common site. About one half of all KCOTs occur at the angle and ramus of the mandible. In the maxilla, most present in the so called 'globulomaxillary' and molar area. A considerable number of KCOTs are asymptomatic and hence detected by incidental radiographic findings. When there are presenting signs and symptoms, swelling and intraoral drainage appear to be most common (Fig. 5-1-12A). The radiographical presentation of KCOT is variable. Typical features such as scalloped margins or a multilocular appearance (Fig. 5-1-12B, 5-1-13, -14) may be indicative, but other odontogenic lesions may present similar radiological features. Thus, there are few unequivocal clinical and radiographic features specific for KCOT, its definitive diagnosis still relies on histological examination.

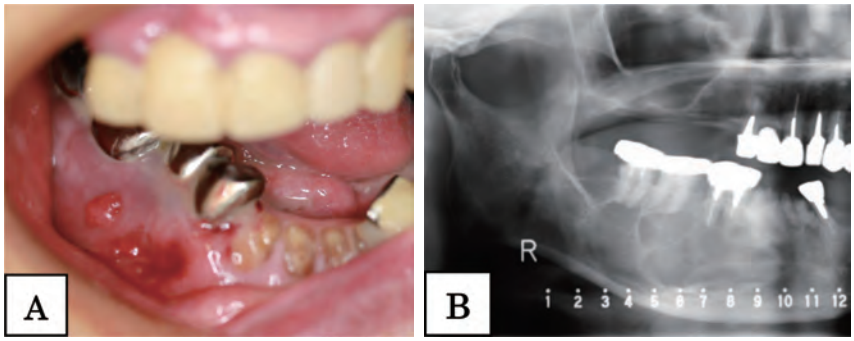



Fig. 5-1-12 Keratocystic odontogenic tumor in the right molar region.
(A) Swelling with pus discharge in the alveolus region is observed at the posterior part of the mandibular body.
(B) Multilocular radiolucent region with a sharp margin is identified in the posterior body of the mandible

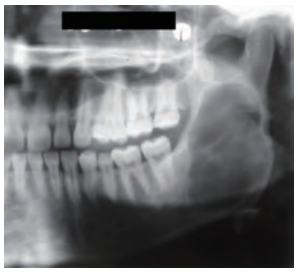


Fig. 5-1-13
Radiograph of a mandibular KCOT involving the angle and ramus region.

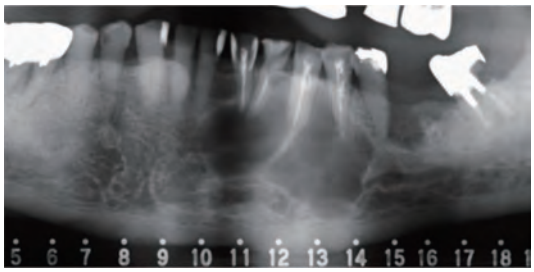


Fig. 5-1-14
Keratocystic odontogenic tumor in the anterior mandible. Multilocular radiolucent lesion with a sharp margin is identified in the anterior body of the mandible.

**Histological features**

The typical morphology of KCOT includes the presence of a thin, uniform lining of stratified squamous epithelium with a tendency to detach from the underlying connective tissue capsule; a thin corrugated surface layer of parakeratin; a spinous cell layer 8 to 4 cells in thickness, often showing intracellular edema; a regular layer of columnar basal cells with palisading of the nuclei; a flat epithelial-fibrous tissue junction usually devoid of epithelial rete ridges; and a relatively thin fibrous capsule which is mostly free from inflammatory cell infiltrate (Fig. 5-1-15, 5-1-16A, 5-1-16B). Where inflammation is present, the adjacent epithelium loses its characteristic structure and may become thicker, develop rete ridges and/or ulcerate. Apparently inactive odontogenic epithelial rests, larger islands of odontogenic epithelium and small satellite cysts are all quite commonly found in the walls of KCOT.

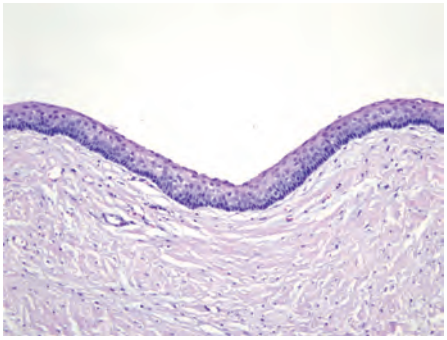


Fig. 5-1-15
The epithelial lining of OKC shows typical features of a corrugated parakeratinized surface layer and a regular layer of columnar basal cells with nuclear palisading. (HE, X200)

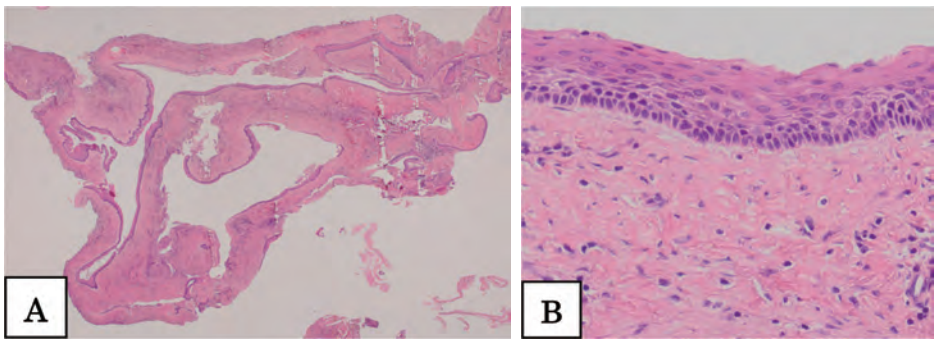



Fig. 5-1-16 Keratocystic odontogenic tumor in the anterior mandible.
(A) Surgical specimens revealed multiple cystic lesions.
(B) The wall of the lesion is lined by parakeratinized stratified squamous epithelium, with the nuclei of the columnar basal cells oriented away from the basement membrane.

Whilst typical KCOT epithelium is parakeratinized with its surface having a characteristically corrugated appearance, there have been a significant number of cases in which an orthokeratinized epithelium lining is prevalent. The orthokeratinized epithelial lining lacks a corrugated appearance, but often shows relatively thick, onion-skin-like orthokeratin layers. A prominent subjacent granular layer beneath the cornified layer and hypocellular spinous cells are consistent findings in the orthokeratinized epithelium. Furthermore, its basal layer cells usually exhibit either a low cuboidal or a flat morphology with little evidence of nuclear hyperchromatin and palisading (Fig. 5-1-17). The recent WHO classification of odontogenic tumors excludes this subtype from typical KCOTs, as the orthokeratinized jaw cyst lacks the typical features of an KCOT, exhibits little if any tendency to recur, and has no apparent association with Gorlin syndrome.

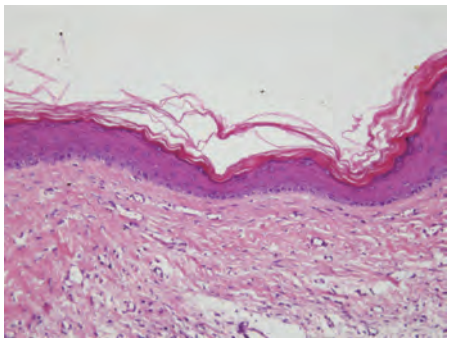


Fig. 5-1-17
The orthokeratinized odontogenic cyst shows onion-skin-like surface orthokeratin layers. Its lining epithelium is hypocellular showing a prominent granular cell layer and flattened basal cells.

**Reasons for recurrence**

The KCOT is of particular interest because it is clinically more aggressive and tends to recur after surgery. The reasons for this may be related to the followings. Firstly, the epithelial lining of KCOT has greater proliferative/growth potential than other cyst types. Then, the occurrence of satellite cysts may be retained during surgical procedure which will cause recurrence. Thirdly, the wall of KCOT is very thin and fragile and the cyst is consequently often removed in fragments. Such fragmentation increases the risk of portions of the epithelial lining and/or satellite cysts being left behind, so increasing the risk of recurrence.

**Association with nevoid basal cell carcinoma syndrome (NBCCS)**

Although KCOT most commonly occurs as a single lesion in the jaw of an otherwise healthy person, about 4-5% of all KCOT patients have multiple cysts

with other features of the so called nevoid basal cell carcinoma syndrome (NBCCS, also known as Gorlin syndrome). NBCCS is a rare autosomal dominant disorder that exhibits high penetrance and variable expressivity. Clinical manifestations are extremely varied and include basal cell carcinoma of the skin, multiple KCOTs of the jaws, palmar or plantar pits, ectopic calcification of the falx cerebri, which are considered as major criteria for diagnosis. Multiple KCOTs are the most consistent and common anomaly in NBCCS, occurring in 65-100% of patients often during the first or second decade of life. In addition, syndrome-associated KCOTs are to be found in both jaws with equal frequency, in contrast to sporadic KCOTs which involve especially the lower jaw. Among the various presentations, KCOTs are often the first signs of NBCCS, frequently antedating the syndromic basal cell carcinomas, thereby allowing earlier diagnosis.

**Treatment**

Enucleation is the basic surgical management. KCOTs with regular spherical outline can be enucleated. Unilocular cysts with loculated periphery may be treated by marginal excision to ensure a safe margin or trimmed with a proper bur after enucleation. Large multilocular lesions may require resection of the involved bone, followed by primary reconstruction. However, our experience suggests that large lesions even with cortical perforation can also be treated by enucleation with excision of the overlying mucosa and/or the other soft tissues. The bony defect should be carefully cauterized with Carnoy's solution. The defect should not be filled with any permanent materials like hydroxyapatite, bone graft, etc. For small defects, primary closure should be tried; for larger defects, temporary filling with iodoform gauze may be required, which should be removed 7 to 10 days after operation.

**Prognosis**

KCOTs have a high tendency to recur. Figures for the incidence of recurrence in various reported series have varied from 2.5 to 62%. The reason for this great variation is partly dependent upon the varied nature of the cases published. For example, some series include cysts from patients with Gorlin syndrome and others exclude them and other important variables include the duration of the follow-up periods and the methods of treatment employed. Patients with KCOT should be followed up regularly for a long period.

(Tie-jun Li, Tomohiro Yamada, Tetsuya Yamamoto)

**Odontogenic epithelium with odontogenic ectomesenchyme with or without hard tissue formation**

**f. Ameloblastic fibroma / fibrodentinoma / fibro-odontoma**

**General description**

Ameloblastic fibroma (AF) consists of odontogenic ectomesenchyme resembling the dental papilla and epithelial strands and nests resembling dental lamina and enamel organs. When there is dentin formation, it is referred to as ameloblastic fibrodentinoma (AFD); when there is dentin and enamel formation, it is referred to as ameloblastic fibro-odontoma (AFO).

**Clinical features**

AF/AFD/AFO occurs mostly in people under 20 years of age with no gender difference. These tumors arise mostly in the molar regions of the mandible. AF/AFD/AFO is associated with slow swelling of the jawbone.

**Diagnosis**

Radiologically, AF/AFD/AFO shows unilocular or multilocular radiolucency. AFO has varying levels of radiopacity. Histologically, a biphasic pattern is seen in ameloblastic and mesenchymal tissues. The mesenchymal component consists of a loose and primitive mass of stellate cells, and the ameloblastic component consists of thin, anastomosing cords and nests of epithelium resembling the dental lamina with ameloblastic changes (palisading and reverse polarization). Dysplastic dentin is formed in case of AFD; dentin and enamel are formed in case of AFO. (Fig. 5-1-18, -19)

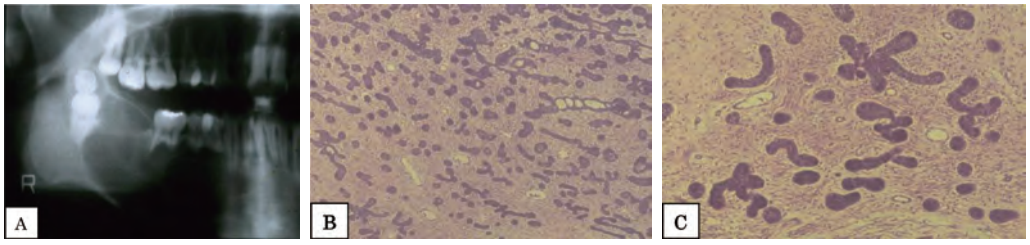



Fig. 5-1-18 Ameloblastic fibroma.
(A) Monolocular radiolucent lesion with a sharp margin in the posterior body of the mandible.
(B, C) Ameloblastic nests are observed within primitive, cellular mesenchymal stroma.

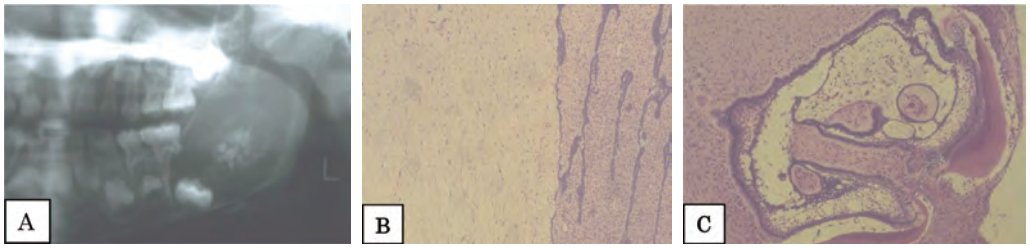



Fig.5-1-19 Ameloblastic fibro-odontoma.
(A) Monolocular radiolucent lesion with many calcified bodies in the ramus of the mandible.
(B, C) Ameloblastic cords are observed within a primitive, cellular mesenchymal stroma. In some parts, hard tissue-like dentin and enamel is observed.

**Treatment**

Treatment consists of enucleation and curettage. Recurrences is rare, careful follow-up is necessary since recurrent AF may become malignant.

(Tomohiro Yamada, Tetsuya Yamamoto)

**g. Odontoma, complex type / compound type**

**General description**

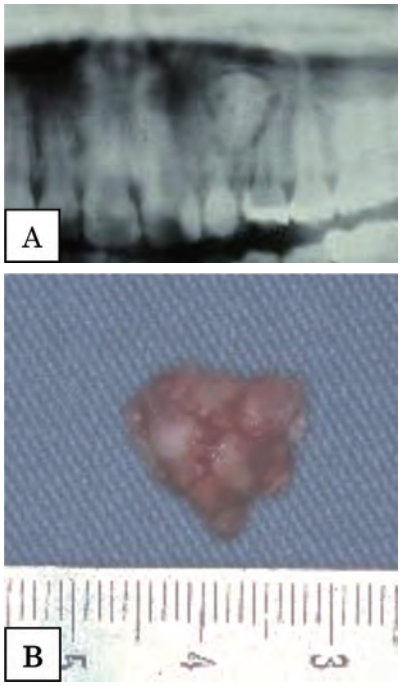
Odontoma is a tumor-like malformation (hamartoma), involving enamel, dentin, and cementum (odontoma, complex type; OC), or varying numbers of tooth-like elements (odontoids) (odontoma, compound type; OCp). Odontoma is the most common of all odontogenic tumors/tumor-like lesions.

**Clinical features**

OC/OCp is a painless slowly growing lesion, and growth stops when fully matured. Most cases are diagnosed based on asymptomatic radiographic findings in subjects between 10 and 30 years of age. OC occurs commonly in the mandibular molar region, whereas OCp occurs primarily in the maxillary anterior region.

**Diagnosis**

Radiologically, OC shows spherical or ovoid radiopacity surrounded by a radiolucent zone. OCp appears as a collection of tooth-like structures surrounded by a radiolucent zone. Histologically, OC consists of an irregular arrangement of dentin and enamel prisms and entrapped odontogenic epithelium. OCp consists of an encapsulated mass of numerous, tiny, single-rooted toothlets admixed with fibrous connective tissue. (Fig. 5-1-20, -21)



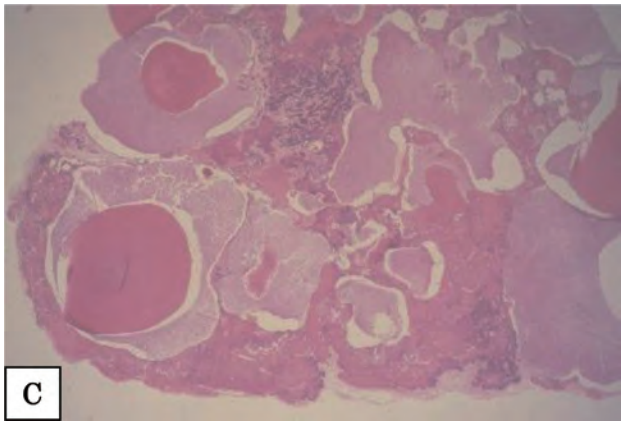
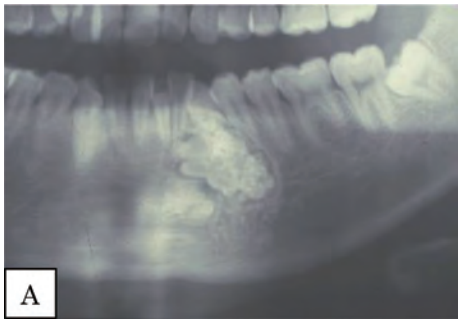




Fig. 5-1-20 Odontoma, complex type.
(A) Monolocular inhomogeneous radiopaque lesion surrounded by a radiolucent area.
(B) Extirpated tumor was a ragged, hard mass covered with thin soft-tissue.
(C) Disorganized mass of dentinoid material and enamel prisms are observed.



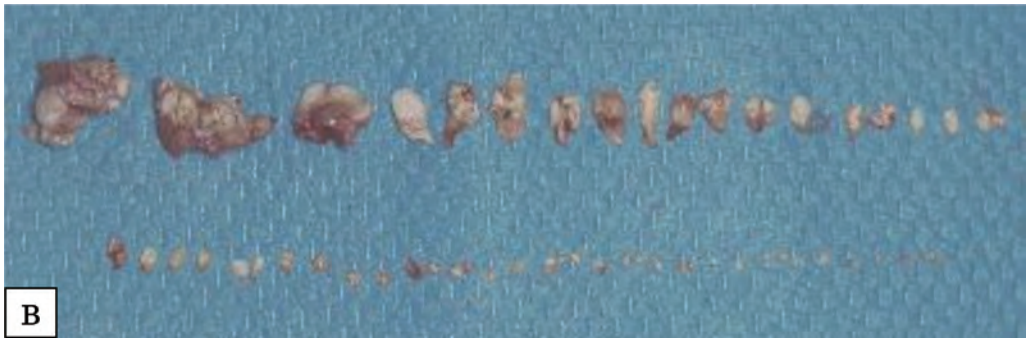




Fig. 5-1-21 Odontoma, compound type.
(A) Monolocular area with many tooth-like calcified bodies surrounded by a radiolucent area in the canine region of the mandible.
(B) Extirpated tumor consisted of numerous tooth-like bodies of various sizes.

**Treatment**

OC/OCp is treated by local excision. It seldom recurs.

(Tomohiro Yamada, Tetsuya Yamamoto)

**h. Odontoameloblastoma**

**General description**

Odontoameloblastoma (OA) combines the features of ameloblastoma and odontoma.

**Clinical features**

OA shows bone expansion, root resorption, tooth displacement and occasional pain. It occurs commonly in the molar region of both jawbones in people under 15 years of age. The tumor grows slowly.

**Diagnosis**

Radiologically, OA appears as a well-defined unilocular or multilocular radiolucent lesion, sometimes with radiopaque material. Histologically, the enamel component consists of islands and cords of odontogenic epithelium demonstrating follicular and plexiform patterns. In addition to fibrous stroma, mineralized dental tissues are formed in varying amounts.

**Treatment**

OA is a locally aggressive neoplasm; therefore, treatment is consistent with ameloblastoma.

(Tomohiro Yamada, Tetsuya Yamamoto)

**i. Calcifying cystic odontogenic tumor (Gorlin cyst) / dentinogenic ghost cell tumor**

**General description**

Calcifying cystic odontogenic tumor (CCOT) and Dentinogenic ghost cell tumor (DGCT) were called calcifying odontogenic cysts, as initially reported by Gorlin in 1962. As they both have tumorous characteristics, they were renamed and subdivided into the current classifications by the WHO (2005). Both lesions are characterized by the appearance of ghost cells and are often associated with odontoma.

**Clinical features**

CCOT and DGCT may present as an intraosseous or extraosseous lesion. There is no predilection in gender and the lesions may occur with equal frequency in the

upper or lower jaw. They commonly occur in the anterior region. CCOT and DGCT are characterized by asymptomatic, slowly growing expansion of the jaw. They are usually asymptomatic.

**Diagnosis**

Radiologically, intraosseous lesion generally shows unilocular radiolucencies with a well-circumscribed border. Variable amounts of radiopaque materials are also seen depending on the amount of calcification.

Histologically, CCOT is characterized as cystic lesion lined by an ameloblastoma-like epithelium with ghost cells that may calcify. DGCT is characterized by ameloblastoma-like islands of epithelial cells in a mature connective tissue stroma. Aberrant keratinization may be found in the form of ghost cells in association with varying amounts of dysplastic dentin (Fig. 5-1-22).

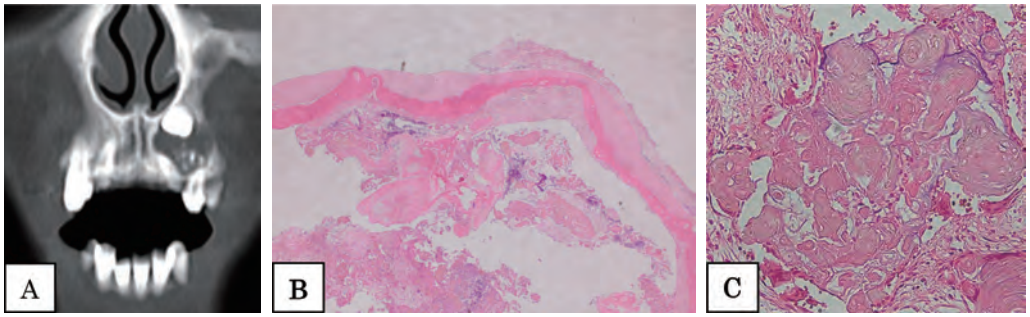



Fig. 5-1-22 Calcifying cystic odontogenic tumor.
(A) Monolocular cystic radiolucent lesion with many small calcified bodies located in the canine region of the maxilla.
(B) The cystic lesion lined with aberrant keratinization.
(C) Histologically aggregated ghost cells, enlarged eosinophilic epithelial cells without nuclei seen.

**Treatment**

Enucleation is the appropriate treatment for most cases of CCOT and extraosseous DGCT. Intraosseous DGCT may be aggressive and wide local resection is recommended, consistent with the approach for ameloblastoma.

**Ghost cell**: an enlarged eosinophilic epithelial cell with eosinophilic cytoplasm but without a nucleus

(Tomohiro Yamada, Tetsuya Yamamoto)

**Mesenchyme and/or odontogenic ectomesenchyme with or without odontogenic epithelium**

**j. Odontogenic fibroma**

**General description**

Odontogenic fibroma (OF) is a rare tumor with various amounts of inactive-looking odontogenic epithelium embedded in a mature, fibrous stroma.

**Clinical features**

OF preferably occurs in people in their 10's, 20's and 30's with female predominance. These lesions occur mostly in the molar regions of the mandible. OF presents as a slow swelling of the jawbone and is mostly asymptomatic.

**Diagnosis**

Radiologically, OF shows unilocular or multilocular radiolucency. Histologically, scattered, inactive epithelial odontogenic nests are seen in interlacing fascicles of mature fibrous connective tissue. Occasionally, small, spherical basophilic calcifications are seen.

**Treatment**

OF can be cured by local enucleation.

(Tomohiro Yamada, Tetsuya Yamamoto)

**k. Odontogenic myxoma / myxofibroma**

**General description**

Odontogenic myxoma (OM) is an intraosseous tumor with stellate and spindle-shaped cells embedded in myxoid or mucoid extracellular matrix. Odontogenic myxofibroma is a variation with a greater amount of collagen. OM accounts for 3-20% of all odontogenic tumors and is the third most common (after odontoma and ameloblastoma).

**Clinical features**

OM occurs mainly in people between the ages of 10 and 50 with a slight preference for females. Two thirds of the cases of OM are located in the mandible, and commonly in the molar regions. Asymptomatic expansion of the bone is seen; however, growth is usually relatively fast.

**Diagnosis**

Radiologically, OM appears as unilocular or multilocular radiolucency with a fine crisscrossing of bone trabeculae showing a “soap bubble” or “honeycomb” appearance. Histologically, OM is characterized by randomly oriented stellate, spindle-shaped and round cells in an abundant mucoid or myxoid stroma (Fig. 5-1-23). The tumor is positive for vimentin and focally positive Odontogenic myxofibroma has dense fibrous tissue.

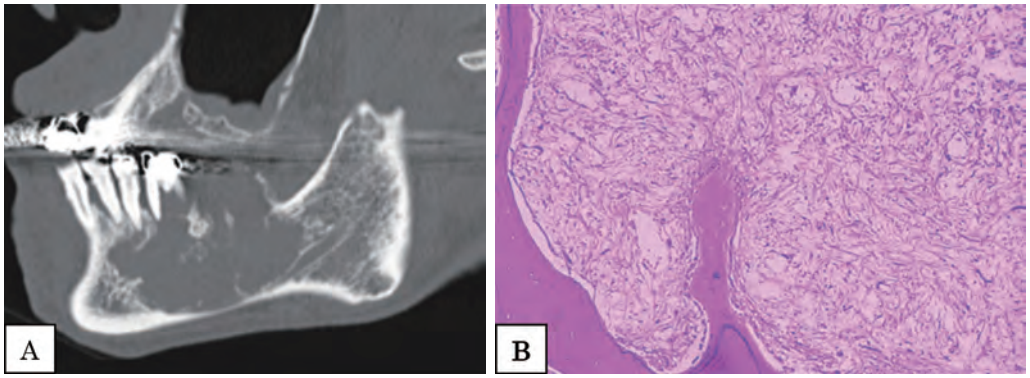



Fig. 5-1-23 Odontogenic myxoma.
(A) An ill-defined multilocular radiolucent lesion is observed.
(B) Randomly oriented stellate and spindle-shaped cells are seen in an abundant myxoid stroma.

**Treatment**

Enucleation or curettage is usually not enough, because OM tends to permeate into marrow spaces. Excision with a safe margin is recommended.

(Tomohiro Yamada, Tetsuya Yamamoto)

**l. Cementoblastoma**

**General description**

Cementoblastoma is a tumor forming cementum-like tissue connected to the root of a tooth.

**Clinical features**

Cementoblastoma occurs most commonly in people between 10 and 30 years of age with no gender difference. The tumor usually arises in the first molar of the mandible. A cementoblastoma provokes pain and swelling of the alveolus.

**Diagnosis**

The electric vitality test of the involved tooth usually indicates that it has remained intact. Radiologically, a calcified mass attached to a tooth root is seen. The radiopaque lesion is surrounded by a fine radiolucent line. Histologically, it consists of dense masses of acellular cementum-like material, containing basophilic incremental lines, in a well vascularized fibrous stroma (Fig. 5-1-24).

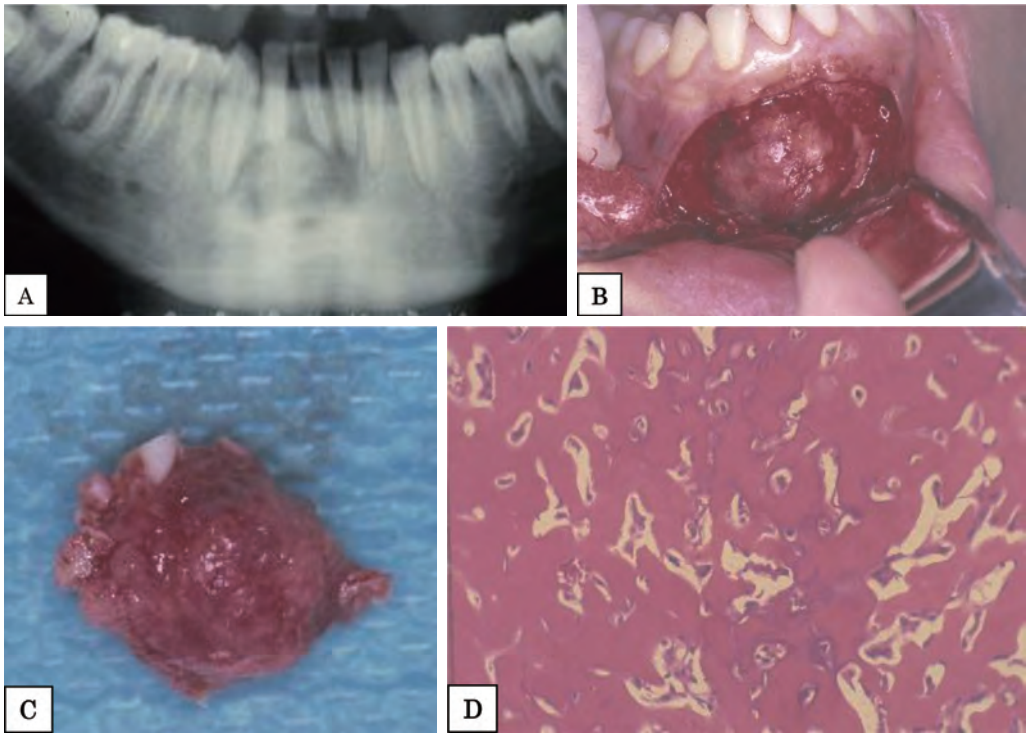



Fig. 5-1-24 Cementoblastoma.
(A) An ill-defined, monolocular radiopaque lesion surrounded by a radiolucent area is observed. The lesion seems to be attached to the mandibular right lateral incisor.
(B, C) Intra-operative view and extirpated lesion. The lesion was demarcated with fibrous soft tissue.
(D) Acellular cementum-like material, containing basophilic incremental lines was seen.

**Treatment**

Cementoblastoma can be treated by removal of the tooth and tumor enucleation.

(Tomohiro Yamada, Tetsuya Yamamoto)

**Bone-related lesions**

**m.Ossifying fibroma**

**General description**

Ossifying fibroma (OF) is a well-demarcated tumor with fibrocellular tissue and mineralized material of varying appearances. It is thought to be a true neoplasm derived from the periodontal ligament. Juvenile trabecular ossifying fibroma (JTOF) and juvenile psammomatoid ossifying fibroma (JPOF) are two histological variants.

**Clinical features**

OF predominantly occurs in people from 10 to 40 years of age with female preference. JTOF and JPOF occur in people of younger ages. OF arises mostly in the posterior region of the mandible. JPOF mainly arises in the bony walls of the paranasal sinuses whereas JTOF generally localizes in the maxilla. OF causes painless swelling and expansion of the bone. JTOF usually expands rapidly.

**Diagnosis**

Radiographically, OF shows a demarcated radiolucent lesion with radiodensity depending on the varying contributions of soft and hard tissue components. Histologically, OF consists of cellular fibrous tissue mixed with cemento-osseous trabeculae and calcific spherules. Woven bone trabeculae are lined with plump osteoblasts (Fig.5-1-25). In JPOF, fibroblastic stroma contains small ossicles resembling psammoma bodies.

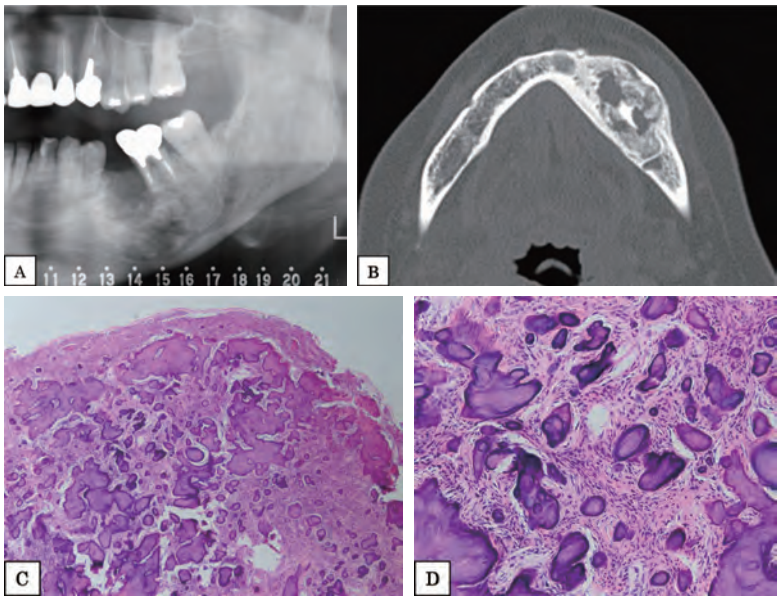



Fig. 5-1-25 Ossifying fibroma.
(A, B) An ill-defined inhomogeneous radiopaque lesion is observed in the posterior region of the mandibular body.
(C, D) Cemento-osseous trabeculae and calcific spherules are seen in cellular fibrous tissue

**Treatment**

OFs continue to enlarge when untreated. They should be removed completely.

(Tomohiro Yamada, Tetsuya Yamamoto)

**n. Fibrous dysplasia**

**General description**

Fibrous dysplasia (FD) is a genetically-based sporadic disease of the bone. The bone lesion may be in one or multiple bones. FD may be a component of the McCune-Albright syndrome.

**Clinical features**

FD preferably occurs in teenagers and young adults with no gender predominance. It occurs more often in the maxilla than in the mandible. It manifests as a slowly growing, painless expansion of bone, producing facial asymmetry.

**Diagnosis**

Radiographically, FD shows ground glass or orange peel radiopacity. Superior displacement of the mandibular canal, narrowing of the periodontal ligament space, and effacing of the lamina dura, are common findings suggesting FD. Histologically, uniform patterns of evenly distributed, variably shaped woven bone trabeculae are seen in a cellular fibrous stroma (Fig.5-1-26).

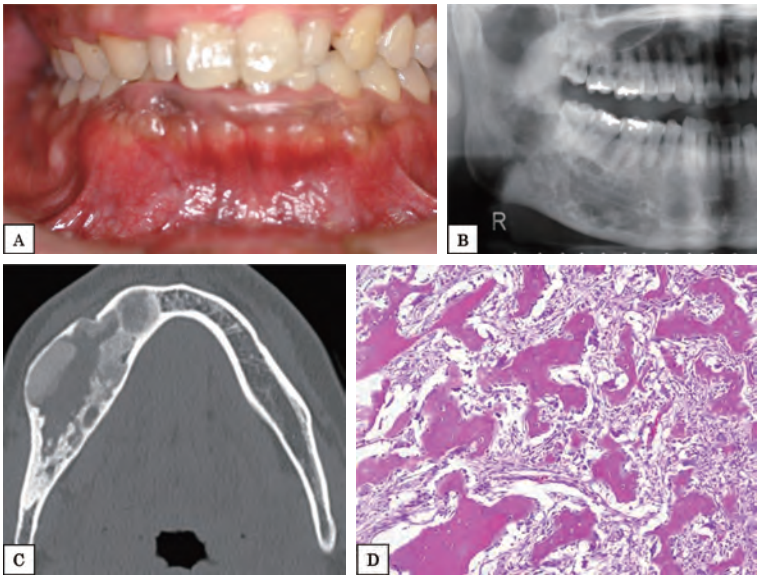



Fig. 5-1-26 Fibrous dysplasia.
(A) Diffuse swelling is observed in the posterior region of the mandibular alveolus.
(B, C) An ill-defined inhomogeneous ground-glass-like radiopaque lesion is observed in the posterior region of the mandibular body.
(D) Differently shaped woven bone trabeculae are seen in a cellular fibrous stroma.

**Treatment**

Observation or surgical recontouring is applied. Very rarely, sarcoma development has been reported.

(Tomohiro Yamada, Tetsuya Yamamoto)

**o. Osseous dysplasia**

**General discription**

Osseous dysplasia (OD) is characterized by the replacement of normal bone by fibrous tissue and metaplastic bone in the periapical region. OD is also called cemento-osseous dysplasia, periapical cemental dysplasia, or periapical osseous dysplasia.

**Clinical features**

OD is generally asymptomatic. It is usually found incidentally by radiological examination. If the lesion is infected, pain and fistula are evident.

**Diagnosis**

Radiographically, OD is shown as a mixed radiolucent and radiopaque lesion in the periapical region. The involved tooth remains vital. Histologically, OD consists of cellular fibrous tissue, woven as well as lamellar bone and masses of cementum-like material (Fig. 5-1-27).

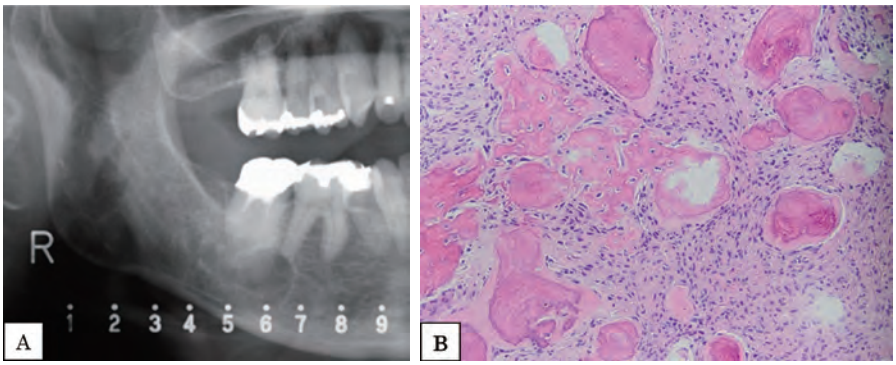



Fig. 5-1-27 Osseous dysplasia.
(A) Monolocular radiolucent lesion mixed with some radiopacity in the periapical region of the mandibular right second molar.
(B) Cemento-osseous trabeculae are seen in cellular fibrous tissue.

**Treatment**

ODs do not require treatment unless complications occur such as infection.

(Tomohiro Yamada, Tetsuya Yamamoto)

**p. Central giant cell lesion**

**General description**

Central giant cell lesion (CGCL) is a localized benign but sometimes aggressive osteolytic proliferation consisting of fibrous tissue with haemorrhage and haemosiderin deposits, with the presence of osteoclast-like giant cells and reactive bone formation.

**Clinical features**

CGCL causes asymptomatic swelling. Larger lesions can be painful. Most cases are diagnosed in patients less than 30 years of age.

**Diagnosis**

Radiographically, CGCL shows unilocular or multilocular radiolucency. A large lesion may destroy the cortical bone and cause tooth resorption. Histologically, cellular fibrous connective tissue containing plump spindle cells, and clusters of multinucleated giant cells are noted.

**Treatment**

Curettage, radical surgery, and/or the injection of corticosteroids, calcitonin, and interferon.

(Tomohiro Yamada, Tetsuya Yamamoto)

**q. Cherubism**

**General discription**

Cherubism is an autosomal dominant inherited disease, characterized by symmetrical extension of the jaws. The histology is indistinguishable from that of a central giant cell lesion.

**Clinical features**

All four quadrants of the jaws can be involved. Symmetrical painless swellings of the jaw occur from 2-5 years of age, making the afflicted subject look like an angel or cherub. The swelling regresses after the cessation of bone growth.

**Diagnosis**

The diagnosis is supported by clinical presentation of bilateral enlargement of the child's jaws, and radiographical findings of uni/multilocular radiolucencies and expansile osteolytic lesions. Histological findings are the same as for central giant cell lesions.

**Treatment**

As the lesions regress after puberty, surgery is performed only in cases of severe functional disturbance.

(Tomohiro Yamada, Tetsuya Yamamoto)

**r. Aneurysmal bone cyst**

**General description**

Aneurysmal bone cyst (ABC) is an expansile osteolytic lesion with blood filled spaces separated by fibrous septa containing osteoclast-type giant cells and reactive bone.

**Clinical features**

ABC occurs primarily in people under 30 and is localized to the jaws in about 1-3% of patients. ABC may show marked swelling and few symptoms. Malocclusion, tooth displacement, and root resorption may occur. Mandiblular posterior region is the most common site.

**Diagnosis**

Unilocular or multilocular radiolucent lesions are seen. Occasionally, mixed radiopaque-radiolucent patterns can be found. Borders are well delineated; however, cortical bone destruction and extension into the soft tissues can occur. On MRI, "fluid-fluid levels" in lesional cavities by sedimentation of blood cells are characteristic (Fig. 5-1-28). Histologically, the blood-filled spaces are not lined with

endothelial cells, but by macrophages. The septa are composed of granulation tissue with foci of multinucleated giant cells, hemorrhage, hemosiderin, and reactive woven bone trabeculae.

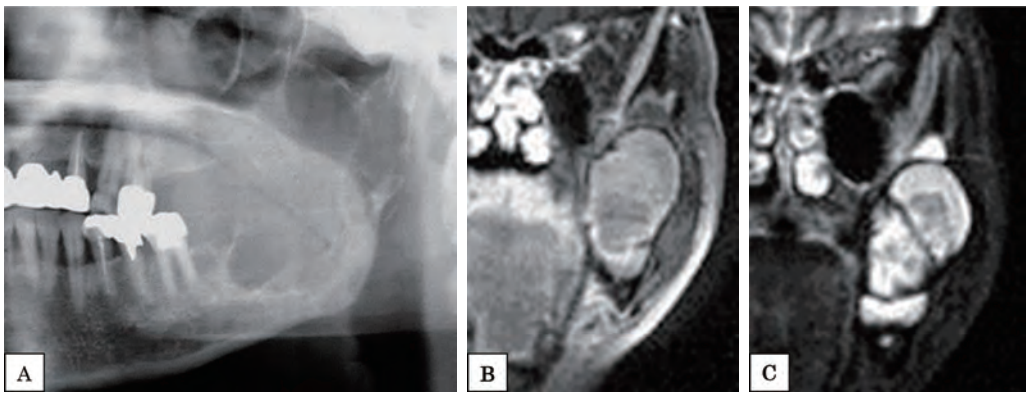



Fig. 5-1-28 Aneurysmal bone cyst.
(A) Multilocular radiolucent lesion in the ramus of the mandible.
(B) T1-weighed MR image.
(C) STIR MR image. Fluid-fluid level is seen in lesional cavities.

**Treatment**

ABC can be treated with curettage, enucleation, or surgery. Successful embolization has also been reported.

(Tomohiro Yamada, Tetsuya Yamamoto)

**s. Simple bone cyst**

**General description**

Simple bone cyst (SBC) is an intraosseous pseudocyst without epithelial lining.

**Clinical features**

SBC occurs preferentially in males under 20 years of age, most commonly in the mandible. SBC is generally asymptomatic and discovered incidentally.

**Diagnosis**

SBC is radiolucent and unilocular with no or slight expansion of the bone. Superior margins between the dental roots are characteristically scalloped (Fig. 5-1-29). Final diagnosis is aided by finding an empty cavity at surgical intervention.

Histologically, SBC is an empty bone cavity lined by loose fibrous connective tissue. Small amounts of new bone formation and collagen deposits may be present.

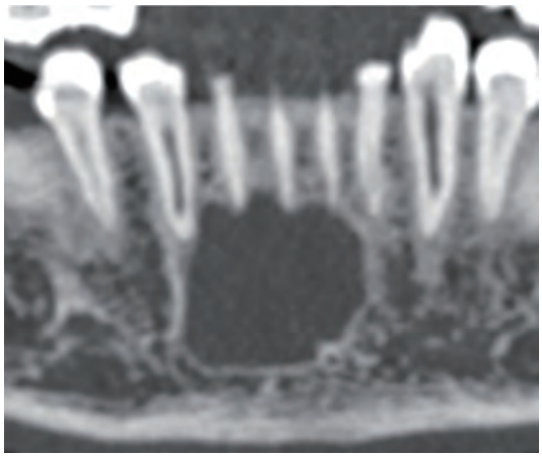


Fig. 5-1-29 Simple bone cyst.
Monolocular radiolucent lesion with a scalloped superior margin is observed in the anterior region of the mandible.

**Treatment**

Even biopsy leads to bone healing within one year.

(Tomohiro Yamada, Tetsuya Yamamoto)

# 5-2. Non-odontogenic tumor

**a. Papilloma**

**Overview**

Papillomas are tumors that arise from the oral mucosal epithelium, appearing papillomatous or dendritic to the naked eye and exhibiting exophytic growth. In many cases, they are reactive growths caused by persistent or chronic irritation, and growths regarded as true tumors are infrequent, but their firm identification is difficult. They are seen in all age groups, but are comparatively more common among the elderly, and commonly occur on the tongue, palate, gingiva and lips. (Fig. 5-2-1)

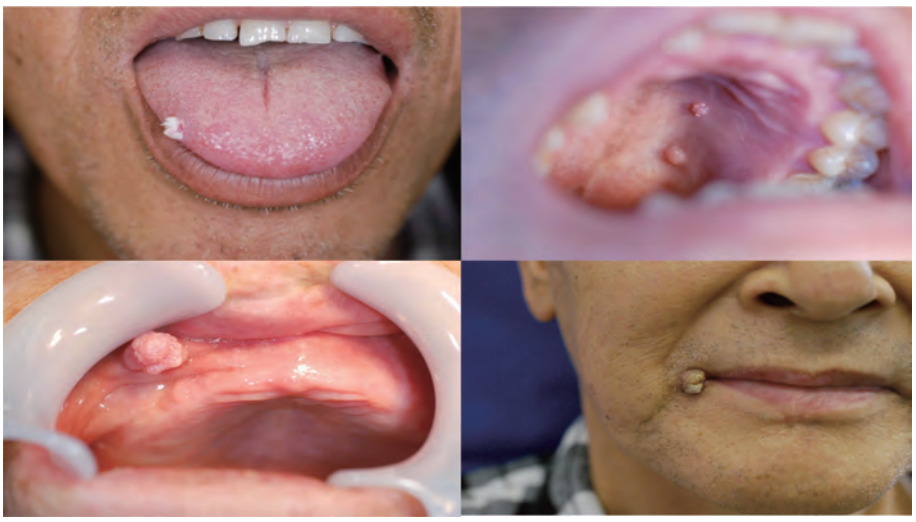


Fig. 5-2-1 Papilloma (tongue, palate, gingiva, lip)

In addition to a range of types of persistent or chronic irritation, the human papilloma virus (HPV) is also involved in the etiology of papilloma. Around 100 genetic types of HPV have been reported, and HPV infection is believed to contribute to tumor formation in humans. Various different types of HPV (including 1, 2, 4, 6, 11, 16 and 59) have been reported in papilloma in the oral region.

Multiple papillomas across a wide area of the oral mucosa are known as papillomatosis. This condition is also called papillary hyperplasia, and is closely associated with HPV. It commonly occurs in elderly individuals in the hard palate or labial mucosa, frequently as a result of chronic irritation from ill-fitting dentures or poor oral hygiene. These may also appear as localized, irregular papillomatous or nodular protuberances across a wide area.

**Diagnosis**

Papillomas are dendritic, pendunculated, with a broad base, with a white appearance if the surface is keratinized. Their growth is generally slow. Histopathologically, they are formed by the papillomatous proliferation of stratified squamous epithelium, with the interior containing hyperplastic fibrous connective tissue. In addition to hypertrophy of the stratum spinosum, hyperkeratosis and parakeratosis may also be evident (Fig. 5-2-2).

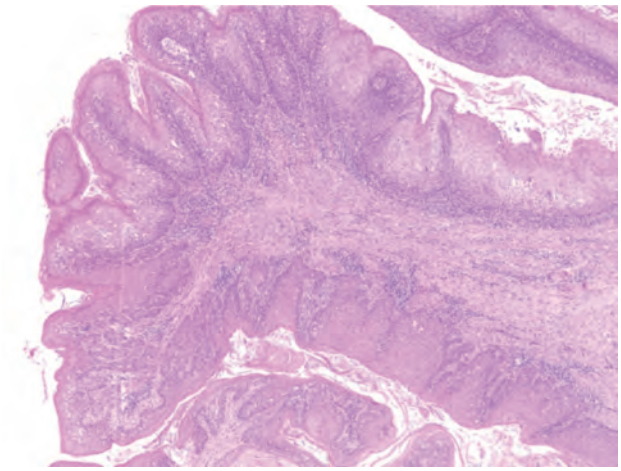


Fig. 5-2-2 Papilloma ( histopathological findings )

**Treatment**

The papilloma is resected, including the base. After resection, the cause of irritation is eliminated. Prognosis is good, but some tumors may become malignant, and adequate follow-up is therefore important.

**b. Fibroma and similar disorders**

**1. So-called fibroma**

**Overview**

So-called fibromas are tumorous lesions consisting of the proliferation of fibrous connective tissue in the oral mucosa and other soft tissues. Most represent inflammatory or reactive hyperplasia of fibrous tissue, and the majority of growths clinically regarded as fibromas are not actually tumorous lesions. Local, chronic mechanical irritation is believed to be involved, and those growths caused by ill-fitting dentures are known as denture fibromas. In rare cases, fibromas may also arise within the jawbone, but these are regarded as odontogenic tumors.

**Diagnosis**

Fibromas arise from the oral mucosal epithelium in areas such as the gingiva, buccal mucosa, palate, and lips. There is no spontaneous pain, tenderness, hemorrhage or other symptoms. They appear as flat, painless, slow-growing tumors with a surface similar in color to healthy mucosa. Fibromas occur in a wide variety of age groups, from young to elderly. They are broad-based tumors that are polypoid or pedunculated in shape(Fig. 5-2-3).

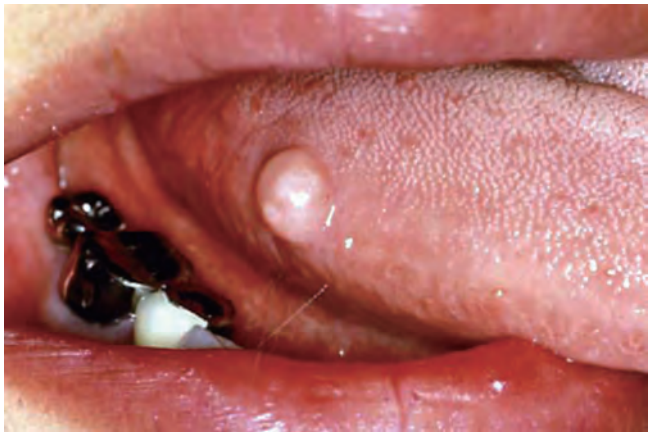


Fig. 5-2-3 Fibroma

Most fibromas arising from the lips or buccal mucosa are caused by chronic mechanical irritation from sources such as malocclusion or biting, ill-fitting tooth crown restorations or dental plate margins. Those growths caused by chronic mechanical irritation from ill-fitting dentures are known as “denture fibromas (Fig. 5-2-4).”

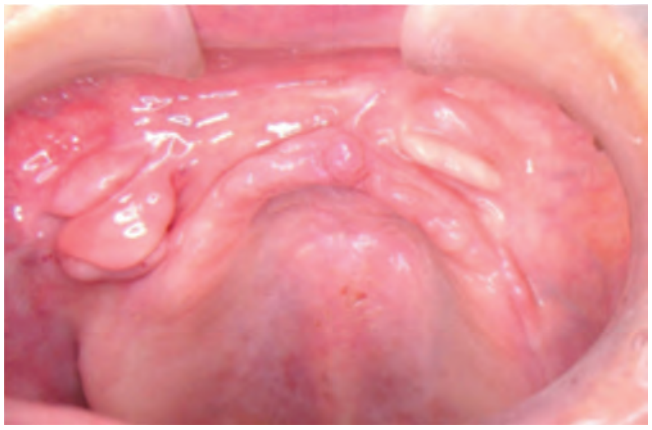


Fig. 5-2-4 Denture fibromas

Histologically, these tumors are covered by hypertophic stratified squamous epithelium, with collagen fibers and fibrous tissue growth associated with fibroblast proliferation beneath the epithelium (Fig. 5-2-5).

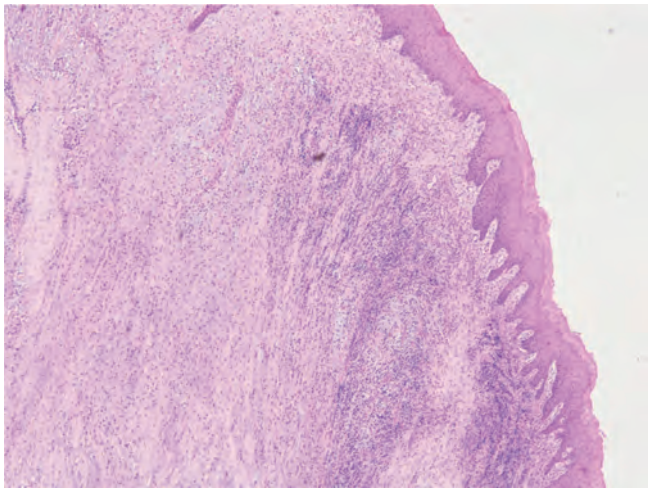


Fig. 5-2-5 Histopathological appearnce of fibroma

**Treatment**

If the cause is chronic irritation by dental plate margins or an ill-fitting restoration, eliminating the cause may result in the disappearance of the fibroma, but normally this tumor is surgically resected. Resection should include a little of the healthy portion of the tumor base. Recurrence is rare and prognosis is good, but it is important to remove ill-fitting prostheses or adjust dentures if these may have caused the problem in order to avoid chronic irritation.

**2. Gingival fibromatosis**

**Overview**

Gingival fibromatosis is a type of developmental abnormality of unknown origin that is mainly seen throughout the upper and lower jaws of young people as a result of diffuse gingival proliferation.

**Diagnosis**

In most cases, gingival swelling occurs in both sexes from the time that the permanent teeth erupt at around 7–9 years of age, on the palatal side in the upper jaw and the labial side in the lower jaw. The gingival surface is covered with normal mucosa, and the elastic-hard, painless tumors have a smooth, lobulated appearance.

The site of origin is the palatal-side gingiva in the upper jaw and the labial-side gingiva in the lower jaw. If the enlargement of the gingiva becomes severe, they also become harder and whiter in color, with most of the crowns of the teeth becoming buried in the gingiva.

Histologically, hypertrophy of the stratum spinosum with extension of the epithelial processes is present, with enlargement of poorly vascularized connective tissue containing densely tangled, thick collagen fibers beneath the epithelium.

**Treatment**

Gingival resection is performed. Prognosis is good, but recurrence is possible.

**c. Myxoma**

**Overview**

Myxomas are benign tumors formed by the proliferation of myxocyte-like cells. Myxoma is a comparatively rare tumor in the stomatognathic region, with an incidence of 3–5.1%. In most cases, it is in the central part of the jawbone, and is regarded as an odontogenic tumor(Fig. 5-2-6).

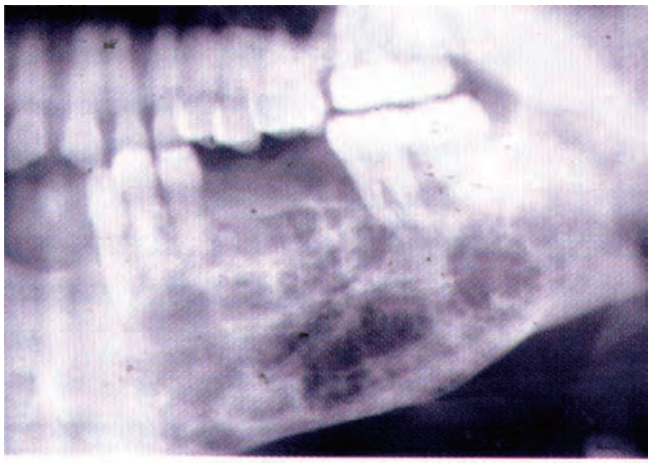


Fig. 5-2-6 Myxoma of the mandible

Myxoma arising from the soft tissues in the stomatognathic region is even more infrequent. Myxoma of the oral soft tissue is more common in males, and frequently occurs in the palate, parotid gland, cheeks, and on the floor of the mouth. Myxoma in soft tissues forms slow-growing tumors, with those that occur in the alveolar mucosa in particular appearing similar to epulis.

With respect to the derivation of myxoma, some regard it as a true tumor due to its structure being similar to fetal connective tissue and the presence of myxoblasts, while others believe it is formed by the differentiation of fibromas or myxoid degeneration.

**Diagnosis**

Myxomas arising from oral soft tissues appear as slow-growing, elastic-soft, painless tumors covered in normal mucosa, and are frequently found in the cheeks, the floor of the mouth, and the palate. The tumor parenchyma is semitransparent, glaucescent and solid, with the appearance of a mucus-rich jelly.

Differential diagnoses for myxomas of the oral soft tissues include epulis, fibroma, pleomorphic adenoma and neurofibroma.

Histopathologically, the main component resembles primitive mesenchymal tissue, with stellate or spindle-shaped cells scattered within a mucoid matrix. The tumors are surrounded by collagen fibers.

Condensed nuclei and stellate or spindle-shaped tumor cells with fine fibers are present singly within a mucoid matrix containing fine fibers. It is rare for only myxocytes to be present, and connective tissue is also usually evident.

Features to distinguish these tumors from odontogenic myxomas in the center of the jawbone include the absence of odontogenic epithelium, with no association with teeth, and no resemblance to dental papilla tissue.

**Treatment**

In principle, extraction is indicated. Prognosis is good.

Partial jawbone resection is indicated for odontogenic myxomas in the center of the jawbone, but recurrence is frequent.

**d. Lipoma**

**Overview**

Lipomas are non-epithelial benign tumors formed by the proliferation of mature adipose tissue. The incidence of lipomas in the oral region is low compared to that in other organs.

**Characteristics**

Lipomas tend to occur in the buccal mucosa, tongue and floor of the mouth. In addition to the skin of the neck, they also rarely occur within the jawbone. They are more common in adults aged over 40 years, with no gender differences. Clinically,

they cause painless swelling and the surface mucosa is normal. They appear as slow-growing, soft tumors with spheroidal elevations. These tumors are covered with a thin connective-tissue capsule that is yellowish in cross-section and soft(Fig. 5-2-7), but which turns white and hard as the amount of connective tissue increases.

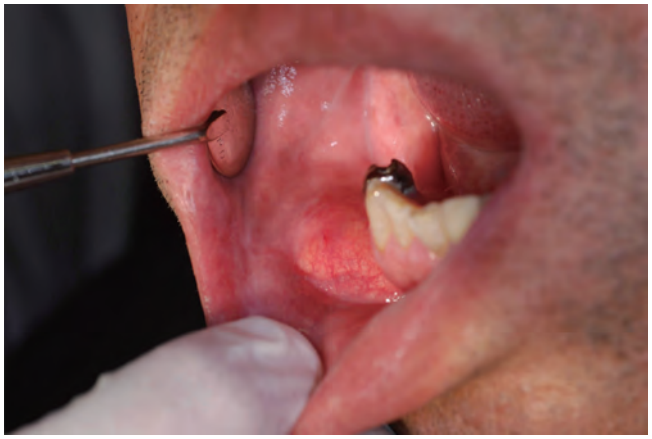


Fig. 5-2-7 Lipoma (buccal)

**Diagnosis**

Histopathologically, the proliferation of mature adipocytes produces a lobulated alveolar structure, with a thin connective tissue capsule in the surface layer. It contains adipocytes in varying stages of maturity. These include immature cells with large fat droplets resembling fat granules, but most are mature adipocytes (Fig. 5-2-8). The interstitium consists of small amounts of fibrous connective tissue and capillary vessels. If fibrous tissue proliferation is also present, they are known as fibrolipomas. It is also possible for adipose tissue to increase within fibrous polyps, producing a similar histological appearance. In rare cases, cartilage or bone metaplasia may be seen within a lipoma.

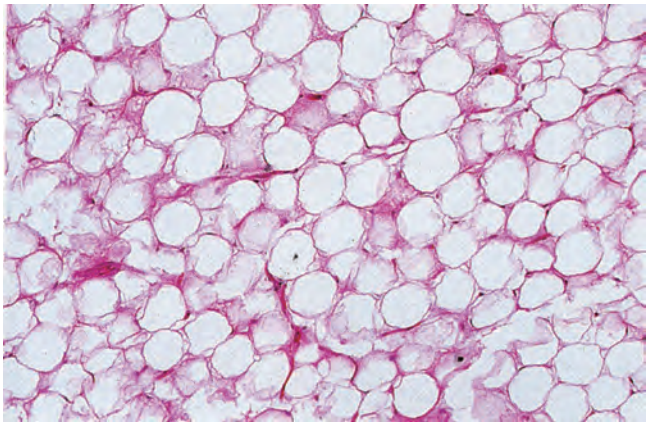


Fig. 5-2- 8 Lipoma ( histopathological findings )

**Treatment**

Tumorectomy is performed, and as the tumor is covered with connective tissue it can easily be enucleated from the surrounding tissue. Prognosis is comparatively good, generally with no recurrence.

**e Neurofibroma**

**1. Neurilemmoma (schwannoma)**

**Overview**

Neurilemmomas are benign tumors arising from the proliferation of Schwann cells derived from the Schwann sheath of peripheral nerves, and are comparatively rare in the oral region.

**Characteristics**

In the head and neck region, neurilemmoma occurs in the cheeks, cheekbones and infratemporal fossa. In the oral region, approximately half of cases occur in the tongue (Fig. 5-2-9), although it is also seen in the palate, buccal mucosa, floor of the mouth, lips, gingiva and salivary glands. This tumor usually arises in the submucosa, but is also rarely seen in the central part of the jawbone. It is most common in people in their 30s and 40s, with no gender differences. Clinically, it appears as a slow-growing, soft tumor with a localized spheroidal or sometimes lobulated elevation. Lesions within the jawbone are most common in the mandibular molar region, are visible on X-rays as resorption of alveolar bone, and may sometimes exhibit pain or nerve paralysis.

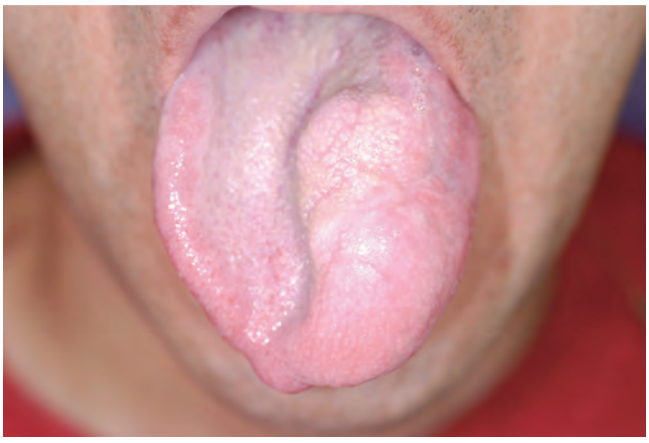
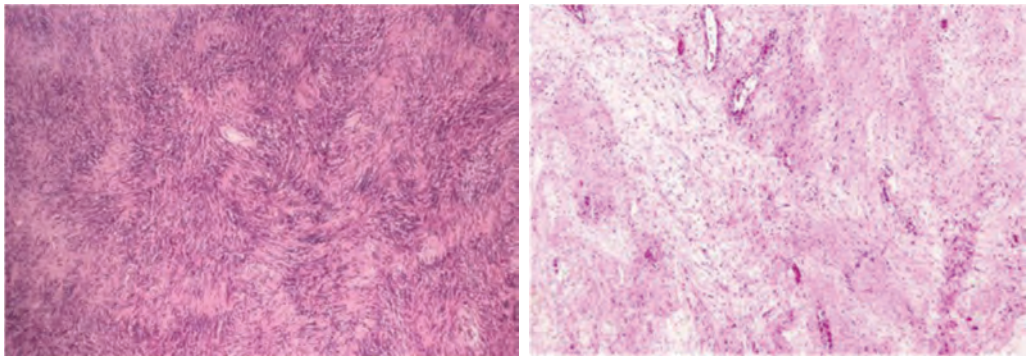


Fig. 5-2-9 Neurilemmoma in the tongue

**Diagnosis**

Histologically, neurilemmoma exhibits an extremely characteristic appearance, and its tissue types are categorized as the fascicular Antoni A pattern and the reticulate Antoni B pattern(Fig. 5-2-10). The Antoni A pattern type consists of bipolar spindle-shaped cells, with nuclei that exhibit a slightly flattened circular shape at both ends and which are arrayed in palisades or ranks, while the anuclear areas that stain pink are known as Verocay bodies. Cell fibers are present between the cells. In the Antoni B pattern, the tumor cells are arrayed more loosely, with widespread degenerative changes including large intercellular deposits of mucoid matrix, the appearance of foam cells, vitrification and hemorrhage. Immunohistochemically, they are positive for S-100 protein, as this protein is produced by peripheral nerve Schwann cells.



Antoni A　　Antoni B

Fig. 5-2-10. Histopathological appearance of neurofibroma

**Treatment**

Tumorectomy is performed, and as the tumor is covered it can easily be enucleated from the surrounding tissue. The prognosis is good, although cases of malignant transformation have been reported.

**2. Neurofibroma**

**2-1) Solitary neurofibroma**

**Overview**

Solitary neurofibromas are believed to be derived not only from Schwann cells but also to involve nerve sheath mesenchymal cells. They commonly arise in the skin and subcutaneously throughout the body, and their occurrence in the mouth is rare.

**Characteristics**

Solitary neurofibroma most often occurs in the tongue, but is also seen in the cheeks, palate, lips, gingiva, floor of the mouth and other sites. It is most common in people in their 30s and 40s, with no gender differences. Clinically, it appears as a slow-growing, soft tumor with a localized spheroidal or sometimes lobulated elevation, but its borders may be poorly demarcated from the surrounding tissue (Fig. 5-2-11).

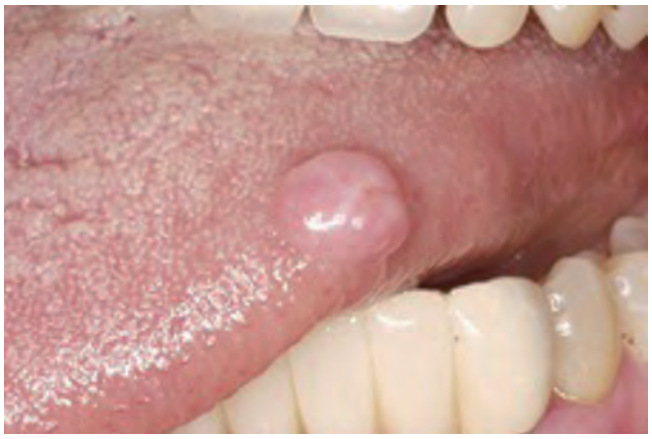


Fig. 5-2-11 Neurofibroma (toungue)

**Diagnosis**

Histologically, neurofibroma has no capsule and its borders are poorly demarcated from their surroundings. Tumor cells consist of Schwann cells with spindle-shaped or undulate nuclei with faint chromatin and spindle-shaped cell bodies, and fibrocytes, with cell fibers between the cells and small amounts of collagen fiber. Nerve fibers may be present within the tumor, and mast cells are sometimes seen in the interstitium. Tumor cell proliferation takes place within the nerve sheath, and tumors with a structure comprising nerve bundles with an irregular course that are surrounded by collagen fibers are known as plexiform neurofibromas.

**Treatment**

Tumorectomy is performed, and as the tumor is covered it can easily be enucleated from the surrounding tissue.

The prognosis is good.

### 2-2) Neurofibromatosis (von Recklinghausen disease)

**Overview**

The main symptoms of neurofibromatosis are multiple neurofibromas in the skin throughout the body, mouth, gastrointestinal tract, and bones, with café au lait spots on the skin (Fig. 5-2-12) and tumors of the central nervous system. It is a chronic, progressive, autosomal dominant disorder of unknown origin.

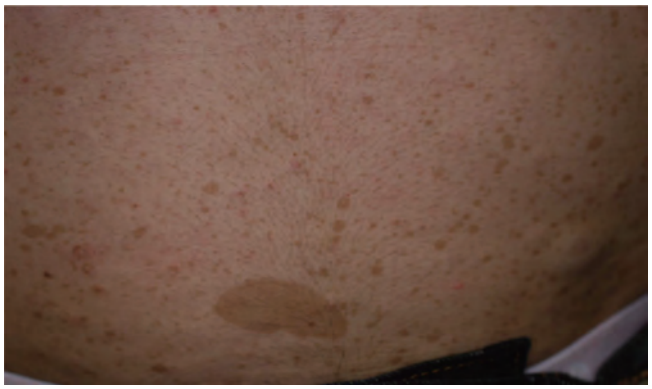


Fig. 5-2-12 von Recklinghausen disease (café aulait spot)

**Characteristics**

Tumors frequently occur on the tongue, and may also occur as solitary or multiple tumors in the gingiva, palate, lips and other areas.

It most commonly develops in early childhood, with no gender differences. Clinically, symptoms that appear in the oral region as part of this syndrome include the development of neurofibroma, and as this enlarges it may cause facial dysmorphia, tooth malalignment, impaired occlusion, macroglossia and other symptoms. Tumors that arise within the jawbone appear as radiolucent areas on X-rays.

**Diagnosis**

Histologically, proliferation of spindle-shaped cells with oval nuclei is evident within connective tissue, and these cells are arranged irregularly, sometimes with a structure similar to that of peripheral nerve neurites. The membrane is unclear.

**Treatment**

There is no curative method of treatment. Surgical resection is performed for functional and cosmetic reasons, but recurrence is extremely common among patients with this syndrome, and malignant transformation to neurofibrosarcoma may also occur.

### 3) Amputation neuroma

**Overview**

Amputation neuromas are not true tumors, but rather consist of the post-traumatic tumorous hyperregeneration of nerve fibers.

**Characteristics**

In the oral region, amputation neuroma frequently occurs in the area of the mental foramen. It commonly occurs after tooth extraction. Clinically, tumor size is approximately 1 cm, and neurogenic symptoms such as tenderness, neuralgia-like pain and paresthesia are evident.

**Diagnosis**

Histologically, amputation neuroma forms nodules from the proliferation of nerve fiber bundles and connective tissue.

**Treatment**

Tumorectomy is performed, but recurrence is very frequent.

### 4) Granular cell tumor

**Overview**

Granular cell tumors are formed by the proliferation of large polygonal or cylindrical cells with eosinophilic granular cytoplasm. They are regarded as neurogenic tumors.

**Characteristics**

Granular cell tumors occur singly in the adult oral mucosa, particularly on the tongue, and are more frequent in women. Clinically, they form elastic-hard, solid tumors that take the shape of bulges of the mucosal surface.

**Diagnosis**

Histologically, there are numerous large polygonal or circular cells with tiny eosinophilic granules in the cytoplasm, proliferating in an alveolar or cingulate configuration. The nuclei are comparatively small, and frequently have eccentrically located concentrated chromatin.

**Treatment**

Tumorectomy is performed. As adhesions to the surrounding tissues are frequent, great caution is required with respect to recurrence.

**f. Hemangioma and lymphoma**

**Hemangioma**

**Overview**

Hemangiomas are lesions in which the growth of vascular tissue is evident, but hamartomatous lesions, reactive vascular proliferation and vascular dilation are not uncommon. They are believed to occur when various types of vascular malformation arise due to some sort of influence on the process whereby primitive blood vessels undergo repeated changes including generation, regression and degeneration.

**Diagnostic signs**

Hemangiomas are benign tumors that are frequently seen in the oral region, and this is the most commonly encountered form of tumor in babies and infants. They may occur at any age, but as a congenital tissue abnormality they are often seen at birth or infancy. In soft tissues, they commonly occur in the tongue, lips and buccal mucosa, but may also be seen in other sites including the gingiva, floor of the mouth and palate(Fig. 5-2-13). They may also occur in the masseter or salivary glands, particularly the parotid gland, and may rarely arise in the jawbone.

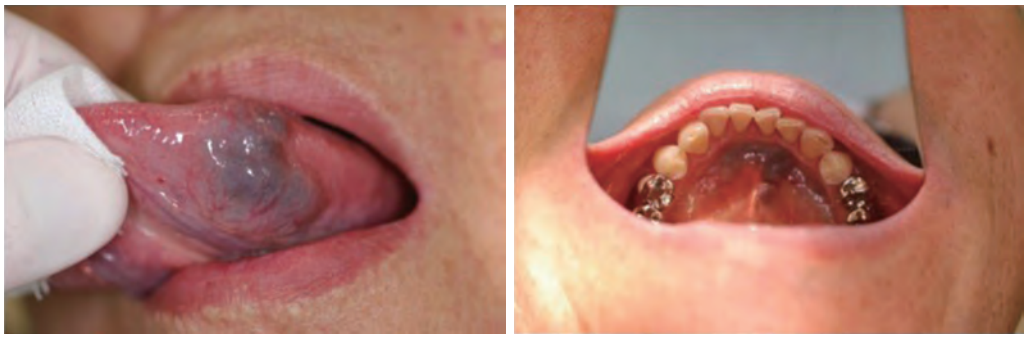


Fig. 5-2-13. Hemangioma (tongue, gingiva-floor of the mouth)

**Diagnosis**

Hemangiomas may be either true hemangiomas that exhibit tumorous proliferation or vascular malformations, which are regarded as a form of congenital dystrophy, and vascular malformations also include a wide range of lesions, from arteriovenous anomalies to capillary anomalies.

Currently, the 1996 International Society for the Study of Vascular Anomalies (ISSVA) classification is widely used.

In terms of diagnosis, lesions are broadly characterized into surface lesions and

deep lesions on the basis of visual examination, palpation and medical history, and non-invasive diagnostic imaging by MRI is most useful.

**1. Hemangioma**

**1) Infantile hemangioma (IH)**

IH appears from a few days to a few weeks after birth, enlarges rapidly from around 6 months to a year, and then spontaneously regresses over the following several years. It starts as a petechial or macular red lesion, and at its peak resembles a protruding strawberry, for which it is also known as strawberry hemangioma. It is a benign tumor formed by the proliferation of vascular endothelial cells in capillary vessels.

**Diagnosis**

MRI scanning shows moderate intensity on T1-weighted imaging and hyperintensity on T2-weighted imaging.

**Treatment**

The majority of cases regress spontaneously, so in principle, a “watch and wait” policy is adopted, but if spontaneous regression does not occur, then dye laser irradiation, oral steroid treatment or local injection and resection may be performed.

**2) Congenital hemangioma (CH)**

CH is a form of hemangioma that is present at birth. It includes rapid involuting congenital hemangioma (RICH), which rapidly contracts after birth, and non-involuting congenital hemangioma (NICH), which does not change in size.

**2. Vascular malformation**

**1) Capillary malformation (CM)**

CM, also known as hemangioma simplex or port-wine birthmark, exhibits a red appearance due to dilation of the dermal capillary vessels. It is present from birth, and although the color may change and or may come to protrude as the child grows, it does not regress spontaneously.

Multiple CMs in the region of the 1st and 2nd branches of the trigeminal nerve may be a sign of Sturge-Weber syndrome(Fig. 5-2-14).

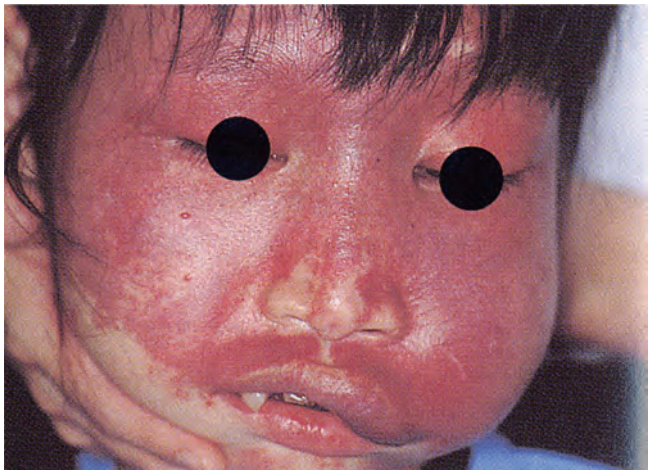


Fig. 5-2-14 Sturge-Weber Syndrome

**Diagnosis**

Contrast-enhanced CT reveals a pronounced contrast effect, while most CMs exhibit moderate intensity on both T1- and T2-weighted imaging.

**Treatment**

As this is a slow-flow vascular malformation in terms of blood flow, a range of treatments is available to avoid cosmetic and functional impairment as far as possible, with laser treatment currently the first choice.

**2) Venous malformation (VM)**

Also known as cavernous hemangioma, this forms a dilated venous lumen from the deep layers of the dermis to the subdermis, in some cases extending as deep as the muscles. The size of the cavity varies, but blood flow within the lesion is slow, and phleboliths are frequently present.

**Diagnosis**

MRI scanning shows moderate intensity on T1-weighted imaging and hyperintensity on T2-weighted imaging. CT can reveal the presence of phleboliths. Histopathologically, cavernous hemangioma consists of vascular proliferation with a markedly dilated vascular lumen, with clots in some of the dilated vessels.

**Treatment**

Conventionally, the basic treatment is removal. The important points for removing a hemangioma from the back of the tongue are: (1) to set the resection

line so that it includes a safe area of healthy tissue around the tumor; (2) to resect the tumor together with a layer of healthy tissue; (3) to be careful not to cut into the tumor when dissecting its borders; (4) to perform hemostasis of vessels entering and leaving the tumor by ligation or electrocoagulation; and (5) not to suture the muscle layer so as to avoid postoperative hemorrhage and dead-space formation, and instead using mattress sutures and single interrupted sutures for the wound edges. As these are slow-flow vascular malformations, sclerotherapy with sclerosing agents and cryosurgery have recently come into use.

**2) Arteriovenous malformation (AVM)**

Also known as racemose angioma, AVM occurs when arteries and veins communicate via an abnormal arteriovenous anastomosis or vascular plexus unmediated by capillary vessels. The absence of communication by capillary vessels means that blood flow through the lesion is fast, and the vein into which it flows is also dilated due to the increase in pressure.

**Diagnosis**

AVM is characterized by a signal void on both T1-weighted and T2-weighted MRI scans. Contrast-enhanced CT reveals a pronounced contrast effect, with comparatively thick arteries visualized within the tumor. Angiography is required for patients with suspected racemose angioma. Preoperative selective vascular embolization is also frequently used during treatment, and as the feeding vessel can be identified and the tumor shadow visualized, the extent of the tumor can be accurately assessed.

**Treatment**

As this tumor is a fast-flow vascular malformation, surgical resection is performed at the site, with complete resection carried out as far as possible. If partial resection is performed, this may exacerbate the severity of the lesion. For this reason, other than for extremely small tumors, ultra-selective arterial embolization and removal are performed and the healthy tissue surrounding the angioma is sutured, enveloping the entire angioma so that it becomes necrotic. Yttrium aluminum garnet (YAG) laser treatment may also be used. Hemorrhage during resection is reportedly controlled by embolization of the feeding artery.
Treatments other than surgery include embolization and embolization/sclerotherapy, and these are regarded as effective in unresectable cases.

**Lymphangioma**

**Overview**

Lymphangioma is believed to constitute congenital dysplasia of the lymph ducts, and although it is histologically benign, infiltration into the surrounding tissue frequently develops, and depending on the size of its site of origin, it is a disorder that may be as difficult to treat as hemangioma. It is formed by the growth of dilated lymph ducts in the dermis or subdermis, and contains lymphatic fluid.

Disease symptoms

There are two theories as to the cause of lymphangioma: that it occurs as a remnant of a primitive lymphatic cyst formed during the fetal period, or that it arises when part of a peripheral lymph duct becomes occluded. It is a comparatively common condition in the head and neck region, but is far less frequently encountered than hemangioma. In many cases it is present at birth, and there are believed to be no gender differences.

Lymphangioma most commonly occurs in the neck and lower jaw, followed by the back of the tongue, buccal mucosa, lips and floor of the mouth. If it is localized, it generally causes no subjective symptoms but if it is accompanied by inflammation or trauma it may cause disorders such as macroglossia, speech impairment, masticatory disturbance or malocclusion. It is present from birth and grows as the body develops. Superficial lymphangioma appears as a semitransparent, pale pink vesicular or granular protuberance(Fig. 5-2-15), while deep lymphangioma forms a poorly demarcated, soft mass.

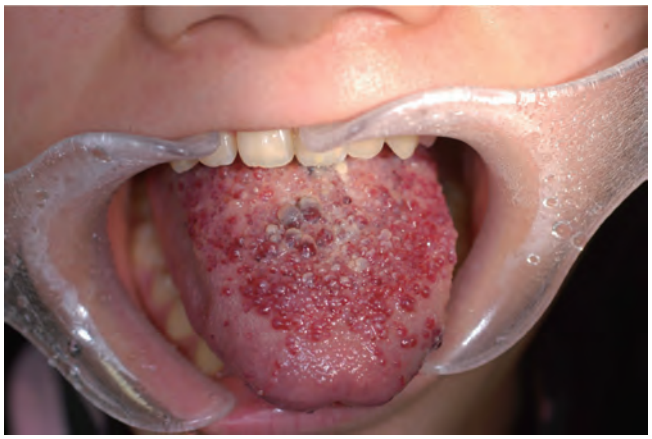


Fig. 5-2-15 Lymphangioma (tongue)

**Diagnostic method**

Superficial lymphangioma can frequently be diagnosed on the basis of clinical signs. Diagnostic imaging such as MRI, CT or ultrasound is required for the diagnosis of deep lymphangioma. On MRI, lymphangioma exhibits hyperintensity on both T1-weighted and T2-weighted imaging, and is not enhanced on Gd-DPa contrast-enhanced images.

**Treatment**

Conventionally, lymphangioma is removed, and if complete removal is feasible then the prognosis is good, but damage to nerves and surrounding healthy tissue as a result of surgery has frequently been reported, as has partial removal due to the poorly demarcated borders between the tumor and healthy tissue, with subsequent recurrence. Sclerotherapy with various sclerosing agents has been reported in recent years. Studies of the combined use of drug injection and surgical resection have found that injection with agents including OK-432, anhydrous ethanol, and bleomycin, is effective.

**g. Osteoma**

**Overview**

In general, osteomas are benign tumors formed by the proliferation of mature lamellar bone. The cause of this tumor is unknown, but it is generally believed to stem either from hyperostosis as a reaction to trauma or infection, or from developmental abnormalities. It may occur as central osteoma within the jawbone, or peripheral osteoma of the periosteum (Fig. 5-2-16, -17).

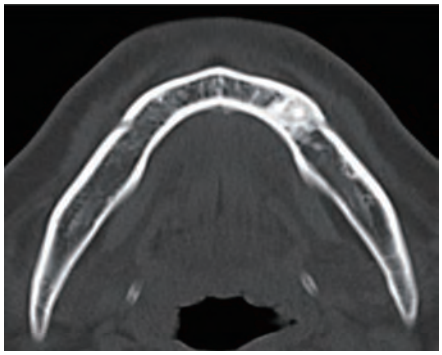


Fig. 5-2-16 Central osteoma (mandible) (CT findings)

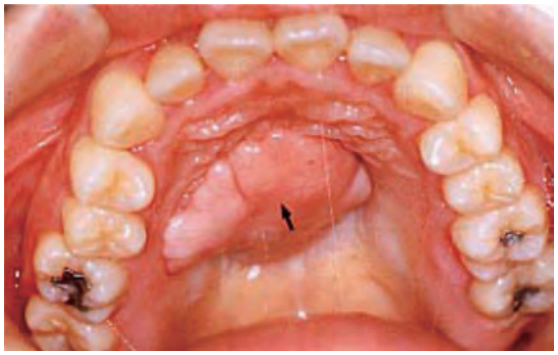


Fig. 5-2-17 Peripheral osteoma (hard palate)

**Disease symptoms**

Osteomas are slow-growing tumors. They are frequently asymptomatic and discovered by chance on X-ray images.

There are no gender differences, and osteoma is most commonly reported up to age 20 years. It most commonly occurs in the canine fossa, hard palate, maxillary sinus, mandibular angle and mentum. Multiple osteomas may be seen as a partial symptom of Gardner syndrome(Fig. 5-2-18).

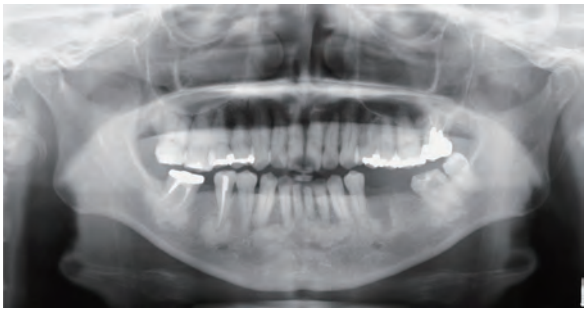


Fig. 5-2-18 Gardner syndrome (multiple osteomas)

**Diagnosis**

Central osteoma appears on X-ray images as a poorly demarcated, comparatively homogenous radioopaque tumor. Peripheral osteoma appears as a clearly demarcated, broad-based or pedunculated, painless, bony-hard tumor.

Histopathologically, in central osteoma the bony substance is compact, with little bone marrow formation. Proliferation of mature lamellar bone is evident in peripheral osteoma (Fig. 5-2-19, -20).

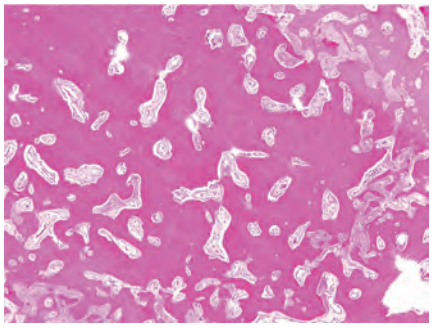


Fig. 5-2-19 Central osteoma
(histopathological findings )

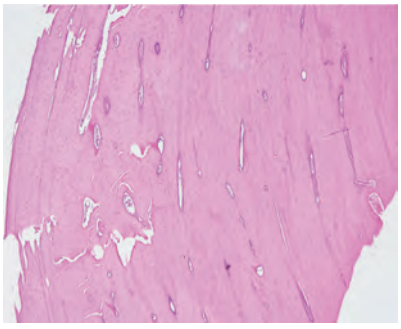


Fig. 5-2-20 Peripheral osteoma
(histopathological findings )

**Treatment**

Surgical resection or removal is performed, although the patient's condition may be monitored if surgery is not indicated.

(Yutaka Imai, Yutaka Doi)

## 5-3. *Odontogenic carcinoma*

Malignant odontogenic tumors are classified by the WHO as odontogenic carcinoma and odontogenic sarcoma. All of these tumors are exceedingly rare and many are still reportable cases. Table 1[1] shows WHO classification of malignant odontogenic tumors.

Table 1. Malignant tumors

| |
|---|
| **Odontogenic carcinomas** |
| Metastasizing (malignant) ameloblastoma |
| Ameloblastic carcinoma-primary type |
| Ameloblastic carcinoma-secondary type (dedifferentiated), intraosseous |
| Ameloblastic carcinoma-secondary type (dedifferentiated), peripheral |
| Primary intraosseous squamous cell carcinoma-solid type |
| Primary intraosseous squamous cell carcinoma derived from keratocystic odontogenic tumor |
| Primary intraosseous squamous cell carcinoma derived from odonto genic cysts |
| Clear cell odontogenic carcinoma |
| Ghost cell odontogenic carcinoma |
| **Odontogenic sarcomas** |
| Ameloblastic fibrosarcoma |
| Ameloblastic fibrodentino-and fiblo-odontosarcoma |

**a. Metastasizing (malignant) ameloblastoma**

Metastasizing ameloblastoma shows typically benign histological appearance, but has given rise to pulmonary or nodal metastases. Judging from some literatures which have already reported, it is considered that in 80% of cases the metastases were of a pure or mixed plexiform type and, histologically, did not differ significantly from conventional, nor metastasizing ameloblastoma[2]. It is therefore not possible to predict on the basis of morphology whether an ameloblastoma would metastasize.

**b. Ameloblastic carcinoma**

Ameloblastic carcinoma is a rare odontogenic malignancy that combines the histological features of ameloblastoma with cytological atypia, even in the absence of

metastases, and is classified into three entities in WHO classification of odontogenic carcinomas[3]: (1) ameloblastic carcinoma – primary type, (2) ameloblastic carcinoma - secondary type (dedifferentiated), intraosseous, and (3) ameloblastic carcinoma – secondary type (dedifferentiated), peripheral. Secondary ameloblastic carcinoma, either intraosseous or peripheral, arises in preexisting benign ameloblastoma. Metastasizing (malignant) ameloblastoma is differentiated from ameloblastic carcinoma by its benign histologic appearance, despite its ability to metastasize.

**Epidemiology**

The incidence of ameloblastic carcinoma is unknown, as fewer than 70 cases have been reported. According to Benlyazid's report,4)the median age of these patients was 44 years, however the tumor occurred in a wide age range of patients, with a sex ratio of 1.75 male to 1 female. The mandible is involved more frequently than the maxilla (ratio 2.14:1), and most cases involved the posterior portion of the jaw.

**Clinical features**

The most common signs and symptoms are swelling with rapid growth, perforation of the cortex of jaw, pain, and paresthesia. Radiographically, ameloblastic carcinoma is seen as cup-shaped radiolucent lesion or as a unilocular radiolucency with ill-defined ragged borders.

**Histopathology**

Ameloblastic carcinoma is characterized by malignant cytologic features in combination with the overall histological pattern of an ameloblastoma. In other words, all variants of ameloblastic carcinoma are histologically characterized by tall columnar cellular morphology and pleomorphism, mitotic activity, focal necrosis, perineural invasion and nuclear hyperchromatism may be present.

**Behavior and management**

Optimal treatment of ameloblastic carcinoma is unknown, but radical surgical resection appears to be the treatment of choice, as most investigators have concluded. There is no evidence about the efficacy about adjuvant chemotherapy and irradiation. Local recurrence or distal metastasis cases have been reported[4, 5]. Therefore, long-term follow-up after surgery is mandatory to detect the recurrence and metastasis.

**c. Primary intraosseous squamous cell carcinoma**

Primary intraosseous squamous cell carcinoma (PIOSCC) is a rare form of squamous cell carcinoma, arising within the jawbones; it has no initial connection with the oral mucosa and develops from remnants of odontogenic epithelium.

According to the 2005 WHO classification of Tumors[1], there are three subcategories of primary intraosseous squamous cell carcinomas: (1) solid tumor that invades marrow spaces and induces osseous resorption (de novo), (2) those arising from the lining of an odontogenic cyst, making a subdivision in carcinomas arising in a keratocystic odontogenic tumor and carcinoma arising in other odontogenic cysts, and (3) those in association with other benign epithelial odontogenic tumors. In this classification, ameloblastic carcinoma is separated from primary intra osseous carcinoma (PIOC), and then PIOSCC is used instead of PIOC to avoid taxonomic problems.

**Epidemiology**

The male –to-female ratio is about 2:1, and the mean age of the patients is about 60 years (range 1.3-90 years)[6]. The common sites of PIOSCC are the same as for non-malignant cysts, most commonly the mandibular third molar, maxillary canine and third molar and mandibular second premolar regions. Bodner et al[6] reported the mandible was involved in 92 cases (79%) and maxilla in 24 cases (21%) from the analysis of 116 cases reported in the literature

**Clinical features**

The presenting symptoms are commonly jaw swelling and pain in the site of lesions. Sometimes paresthesia or decreased sensation may be present, which is a suspicious sign suggesting malignancy.

Radiographic examination is one of the most effective methods to detect PIOSCC. Radiographic feature of PIOSCC reveals a radiolucent lesion and an indistinct margin without sclerotic outline. In lager cases, the CT findings show expansion and destruction of the cortical bone of jaws. However, PIOSCCs show great variation in size and shape and in the appearance of their borders.

**Histopathology**

PIOSCC is typically a well-differentiated squamous cell carcinoma that may or may not be keratinizing. According to the type, there may be microscopic evidence of an origin in a cyst or tumor.

**Behavior and management**

The prognosis of PIOSCC is generally poor, although well-differentiated squamous cell carcinoma is reported to have a better prognosis[7]. Cervical lymph node metastasis is a significant prognostic factor affecting both recurrence and survival. The rate of lymph node metastasis was higher in the de novo group.

Surgery is the optimal form of treatment. Especially, radical surgery with radiotherapy and /or chemotherapy has been advised[8].However, adjuvant chemoradiotherapy protocols have not yet been established.

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(Yoshiya Ueyama)

## *5-4. Non-odontgenic malignant tumor*

**a. Squamous cell carcinoma**

Squamous cell carcinomas (SCC) of the oral cavity are cancers that arise from the superficial tissues of the mouth. These tissues include the lip, tongue, floor of mouth, hard palate, cheek mucosa and alveolus (gums) (Fig. 5-4-1). There are several types of oral cancers, but around 90% are SCC. Men are affected twice as often as women. The incidence of SCC increases with age; most cases occur after 40 years of age.

Tobacco smoking and alcohol use are the principal risk factors for developing oral cavity SCC. Human papillomavirus 16, periodontal disease, poor oral hygiene, ill- fitting dentures and other rough surfaces on the teeth, radiation and immune deficiency are also risk factors. Patients after hematopoietic stem cell transplantation (HSCT) are at a higher risk for oral SCC. Post-HSCT oral cancer may have more aggressive behavior with poorer prognosis, when compared to oral cancer on non-HSCT patients. This effect is supposed to be due to the continuous lifelong immune suppression and chronic oral graft-versus-host disease[1)].

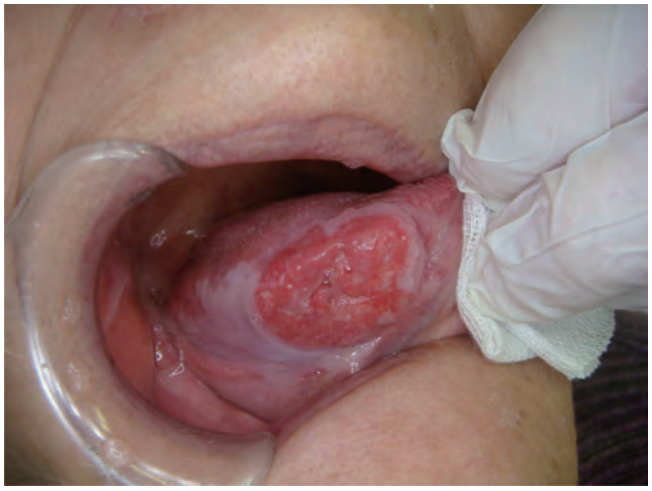

Fig. 5-4-1 Exophytic oral carcinoma arising from the tongue

**Clinical features**

Symptoms of oral cavity cancer include discolored patches, an ulcer or sore that will not heal, bleeding, loose teeth, difficulty in wearing dentures, pain when swallowing, a lump in the neck and paresthesia of lower lip and chin[2)].

**Diagnosis**

SCC is diagnosed by histopathologically examining a representative biopsy of the neoplastic tissue. Common to all lesions is the presence of invasion into the underlying connective tissue and the inherent potential of malignant cells to erode the lymphatic and blood vessel walls. Tumors that produce significant amounts of keratin and exhibit some features of maturation from basal cells to keratin are considered as well differentiated (Fig. 5-4-2). Tumors that produce little or no keratin but in which the epithelium still is recognizable as stratified squamous, despite its significant deviation from normal, are regarded as moderately differentiated. Tumors that produce no keratin, bear little resemblance to stratified squamous epithelium, exhibit a significant lack of normal architectural pattern and cohesiveness of cells, and exhibit extensive cellular abnormalities are designated as poorly differentiated[3].

TNM classification and clinical staging of carcinoma patients is used to designate the extent of disease in patients and to match it with what has been determined to be the most appropriate treatment for patients with comparable staging. The diagnostic examinations such as computed tomography (CT) (Fig. 5-4-3), magnetic resonance imaging (MRI) and positron emission tomography (PET) can result in assignment of a higher clinical stage.

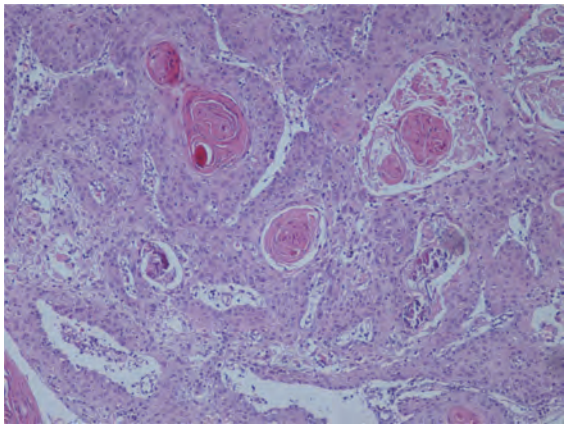

Fig. 5-4-2
Photomicrograph of a keratin pearl that is characteristic of SCC (hematoxylin-eosin stain, original magnification ×100)

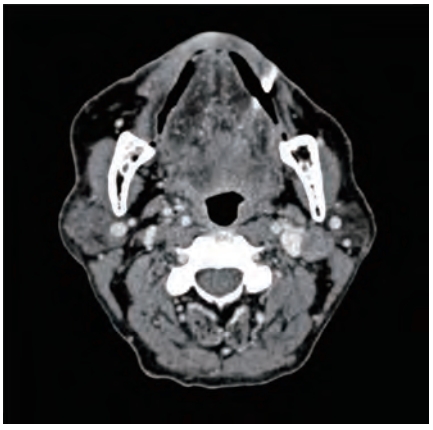

Fig. 5-4-3
Enhanced axial computed tomographic scan of the neck shows lymph node metastasis (arrow)

**TNM definitions**

T: Primary tumor

TX: Primary tumor cannot be assessed

T0: No evidence of primary tumor

Tis: Carcinoma in situ

T1: Greatest diameter < 2cm

T2: Greatest diameter > 2cm but < 4cm

T3: Greatest diameter > 4cm

T4a: Tumor invades through critical bone, into deep muscle of tongue, maxilary sinus, or skin of face

T4b: Tumor invades masticator space, pterygoid plates, or skull base and/or encases internal carotid artery

N: Regional lymph nodes

NX: Regional lymph nodes cannot be assessed

N0: No regional lymph node metastasis

N1: Metastasis in a single ipsilateral lymph node, 3cm or less in greatest dimension

N2a: Metastasis in a single ipsilateral lymph node, more than 3cm but not more than 6cm in greatest dimension

N2b: Metastasis in multiple ipsilateral lymph nodes, none more than 6cm in greatest dimension

N2c: Metastasis in bilateral or contralateral lymph nodes, none more than 6cm in greatest dimension

N3: Metastasiss in a lymph node more than 6cm in greatest dimension

M: Distant metastasis

MX: Distant metastasis cannot be assessed

M0: No distant metastasis

M1: Distant metastasis present

**Staging of oral cancer**

Stage 0: Tis, N0, M0

Stage I: T1, N0, M0

Stage Ⅱ: T2, N0, M0

Stage Ⅲ: T3, N0, M0, or T1-3, N1, M0

Stage ⅣA: T4a, N0-1, M0, or T1-4a, N2, M0

ⅣB: T4b, any N, M0, or Any T, N3, M0

ⅣC: Any T, any N, M1

**Treatment and prognosis**

Treatment for oral cavity SCC usually depends on the extent, or stage, of the disease. SCC of stage I and II are small tumors that have not spread beyond the adjacent tissue. In general, treatment options are either surgery or radiation therapy

(RT). Surgery is the preferred approach because it is associated with less toxicity, both in the immediate post-treatment time period and over the long term.

SCC of stage III and IV represents either big tumors or indicates that cancer has spread outside the local tissue, either to lymph nodes or other distant tissues. Again, whenever possible, surgery is the preferred method of treatment. Surgical resection may require large areas of the oral cavity and adjacent structures to be removed, sometimes requiring reconstruction.

1) Treatment for the neck
   1. Radical neck dissection (RND): No structures are preserved.
   2. Modified RND: The accessory nerve and/or internal jugular vein and/or sternocleidomastoid muscle are preserved.
   3. Supraomohyoid neck dissection: Nodes are removed from level I to III.

In a clinically negative neck, supraomohyoid neck dissection is adequate. In a clinically positive neck, RND or modified RND is advised. If the cancer involves the multiple lymph nodes or there is an extranodal invasion of the cancer, postoperative RT is generally recommended.

For the patients with advanced SCC who are not candidates for surgery, due to the extent of their disease or their overall medical condition, chemotherapy, RT, or a combination of both may be recommended. However, this type of treatment is associated with significant side effects, including inflammation, ulcer formation, and even necrosis of the oral tissue and adjacent bone.

Survival rate for stage I disease are approximately 90% at five years, hence the emphasis on early detection to increase survival outcome for patients. Survival rate for stage IV disease is 30-40% and the prognosis of advanced disease is very poor[2].

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(Yoshiya Ueyama)

**b. Kaposi's sarcoma**

Kaposi's sarcoma (KS) is a tumor caused by human herpes virus 8 (HHV8), also known as Kaposi's sarcoma-associated herpes virus (KSHV). It was originally described by Moritz Kaposi in 1872. It became more widely known as one of the AIDS defining illnesses in the 1980s.

**Clinical features**

Kaposi's sarcoma lesions are nodules or blotches that may be red, purple, brown, or black, and are usually popular. They are typically found on the skin. The mouth, gastrointestinal tract and respiratory tract are also commonly affected. Growth can range from very slow to extremely fast, and is associated with significant mortality and morbidity.

(1) Skin: Skin lesions commonly involve the lower limbs, face, mouth and genitalia. They may be involved in skin breakdown with resulting fungating lesions. Associated swelling may be from either local inflammation or lymphoedema. Skin lesions may be quite disfiguring for the sufferer, and a cause of much psychosocial pathology.

(2) Mouth: Intraoral Kaposi's sarcoma lesion with an overlying candidiasis infection is involved in about 30%, and is the initial site in 15% of AIDS related Kaposi's sarcoma. In the mouth, the hard palate is most frequently affected, followed by the gingiva. Lesions in the mouth may interfere with eating or speaking.

(3) Gastrointestinal tract: Involvement can be common in those with transplant related or AIDS related Kaposi's sarcoma, and it may occur in the absence of skin involvement. The gastrointestinal lesions may be silent or cause weight loss, pain, nausea/vomiting, diarrhea, bleeding, malabsorption, or intestinal obstruction.

(4) Respiratory tract: Involvement of the airway can present with shortness of breath, fever, cough, hemoptysis, or chest pain, or as an incidental finding on chest x-ray. The diagnosis is usually confirmed by bronchoscopy when the lesions are directly seen, and often biopsied.

**Pathology**

Kaposi's sarcoma lesions contain tumor cells with a characteristic abnormal elongated shape (spindle cells). The tumor is highly vascular, containing abnormally dense and irregular blood vessels, which leak red blood cells into the surrounding tissue and give the tumor its dark color. KSHV proteins are uniformly detected in Kaposi's sarcoma cancer cells.

**Diagnosis**

Although Kaposi's sarcoma may be suspected from the appearance of lesions and the patient's risk factors, a definite diagnosis can only be made by biopsy and pathological examination. Detection of the KSHV protein LANA in tumor cells confirms the diagnosis.

**Treatment**

Kaposi's sarcoma is not curable, but it can often be effectively palliated for many years. Patients with a few local lesions can be treated with radiation therapy or cryosurgery. Surgery is generally not recommended as Kaposi's sarcoma can appear in wound edges. Wide spread disease, or disease affecting internal organs, is generally treated with systemic therapy with interferon alpha, liposomal anthracyclines (such as Doxil) or paclitaxel.

In Kaposi's sarcoma associated with immunodeficiency or immunosuppression, treating the cause of the immune system dysfunction can slow or stop the progression of the tumor. In 40% or more of patients with AIDS-associated Kaposi's sarcoma, the Kaposi lesions will shrink upon first starting highly active antiretroviral therapy (HAART). However, in a certain percentage of such patients, Kaposi's sarcoma may again grow after a number of years on HAART, especially if HIV is not completely suppressed.

(Chuan-bin Guo)

**c. Fibrosarcoma**

Fibrosarcoma is a tumor of mesenchymal cell origin that is composed of malignant fibroblasts in a collagen background. It can occur as a soft-tissue mass or as a primary or secondary bone tumor. Fibrosarcoma was diagnosed much more frequently in the past; it is now more reliably distinguished histologically from similar lesions, such as desmoid tumors, malignant fibrous histiocytoma, malignant schwannoma, and high-grade osteosarcoma.

Radiotherapy to the local site is known to increase the risk of fibrosarcoma development but there are no other known etiologic factors. On the perioral skin, occasional cases develop at the site of thermal damage or of a pre-existing scar.

**Clinical Features**

Fibrosarcoma is rare in the oral and oropharyngeal region, but it is the most common mesenchymal cancer of the region, representing more than half of all sarcomas. Twenty-three percent of head and neck fibrosarcomas occur within the oral cavity and any submucosal site may be involved, although the buccal mucosa and tongue account for three-fourths of oral lesions. It usually affects patients of 30-50 years of age, but there is a wide age range and many patients are less than 20 years old. There is no apparent gender predilection.

Fibrosarcoma most often presents as a lobulated, sessile, painless and nonhemorrhagic submucosal mass of normal coloration. It may, however, be a rapidly enlarging, hemorrhagic mass similar in clinical appearance to an ulcerated pyogenic granuloma or peripheral giant cell granuloma. Even lesions which do not demonstrate surface ulceration or rapid growth may show destruction of underlying muscle and bone.

Fibrosarcoma seldom metastasizes except late in its clinical course, but when this does occur the metastatic deposits are usually blood-borne and carried to distant sites, especially the lungs, liver and bones.

**Pathology**

Fibrosarcomas vary in histologic grade. Well-differentiated forms have multiple plump fibroblasts with deeply staining nuclei in a rich collagen background. Intermediate-grade tumors have the typical herringbone pattern, showing the diagnostic parallel sheets of cells arranged in intertwining whorls. A slight degree of cellular pleomorphism exists. High-grade lesions are very cellular, with marked cellular atypia and mitotic activity. The matrix is sparse. No malignant osteoid formation should be present. Higher grades are extremely anaplastic and pleomorphic, with bizarre nuclei that bring to mind the histologic features of malignant fibrous histiocytoma.

**Diagnosis and differential diagnosis**

Diagnosis of fibrosarcoma is usually based on its clinical features and biopsy results. CT, MRI, and bone scanning using technetium-99m are useful in the evaluation of tumor size, location, and stage.

Fibrosarcoma of the oral region must be differentiated from a variety of other malignant tumors and benign spindle cell proliferations. They include malignant fibrous histiocytoma, malignant peripheral nerve sheath tumor (malignant schwannoma), dermatofibrosarcoma protuberans, leiomyosarcoma, and certain

carcinomas such as desmoplastic (sarcomatoid) melanoma, spindle cell (sarcomatoid) carcinoma and myoepithelial carcinoma.

**Treatment and prognosis**

Well-differentiated fibrosarcoma is treated by wide local excision, while more poorly differentiated tumors require more radical surgery, including removal of potentially invaded muscle and bone. Adjunctive therapy, such as radiation treatment and chemotherapy, can improve local control and may make the appearance of clinically evident metastatic disease less likely. The use of chemotherapy is controversial, but chemotherapy is generally used in bone lesions. Radiation therapy is used in conjunction with surgery for soft-tissue fibrosarcomas, with or without chemotherapy.

The five-year survival rate for this disease is poor, ranging from 20 to 35%.

(Chuan-bin Guo)

**d. Osteosarcoma**

Osteosarcoma is a malignant tumor that arises from bone itself. It tends to affect regions around the knee in 60% of cases, 15% around the hip, 10% at the shoulder, and only 8% in the jaw. There are numerous theories regarding the causes of osteosarcoma. Many cases occur during a time of rapid bone growth, as in teenagers or people with Paget's disease. This suggests that the cancer may develop when the body loses its ability to control the multiplication of certain bone cells. Some cases of osteosarcoma are likely to have a genetic basis, and numerous genetic abnormalities have been found in patients with osteosarcoma. Osteosarcoma is also the most common second cancer to develop in survivors of retinoblastoma, a cancer of the eye that often has a genetic cause. Other cases arise in people who have been exposed to radiation, either accidentally or as part of a medical treatment.

**Clinical features**

Osteosarcoma occurs most frequently during childhood or adolescence. About 60% of cases of this disease develop during the second decade of life. The incidence of osteosarcoma rises again among people in their 40s and 50s. Osteosarcoma in the jaw generally occurs 10-20 years later than in the long bone. Males may be more easily affected than females. It arises more often in the

mandible than the maxilla.

Osteosarcoma starts growing within a bone and forms an expanding, ball-like mass (Fig. 5-4-4). The most common early symptoms of osteosarcoma are often vague. There may be pain or swelling at the site of the tumor. The tumor eventually breaks through the surface of the bone and begins to invade adjoining structures such as muscles, causing deformity of the face and teeth shifting. If untreated, the disease usually metastasizes to distant parts of the body, such as the lungs.

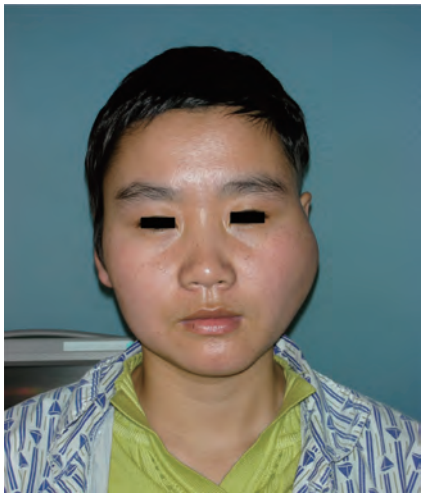

Fig. 5-4-4
Osteosarcoma presents as an expanding, ball-like mass

**Pathology**

The characteristic feature of osteosarcoma is presence of osteoid within the tumour. Tumor cells are very pleomorphic with numerous atypical mitoses. These cells produce osteoid describing irregular trabeculae with or without central calcification - tumor bone. Tumor cells are included in the osteoid matrix. Depending on the features of the tumour cells, the tumour can be classified as low grade, intermediate, or high grade. If the tumor has few dividing cells, it is a low-grade osteosarcoma. If the tumor has many dividing cells, it is a high-grade osteosarcoma. A high-grade osteosarcoma also has a lot of dead cells in the tumor. This usually means the cancer is growing so fast it outgrows its source of nutrition (Fig. 5-4-5A,B).

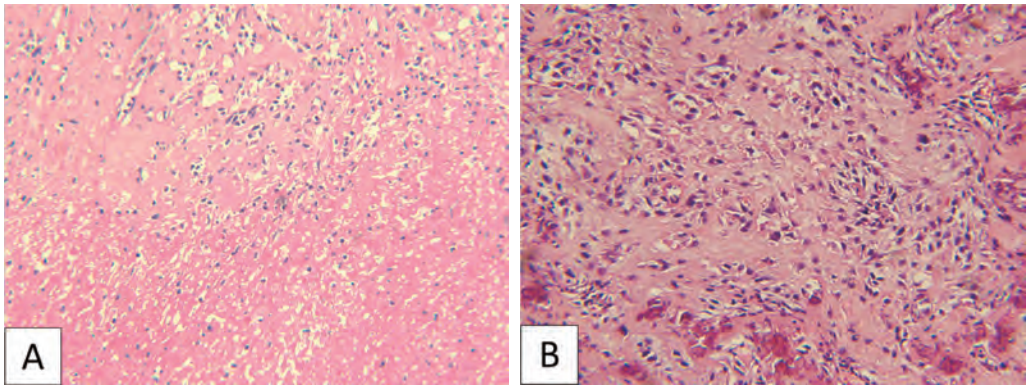


Fig. 5-4-5 Pathological features of low-grade osteosarcoma.
(A) Osteoid exhibits irregular trabeculae with or without central calcification and tumor cells are included in the osteoid matrix (H&E, x100).
(B) Pleomorphic tumor cells with numerous atypical mitoses (H&E, x200).

**Diagnosis**

Initial diagnosis begins with x-ray images of the affected area. These pictures will show a destructive growth within the bone, which is often described as having a "moth-eaten appearance" (Fig. 5-4-6). The patient then requires further imaging tests such as computed tomography or magnetic resonance scans of the tumor, a chest x-ray series or chest CT, and a nuclear medicine scan of the entire skeleton (bone scan). Blood tests, such as measurements of alkaline phosphatase provide additional information. These tests all help determine the stage of the cancer. Final diagnosis requires a biopsy.

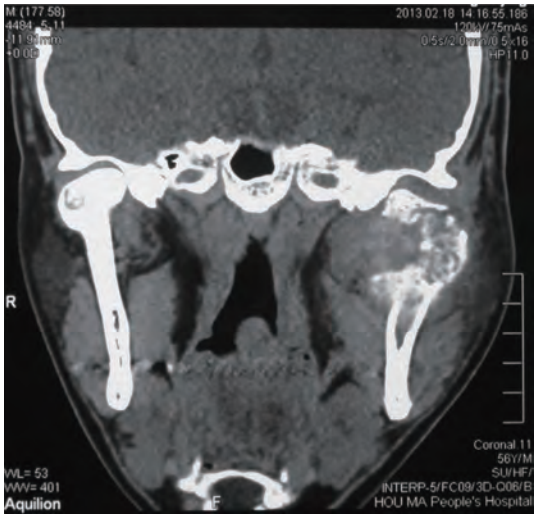


Fig. 5-4-6
CT shows moth-eaten appearance of osteosarcoma

**Treatment**

Current standard treatment is to use neoadjuvant chemotherapy (a combination of high dose methotrexate with leucovorin rescue, intra-arterial cisplatin, adriamycin, ifosfamide with mesna, BCD, etc.) followed by surgical resection. The percentage of tumor cell necrosis seen in the tumor after surgery gives an idea of the prognosis and suggestions for modification of the chemotherapy regime.

**Prognosis**

Osteosarcoma in the jaw has better prognosis. Its five year survival rate is about 40%. The main death cause is uncontrollable local recurrence.

(Chuan-bin Guo)

**e. Malignant melanoma**

Malignant melanoma is defined simply as a malignant neoplasm of melanocytes. Mucosal malignant melanomas of the oral cavity represent less than 1% of the total melanomas of the body. Melanomas of the oral cavity arise between 20 and 80 years, with an average age of about 55 years. There is a male predominance with a ratio of 3:1. The palate and maxillary gingiva are the most prevalent sites of oral melanomas, accounting for about 80%. Oral melanomas typically reveal multiple or widespread macular pigmentation with areas of nodular growth (Fig. 5-4-7) Ulceration is occasionally seen. There is a rare variant of amelanotic melanoma, which reveals a nodular lesion covered by a non-pigmented mucosa (Fig. 5-4-8).

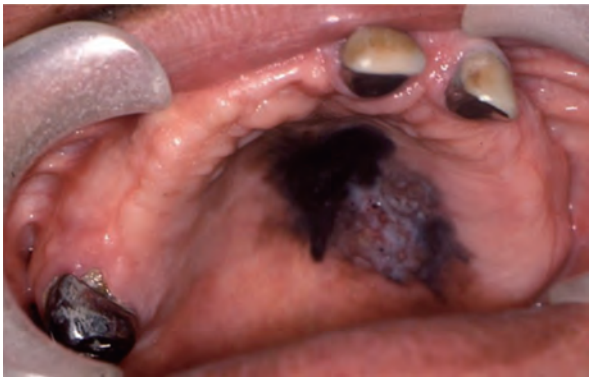

Fig. 5-4-7
Malignant melanoma in a 67-year-old man. Widespread macular pigmentation with a nodular lesion is observed in the palatal mucosa.

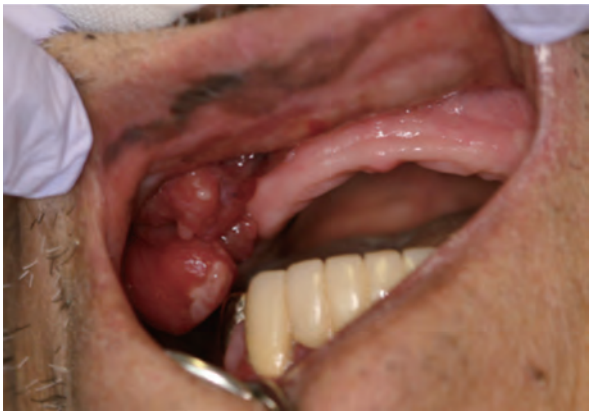

Fig. 5-4-8
Amelanotic melanoma of the upper alveolus in a 73-year-old man. A fungating nodular lesion without black pigmentation is observed in the vestibule of the posterior maxilla

Histologcally, oral melanomas are similar to acral letiginous melanoma of the skin. They are classified as in-situ oral mucosal melanoma, invasive oral mucosal melanoma and mixed lesions. Melanoma cells show sheets or islands of epithelioid cells containing melanin pigments (Fig. 5-4-9). Occasionally lesions may be composed of sheets or fascicles of spindle cells (Fig. 5-4-10, -11A). Melanins can be identified by Masson-Fontana stain (Fig. 5-4-11B). Immunohistochemical markers include S100, HMB45, Melan-A and anti-tyrosinase (Fig. 5-4-11C, D).

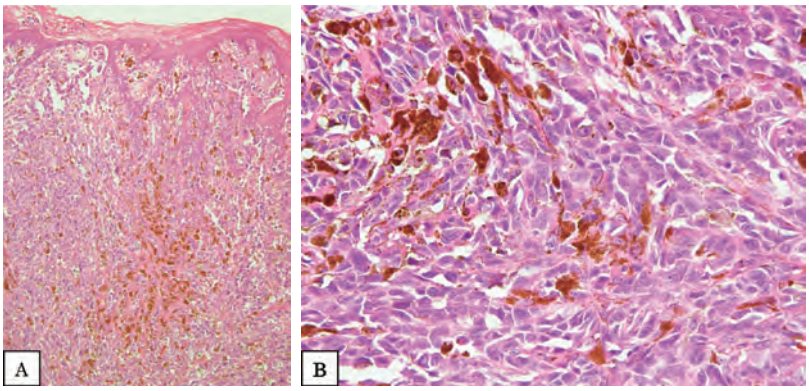


Fig. 5-4-9
A. Melanoma cells show junctional activity in the epithelial-connective tissue interface, and proliferate in the subepithelial connective tissue.
B. The lesion consists of sheets of epithelioid cells containing melanin granules Hematoxylin-eosin stain. Please include magnification

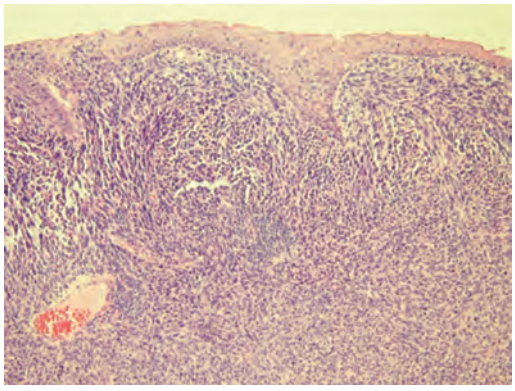

Fig. 5-4-10
The lesion is composed of fascicles or sheets of spindle melanoma cells in the subepithelial tissue. Hematoxylin-eosin stain.

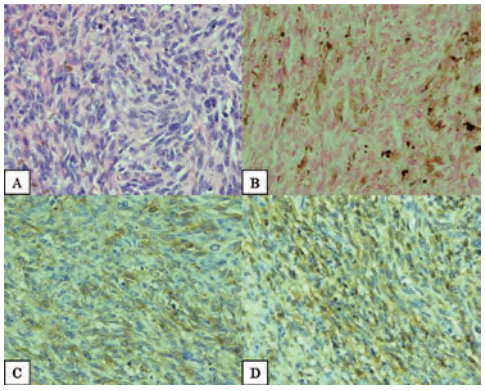


Fig. 5-4-11
Melanoma cells show spindle shape with an interlacing arrangement (A, Hematoxylin-eosin stain).
Melanin is demonstrated by Masson-Fontana stain (B). Immunohistochemical stains show positivity of melanoma cells against HMB45 (C) and S100 (D).

The treatment is to attempt complete excision of the primary tumors, followed by postoperative radiotherapy for residual disease or nodal involvement. However, these tumors are unresponsive to conventional radiotherapy. Newer methods, such as hypofractionation and neutron beam therapy, may play an adjunctive role. Chemotherapy using dacarbazine alone or in combination with other agents is often carried out, though it has not affected survival outcome. The reported prognosis of oral melanoma is quiet poor. Rapini et al reported a 5-year survival of only 13%. Local recurrence and subsequent distant metastasis are the most common causes of failure.

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(Kenji Kawano)

**f. Wegener's Granulomatosis**

Wegener's Granulomatosis (WG) is an uncommon disease. There is no known cause of WG. It is systemic, affecting the upper (sinuses and nose), and lower (lungs), respiratory system and frequently involves the kidneys, lungs, eyes, ears, throat, skin and other body organs. Symptoms are due to inflammation that can affect many tissues in the body, including blood vessels (vasculitis).

**Clinical features**

WG can occur at any age. It most often occurs in the 4th and 5th decade of life. Patients are divided equally between males and females. It appears that Caucasians are far more commonly affected than other racial groups.

Onset of WG may be indolent or rapid and severe. About 90% of patients have symptoms of a cold or runny nose or sinusitis that fail to respond to the usual

therapeutic measures and last considerably longer than the usual upper respiratory tract infection. Other symptoms include nasal membrane ulcerations and crusting, saddle-nose deformity, inflammation of the ear with hearing problems, inflammation of the eye with sight problems, cough (with or without the presence of blood), pleuritis, rash and/or skin sores, fever, lack of energy, weakness, fatigue, loss of appetite, weight loss, arthritic joint pain, night sweats, and blood in urine which may or may not be indicated by a change in urine color.

**Pathophysiology**

Inflammation with granuloma formation against a nonspecific inflammatory background is the classical tissue abnormality in all organs affected by WG.

It is now widely presumed that the anti-neutrophil cytoplasmic antibodies (ANCAs) are responsible for the inflammation in WG. The typical ANCAs in Wegener's are those that react with proteinase 3, an enzyme prevalent in neutrophil granulocytes.

**Diagnosis**

Not all WG patients experience all symptoms. Different patients experience different symptoms, and the severity of the disease is also different for each WG patient. If any of the above symptoms persist, consider a possible diagnosis of WG and arrange to have a complete evaluation, including health history, physical exam, laboratory studies, including a urinalysis and an ANCA test.

Diagnosis is established by clinical and laboratory findings such as the ANCA blood test, other blood and urine tests, x-rays, and tissue biopsy, if needed. Many biopsies can be nonspecific and 50% provide too little information for the diagnosis of WG.

**Treatment**

The treatment of WG can be divided into two stages: the induction of disease remission and the maintenance of disease remission. Medication usually consists of cytotoxic agents, using relatively low doses of Cytoxan, and/or methotrexate and/or azathioprine, and glucocorticoids.

Treatment will vary based on patient symptoms, disease activity, organ involvement and lab test results. Patients with kidney involvement and more severe WG are commonly prescribed Cytoxan and prednisone as initial treatment. Ideally, the use of Cytoxan will be limited to a three to six month period and then replaced, based on kidney function, by methotrexate or azathioprine.

Those with milder forms of WG are commonly prescribed methotrexate and prednisone. These medications will be reduced over time, and even eliminated, if the patient remains in a stable remission. WG patients may also be prescribed calcium supplements and other medications to prevent osteoporosis from extended prednisone use.

Many patients will also be prescribed antibiotics to help prevent secondary lung infections.

(Chuan-bin Guo)

**g. Malignant lymphoma**

There are two main types of lymphocytes: the T cell and the B cell. Lymphomas develop from these two types. B-cell lymphomas are more common among adults, while among children, the incidence of T- and B-cell lymphomas are almost equal. Because there is lymph tissue in many parts of the body, lymphomas can start in almost any organ of the body.

Lymphomas can be divided into two main types: Hodgkin's and non-Hodgkin's. Most non-Hodgkin's lymphomas begin in the lymph nodes; about 20% start in other organs, such as the lungs, liver or gastrointestinal tract.

The exact cause of non-Hodgkin's lymphomas is unknown. People exposed to certain pesticides and ionizing radiation have a higher-than-average chance of developing this disease. Patients who suffer from immune-deficient disorders, as well as those who have been treated with immune-suppressive drugs for heart or kidney transplants, and for conditions such as rheumatoid arthritis and autoimmune diseases, are at an increased risk for this disease. Some studies have shown a loose association between retroviruses, such as HTLV-I, and some rare forms of lymphoma. The Epstein-Barr virus has been linked to Burkitt's lymphoma in African countries. However, a direct cause- and-effect relationship has not been established.

**Clinical features**

Males are at a higher risk than females, and the risk increases with age. Though it can strike people of any age, young and middle-aged people are at the highest risk.
Hodgkin's disease typically presents as painless lymphadenopathy, most commonly in the lower cervical or supraclavicular region. Involved lymph nodes are usually in

localized region, or in contiguous groups. The nodes are nontender, mobile and rubbery. Mediastinal or hilar nodes are frequently involved at presentation. Abdominal involvement is unusual unless the patient has systemic symptoms(weight loss, fever, night sweats), or histologic examination shows the lymphocyte depleted subtype. Primary extranodal Hodgkin's disease is rare.

Patients with non-Hodgkin's lymphoma often have cervical lymphadenopathy, and it is the presenting complaint in 15% of patients. Unlike Hodgkin's disease, non-Hodgkin's lymphoma often presents with both nodal and extranodal disease. The most common extranodal site is Waldeyer's ring (usually tonsil). Primary extranodal lymphoma also occurs in the bone, brain, stomach, intestine, and kidney. Few patients present with localized disease, and contiguous lymph node spreading is uncommon. Mediastinal involvement is rare, and abdomenal involvement is more common. Twelve percent of patients have systemic symptoms(Fever > 38.0, night sweats, weight loss > 10% body weight in 6 months). In higher grade lymphomas, systemic symptoms may be the presenting complaint.

**Diagnosis**

Lymphomas are often difficult to diagnose in their early stages. When lymphoma is suspected, a complete medical history should be taken and a thorough physical examination performed. Enlarged liver, spleen, or lymph nodes may suggest lymphomas. Blood tests will determine the cell counts and obtain information on how well the organs, such as the kidney and liver, are functioning.

A biopsy of the enlarged lymph node is the most definitive way to diagnose a lymphoma. A bone marrow biopsy is also needed Once the exact form of lymphoma is known, it is then staged to determine how aggressive it is, and how far it has spread. This information helps determine the appropriate treatment. Biopsies may also be repeated during treatment to see how the lymphoma is responding to therapy.

Conventional imaging tests, such as X-rays, computed tomography scans (CT scans), magnetic resonance imaging, and abdominal sonograms, are used to determine the extent of spread of the disease.

**Treatment**

Treatment options for lymphomas depend on the type of lymphoma and its stage. In most cases, treatment consists of chemotherapy, radiation therapy, or a combination of the two.

Combination chemotherapy, which uses several drugs, has been found more

effective than single-drug use. Treatment usually lasts about six months, but in some cases may be as long as a year.

Bone marrow transplantation is being tested as a treatment option when lymphomas do not respond to conventional therapy, or when the patient has had a relapse or suffers from recurrent lymphomas.

A new option for lymphoma patients is peripheral stem cell transplantation. In this treatment, stem cells, that normally circulate in the blood are collected, treated to remove cancer cells, then returned to the patient in a process called leukapheresis. Researchers are exploring whether these cells can be used to restore the normal function and development of blood cells, rather than using a bone marrow transplant.

**Prognosis**

When all the different types and stages of lymphoma are considered together, only 50% of patients survive five years or more after initial diagnosis. The survival rate among children is definitely better than among older people. About 90% of children diagnosed with early-stage disease survive five years or more, while only 60-70% of adults diagnosed with low-grade lymphomas survive for five years or more. The survival rate for children with the more advanced stages is about 75-85%, while among adults it is 40-60%.

(Chuan-bin Guo)

# 6

# *Salivary Gland Diseases*

**Anatomy and physiology of salivary glands**

Saliva is the glandular secretion that constantly bathes the teeth and the oral mucosa. It is constituted by the secretions of the three paired major salivary glands, the parotid, submandibular and sublingual glands, the minor salivary glands and the gingival fluid. The presence of saliva is vital to the maintenance of healthy oral tissues.

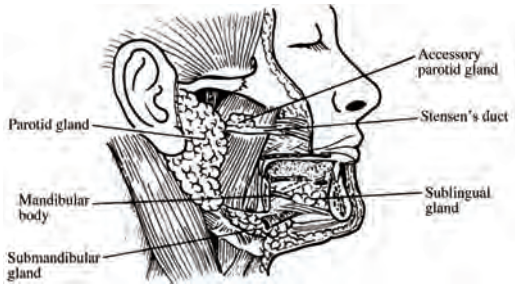


Fig. 6-1 Anatomy of the parotid, submandibular, and sublingual glands

**1. Anatomy**

The type of salivary secretion varies according to the gland. Secretions from the parotid gland are serous or watery in consistency, those from the submandibular and sublingual glands, and particularly the minor mucous glands, are much more viscous due to their glycoprotein content.

The parotids are the largest salivary glands. They are wedge-shaped with the base of the wedge lying superficially covered by fascia and the parotid capsule. They are situated in front of the ear and behind the ramus of the mandible (Fig. 6-1). The apex of the wedge is the deepest part of the gland. The gland is intimately associated with the peripheral branches of the facial nerve.

The parotid duct is thick walled, formed by the union of the ductules, which drain the lobules of the glands. It emerges at the anterior border of the gland on the surface of the masseter muscle and hooks medially over its anterior border. The duct opens into the oral cavity in a papilla opposite the second upper molar tooth.

The submandibular gland is variable in size being about half of the parotid, its superficial part is wedged between the body of the mandible and the mylohyoid muscle. The gland hooks around the sharply defined posterior border of the mylohyoid muscle and its smaller, deep part lies above the mylohyoid in the floor of the mouth (Fig. 6-1). The thin walled duct runs forward in the angle between the side of the tongue and mylohyoid. It opens into the floor of the mouth underneath the anterior part of the tongue, on the summit of the sublingual papilla lateral to the lingual frenulum.

The sublingual gland is the smallest of the paired major salivary glands being about one-fifth the size of the submandibular gland. It is situated in the floor of the

mouth beneath the sublingual folds of mucous membrane (Fig.6-1). Numerous small ducts open into the mouth of the sublingual fold.

Minor salivary glands are situated on the lateral border of the tongue, the posterior part of the palate and in the buccal and labial mucosa. They are small mucosal glands.

**2. Function of saliva**

The functions of saliva are largely protective, however, it also has other functions.

(1) Lubricant: saliva coats mucosa and helps to protect against mechanical, thermal and chemical irritation. It assists smooth air flow, speech and swallowing.

(2) Ion reservoir: solution supersaturated with respect to tooth mineral facilitates remineralization of the teeth. Statherin and acidic proline-rich proteins in saliva inhabit spontaneous precipitation of calcium phosphate salts.

(3) Buffer: saliva helps to neutralize plaque pH after eating, thus reducing time for demineralization.

(4) Cleansing: saliva clears food and aids swallowing.

(5) Antimicrobial actions: saliva contains specific (eg sIgA) and non-specific (eg lysozyme, lactoferrin and myeloperoxidase) antimicrobial compounds which help to control the oral microflora.

(6) Agglutination: agglutinins in saliva aggregate bacteria resulting in accelerated clearance of bacterial cells. Examples are mucins and parotid saliva glycoproteins.

(7) Pellicle formation: some salivary proteins form thin (1-10um) protective diffusion barrier on enamel.

(8) Digestion: the enzyme a-amylase is the most abundant salivary enzyme. It splits starchy foods into maltose, maltotriose and dextrins.

(9) Taste: saliva acts as solvent thus allowing interaction of foodstuff with taste buds to facilitate taste.

(10) Excretion: as the oral cavity is technically outside the body, substances that are secreted in saliva are excreted. This is a very inefficient excretory pathway as reabsorption may occur further down the intestinal tract.

(11) Water balance: under conditions of dehydration, salivary flow is reduced, dryness of the mouth and information from osmoreceptors are translated into decreased urine production and increased drinking.

# 6-1. Sialadenitis

Inflammation of the salivary glands (sialadenitis) is one of the most common diseases of salivary glands. It can arise from various infectious and noninfectious causes. Effective treatment is based on knowledge of the etiology.

**a. Acute suppurative parotitis**

Acute suppurative parotitis is also called as post-operative parotitis. Its frequency has declined in recent decades because more attention is paid to the balance of body fluid for patients undergoing abdominal surgery.

**Etiology and pathogenises**

Acute suppurative parotitis is an unusual form of circumscribed purulent parotitis. It presents after major abdominal operations particularly, but also after other major procedures. Food –inhibition and dehydration are main causes of this disease. Most cases of acute suppurative parotitis are due to Staphylococcus aureus, but they also may arise from Streptococci or other organisms.

The fact that postoperative parotitis can occur even during intensive antibiotic therapy indicates that the cause is not a straightforward bacterial inflammation. The submandibular gland unlike the parotid gland, is only rarely affected, possibly because of its high content of mucinous secretion with particularly active protective agents.

**Clinical features**

The clinical picture is characterized by tender, often fluctuant, circumscribed, or diffuse swelling of the parotid gland (Fig. 6-1-1). The ear lobes may be displaced laterally, and turbid secretion drains from the duct. Occasionally, a fistula forms as a result of an abscess, and purulent secretion drains from it. The abscess may track via the pterygomaxillary fissure into the pterygopalatine fossa or via Santorini's fissure into the external auditory meatus.

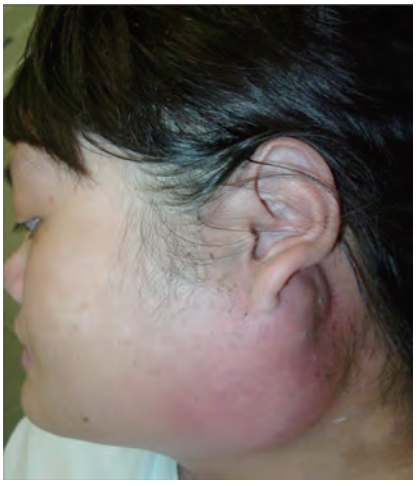

Fig. 6-1-1
Clinical feature of suppurative parotitis.

**Diagnosis**

The differential diagnosis includes arthritis of the temporomandibular joint, masseteric space infection originating from unerupted molars and dental abscess.

Since the diagnosis of acute suppurative parotitis is easily made in most cases, further diagnostic procedures, such as biochemical analysis of the saliva, are unnecessary and usually of no practical value.

**Treatment**

The treatment of acute suppurative parotitis includes appropriate antibiotic therapy and rehydration of the patient to stimulate saliva flow. Surgical drainage may be needed if there is abscess formation.

Although this regimen is usually sufficient, more than 20% mortality rate has been reported in debilitated patients because of spread of the infection and sepsis.

**b. Chronic recurrent parotitis**

Chronic recurrent parotitis is one subtype of chronic parotitis. It is mostly seen in children and rare in adults.

**Etiology and pathogenesis**

Several general factors, such as incomplete development of parotid gland, low immunological ability of patients, genetic potential are possible causes of chronic recurrent parotitis. Based on the general causes, bacterial infection is also related to this disease.

**Clinical features**

It is most common in the early childhood from 3 to 15 years of age. Boys are affected more than girls. The disease is characterized by recurrent tender swelling of one or both parotid glands. The overlying skin of the affected gland may be erythematous. An associated low-grade fever may be present. An egg-white like mucous discharge is often observed from the duct orifice when the gland is milked. The swelling may persist for 5 to 7 days. The interval between episodes of inflammation varies from weeks to months or years. Younger the age, more the chances of recurrence. In symptom-free intervals, the glands may be clinically unremarkable or slightly indurated. As the children grown, recurrence becomes less and less.

Sialogram usually shows snowstorm appearance, diffuse spherical ectasia of the terminal branch ducts, with no obvious change in the main duct (Fig. 6-1-2).

Fig. 6-1-2 Sialogram of chronic recurrent parotitis.

The clinical appearances of chronic recurrent parotitis in adult is similar to that in children, but the symptoms are often more slight and recurrence of episodes is less.

**Treatment**

Chronic recurrent parotitis in children very often resolves spontaneously at adolescence. The principle of treatment thus must be conservative to decrease the recurrence of the disease. The self-protect modality, including massage of the gland to aid the discharge of the saliva in the gland, chewing sugar-free chewing-gum to stimulate the secretion of saliva, drinking more water, and cleaning the mouth with normal saline, is effective to prevent recurrence of the disease. Antibiotic therapy is suggested when there are symptoms of acute inflammation. For patients with frequent recurrence, administration of thymulin is suggested.

The disease in most children is self-limiting. Recurrence of the disease continues in a low-percentage of the patients, which is called as adult recurrent parotitis.

**c. Chronic obstructive parotitis**

Chronic obstructive parotitis is another subtype of chronic parotitis. Differing from chronic recurrent parotitis, local causes are the main etiology of chronic obstructive parotitis.

**Etiology and pathogenesis**

Some local factors, such as sialoliths, structure of the ductal orifice, injury of the surrounding mucosa of the ductal orifice and scar formation, are related to development of chronic obstructive parotitis. The discharge of saliva is obstructed by the sialoliths or structure of the duct and the duct is dilated.

**Clinical features**

The main complaint of patients is recurrent swelling of the parotid gland. It is usually unilateral. The swelling is often related to eating food and this symptom may disappear spontaneously after eating. The patients feel a salty taste of secretion from the parotid gland, especially in the early morning.

Physical examination shows a mild swelling of the parotid gland. An egg-white like or snowstorm like secretion is often observed from the duct orifice when the gland is milked.

The duct ectasia causes an appearance like a string of pearls on the sialogram due to alternating dilation and narrowing of the main duct (Fig. 6-1-3).

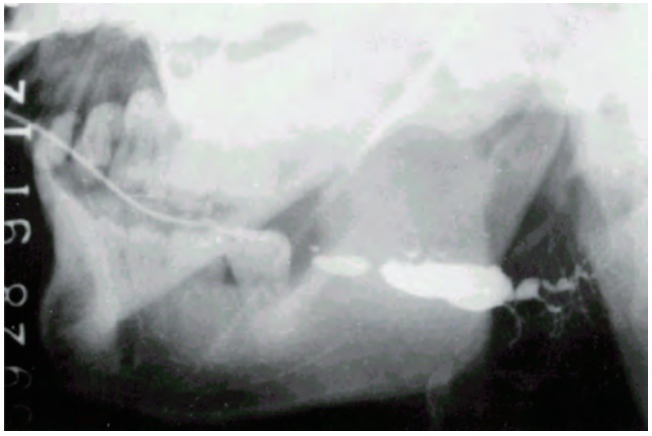

Fig. 6-1-3 Sialogram of chronic recurrent parotitis.

**Treatment**

In the early stage of the lesion, above mentioned self-protect modality is suggested. In the intermittent stage of the lesion, sialoendoscopy is a modality not only for accurate diagnosis, but also for effective treatment. In the end stage of the lesion with highly dilated duct and atrophied gland, superficial parotidectomy is a choice for management. However, the dissection of facial nerve should be done very carefully since the fibers of the facial nerve adhere closely to the chronically inflamed parotid gland tissues. The entire main duct of the affected parotid gland should be removed.

# 6-2. Sialolithiasis and sialadenitis of submandibular gland

Sialolithiasis is a condition characterized by the presence of sialoliths. Sialoliths are calcified structures that develop within salivary ductal system. About 85% sialoliths occur in the submandibular gland, followed by parotid gland, and rarely in the minor salivary gland of lip and sublingual gland. Sialoliths are usually accompanied by secondary inflammation of submandibular gland because of obstruction of the duct.

**Etiology and pathogenesis**

It remains unexplained why such calculi form. Some local factors include foreign body, inflammation, saliva stasis due to various causes. Systemic derangement in calcium and phosphorus may be one of the causes because some patients have calculi in other organs, such as the urinary tract and the gallbladder. Sialoliths are believed to arise from deposition of calcium salts around a nidus of debris within the duct lumen.

There are two reasons why the submandibular gland is the most frequently affected by sialolithiasis. Firstly, the submandibular duct ascends when the body is upright, it bends at the posterior edge of the floor of the mouth, and its course is sinuous. Secondly, the submandibular saliva is rich in mucus and is thus more viscous than the parotid saliva. These facts all favor stasis of secretion, leading to calculus formation.

**Clinical features**

Sialolithiasis can occur at almost any age, but they are most common in young and middle- aged adults.

The calculi may be present for several days to several years before they block the duct and cause symptoms. In such cases, recurrent swelling of the parenchyma may occur during periods of stimulation of secretion, usually during meal times. The swelling is often extremely painful, which is called “salivary gland colic”, but the pain caused by a calculus in the duct system itself is less marked. Pain relieves spontaneously soon after diet in most patients, but may maintain for several hours in some patients. The enlarged gland is tender. If the calculus is not ejected spontaneously, secondary infection almost inevitably occurs. The mucosa around the ductal orifice is red and swollen (Fig. 6-2-1). Purulent discharge may be observed at the orifice of the duct when the affected submandibular gland is milked. For the patients with small calculus, the symptoms are often trivial.

If the calculus lies close to the ostium or in the middle third of the duct, it can be palpated in the floor of the mouth. Radiopaque submandibular calculi are readily

recognized on plain radiographs. Stones in the terminal portion of the submandibular duct are best demonstrated with an occlusal radiograph (Fig. 6-2-2), while stones in the posterior portion of the duct or within the gland are demonstrated well with a lateral view for submandibular gland. Sialography is suggested only in patients without radiopaque calculi, but when obvious symptoms of duct obstruction are present.

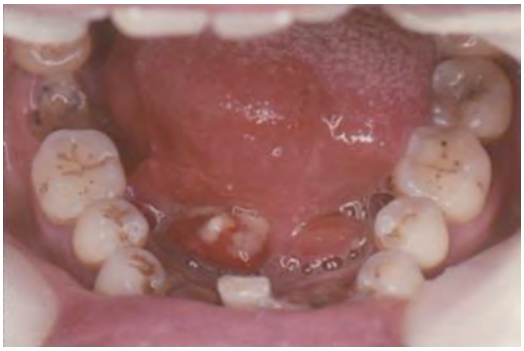

Fig. 6-2-1
Sialolithiasis of submandibular gland.

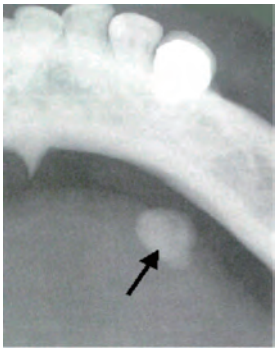

Fig. 6-2-2
Occlusal radiograph demonstrating radiopaque calculi.

**Treatment**

Small sialoliths of the submandibular gland sometimes can be treated conservatively by gentle massage of the gland in an effort to milk the stone toward the duct orifice. Sialagogues also may promote passage of the stone. Surgical removal of large submandibular calculi in an accessible part of the duct (distal two-thirds) is straightforward and can be undertaken under local analgesia.

Sialoendoscopy is a relatively new and minimally invasive technique that has proven useful in removal of sialoliths within the duct system (Fig. 6-2-3). This technique has low morbidity and affords the possibility of retaining a functional gland. If a calculus occurs within the submandibular gland or significant inflammatory damage has occurred with the feeding gland, excision of the gland by an external approach is advocated.

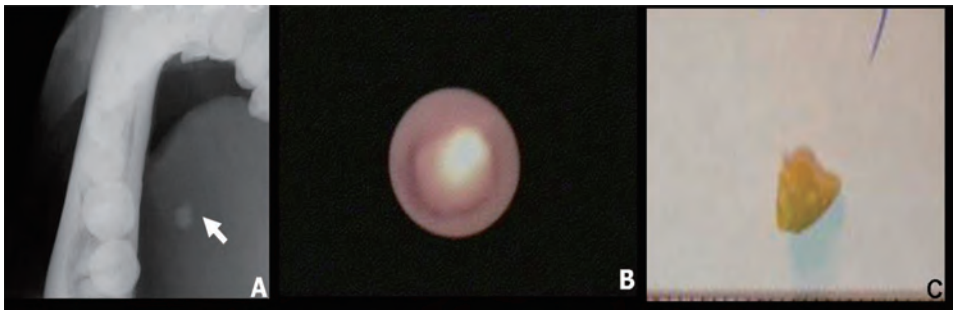


Fig. 6-2-3 Sialoendoscopic appearances of sialoliths in duct of submandibular gland

# 6-3. Sjögren's syndrome

Sjögren's syndrome is a chronic, systemic autoimmune disorder that principally involves the salivary and lacrimal glands, resulting in xerostomia and xerophthalmia. The clinical presentation of both xerostomia and xerophalmia is also called as the "sicca syndrome". The disease is divided into two patterns: primary Sjögren's syndrome (sicca syndrome alone; no other autoimmune disorder is present) and secondary Sjögren's syndrome (the patient manifests sicca syndrome in addition to another associated autoimmune disease).

**Etiology and pathogenesis**

The cause of Sjögren's syndrome is unknown. Immuno-regulatory defect is related to the development of Sjögren's syndrome. Relatives of affected patients have an increased frequency of other autoimmune diseases. In addition, certain histocompatibility antigens (HLAs) are found with greater frequency in patients with Sjögren's syndrome. HLA-DRW52 is associated with both patterns of the disease. HLA-B8 and HLA-DR3 are seen with increased frequency in the primary pattern of the disease. Viruses may be related to the development of Sjögren's syndrome.

**Clinical features**

Females are affected nearly 10 times as frequently as males. Women in middle age or more are predominantly affected.

Three principal symptoms, dry mouth, dry eye, and other symptoms related to autoimmune disorders, occur in Sjögren's syndrome.

Xerostomia, caused by decreased salivary secretion, is the principal oral symptom of Sjögren's syndrome. The severity of this dryness can vary widely from patient to patient. The saliva may appear frothy, with a lack of the usual pooling of saliva in the floor of the mouth. Patients may complain of difficulty in swallowing, altered taste, or difficulty in wearing dentures. The tongue often becomes fissured with atrophy of the papillae (Fig. 6-3-1). The oral mucosa may be red and tender, usually as a result of secondary candidiasis. The lack of salivary cleansing action predisposes the patient to dental decay, especially cervical caries.

Swelling of the parotid gland occurs in about 30% of the patients. This swelling is diffuse, usually bilateral, may be painless or slightly tender.

Sjögren's syndrome can have serious ocular effects. Patients often complain of a scratchy, gritty sensation or a perceived presence of a foreign body in the eye.

Defect of the ocular surface epithelium develops and can be demonstrated with rose bengal dye. Vision may become blurred, and sometimes there is an aching pain. The ocular manifestations are least severe in the morning on wakening and become pronounced as the day progresses.

Sjögren's syndrome is a systemic disease, and the inflammatory process also can affect various other body tissues. The skin is often dry, as are the nasal and vaginal mucosa. Rheumatoid arthritis is the most common connective tissue disease. Other possible associated problems include systemic lupus erythematosus, scleroderma, polymyositis, Raynaud's phenomenon, and interstitial nephritis etc.

The saliva flow rate including pure parotid saliva collected by Lashley cup and whole saliva, is decreased. Schirmer's test confirms the decreased tear secretion. Sialographic examination reveals punctate sialectasia and lack of normal arborization of the ductal system, typically demonstrating a "fruit –laden, branchless tree" pattern (Fig. 6-3-2). Scintigraphy with radioactive technetium -99m pertechnetate characteristically shows decreased uptake and delayed emptying of the isotope.

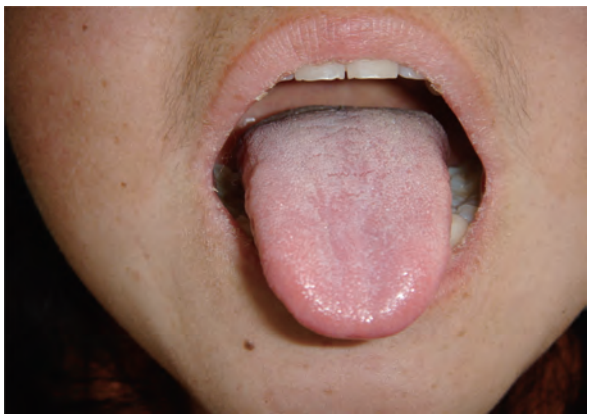

Fig. 6-3-1 Dry mouth of Sjögren's syndrome.

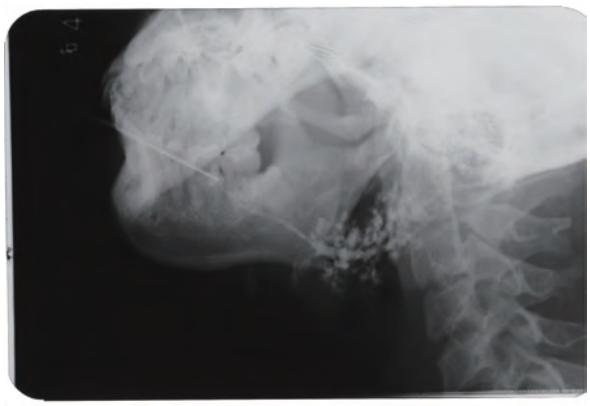

Fig. 6-3-2 Sialogram of Sjögren's syndrome.

In some patients with Sjögren's syndrome, laboratory examination shows elevated erythrocyte sedimentation rate, serum immunoglobulin levels, especially IgG and positive rheumatoid factor (RF). A variety of autoantibodies can be detected, such as antinuclear antibodies (ANA), anti-SS-A (anti-Ro). Anti-SS-B (anti-La), and salivary duct autoantibody.

**Treatment**

The treatment of the patient with Sjögren's syndrome is mostly supportive. Artificial salivas are available for the treatment of xerostomia. Chewing sugar-free chewing gum can help to stimulate the secretion of the salivary glands and keep the mouth moist. Sialagogues, such as pilocarpine and cevimeline, are useful to stimulate salivary flow if enough functional salivary tissue still remains. Daily fluoride application is suggested in dentulous patients because of the increased risk of dental caries. Antifungal therapy often is needed to treat secondary candidiasis.

The dry eyes are best managed by periodic use of artificial tears. Sealing the lacrimal punctum at the inner margin of the eyelids can be helpful by blocking the normal drainage of any lacrimal secretions into the nose.

Patients with Sjögren's syndrome have an increased risk for lymphoma, up to 40 times higher than the normal population. These tumors may arise initially within the salivary glands or within lymph nodes. These tumors are predominantly non-Hodgkin's B-cell lymphoma of the mucosa-associated lymphoid tissue. The detection of immunoglobulin gene rearrangements in labial salivary gland biopsies may prove to be a useful marker for predicting the development of lymphoma.

## *6-4. Tumor-like lesions*

**a. Mucocele**

Mucocele is a common lesion of the oral mucosa and the most common tumor-like lesion in salivary glands.

**Etiology and pathogenesis**

The mucocele results from rupture of a salivary gland duct and spillage of mucin into the surrounding soft tissues. This spillage is often the result of local trauma, although there is no known history of trauma in many cases. The mucocele is not a true cyst because it lacks an epithelial lining.

**Clinical features**

The mucocele is most common in children and young adults, perhaps because younger people are more likely to experience trauma that induces mucin spillage. Mucoceles most often form in the lower lip but occasionally on the buccal mucosa and anterior ventral tongue. They are usually superficial and rarely larger than 1 cm in diameter. In the early stages they appear as rounded fleshy swellings. Later, they are obviously cystic, hemispherical, fluctuant and bluish due to the thin wall (Fig. 6-4-1). Many patients relate a history of a recurrent swelling that periodically may rupture and release its fluid contents.

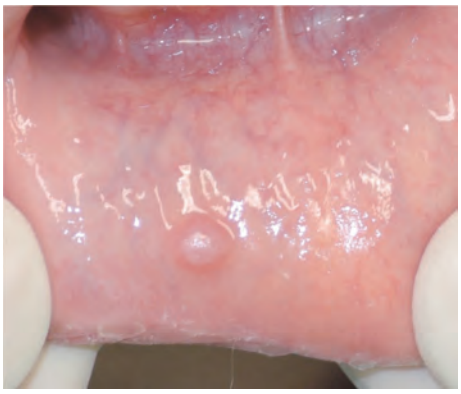

Fig. 6-4-1 Clinical feature of mucocele

**Treatment**

Surgical excision is the choice of treatment of mucocele. A spindle incision is made just through the overlying mucosa and the lesion is excised together with the underlying minor salivary gland of origin.

**b. Ranula**

Ranula is a term used for mucoceles that occur in the floor of the mouth. The name is derived from the Latin word rana, which means frog, because the swelling may resemble a frog's translucent underbelly.

**Etiology and pathogenesis**

Damage to the duct of the sublingual gland causes the formation of a mucous extravasation cyst appearing as a tense bluish swelling in the anterior floor of the mouth just to one side of the midline.

**Clinical features**

Ranula is common in children and young adults. They are usually unilateral and 2 or 3 cm in diameter. Occasionally they extend across the whole of the floor of the mouth, and elevate the tongue. They appear as soft, fluctuant and bluish swelling (Fig. 6-4-2). Deeper lesions may be normal in color. They are typically painless but may interfere with speech or mastication. Like other mucoceles, ranulas may decrease in their size, even disappear after rupture and release their mucin contents, and then re-form. An unusual clinical variant, the plunging ranula, occurs when the spilled mucin dissects through the mylohyoid muscle and produces swelling within the neck (Fig. 6-4-3). A concomitant swelling in the floor of the mouth may or may not be present.

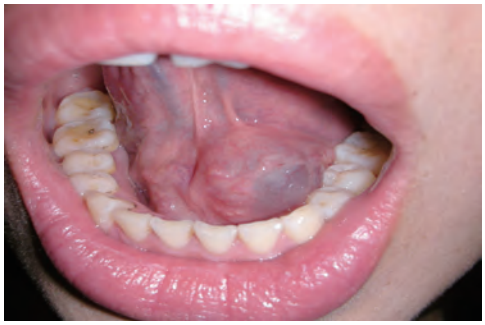

Fig. 6-4-2 Clinical feature of ranula.

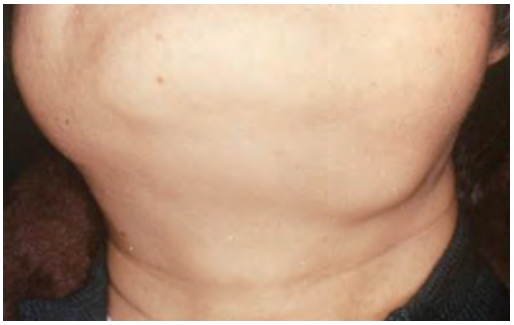

Fig. 6-4-3 Clinical feature of plunging ranula.

**Treatment**

Ranula is one type of extravasation mucocele, other than retention mucocele. Therefore, removal of the feeding sublingual gland is the principle treatment for ranula. It is strongly emphasized that removal of the feeding gland is the key point for preventing a recurrence of the ranula. If the gland is removed, meticulous dissection of the lining of the lesion may not be necessary for the lesion to resolve, even for a plunging ranula.

## *6-5. Salivary gland tumors*

**a. General considerations**

The majority of salivary gland tumors are of epithelial origin. Their pathohistological classification is very complicated. The clinical and imaging appearances, treatment and prognosis of different types of tumors are varied.

**Frequency**

The incidence of salivary gland tumors varies in different countries from 0.25 to 1.8 per 100,000 population. The percentage of major salivary gland tumors compared to tumors of the head and neck is 5%. According to the data from 7 key dental schools in China, among 69,902 cases of tumors in the oral and maxillofacial region, 23,010 cases are salivary gland tumors, accounting for 32.9%.

In different locations of salivary gland tumors, the frequency of parotid tumor is the highest. During the period between 1963 and 2007, 4410 cases of salivary gland tumor were collected by Peking University School of Stomatology. Among them, 2 803 (63.6%) tumors occurred in parotid gland, 398 (9%) in submandibular gland, 89 (2%) in sublingular gland, and 1120 (25.4%) in minor salivary glands. In the minor salivary gland, the tumors of the palate are the most common, accounting for 50%.

The ratio of benign tumors to malignant tumors also varies in different locations of salivary glands. In parotid gland, benign tumors account for 77%, much more than malignant tumors. In submandibular gland, 64% tumors are benign, 36% are malignant. In sublingual gland, most of the tumors (93%) are malignant. In minor salivary glands, malignant tumors (62% ) are more than benign tumors (38% ).

The frequency of different types of tumors varies in the different locations. Almost all of Warthin tumor and oncocytoma occur in the parotid gland. Most of the acinic cell carcinomas, salivary duct carcinomas, epithelial-myoepithelial carcinomas are seen in the parotid gland. Most of the polymorphous low-grade adenocarcinomas occur in the palate. The sublingual gland tumor is rare. However, there is a great possibility of adenoid cystic carcinoma once the tumor occurs.

Salivary gland tumors could occur in patients at any age. In adults, malignant tumors account for 45%, less than benign tumors (55%). However, in children, malignant tumors account for 53%, more than benign tumors (47%). Patients with benign tumors are relatively young in adulthood. However, most patients with Warthin tumor are relatively old, but they are 10 years younger than patients with oral squamous cell carcinoma. Generally speaking, the age difference of patients

between benign tumors and malignant tumors is not as obvious as that of oral squamous cell carcinoma and oral benign tumors.

There is a sex difference in some salivary gland tumors. The ratio of male to female in Warthin tumor is 6:1. On the contrary, the ratio is 1:1.2~1.5 in pleomorphic adenoma.

**Clinical diagnosis**

(1) Case history

Benign tumors grow slowly with long history of several years or more. When tumors grow rapidly in a recent period or the patients have symptoms of pain, malignant transformation should be considered.

Malignant tumors grow rapidly. Most salivary gland tumors appear as painless masses, however, patients with adenoid cystic carcinoma usually have symptoms of local pain. Some patients with Warthin tumor have a history of growth and quiescence alternately, and symptoms of swelling and pain. It should be differentiated from inflammation and malignant tumors.

(2) Clinical examination

Observation: Patients with benign tumors in parotid gland have no signs of facial paralysis. But if the facial nerve is invaded by malignant tumors, facial paralysis can occur. It depends on the histological type of tumor. When mucoepidermoid carcinoma invades the facial nerve, there could be no sign of facial paralysis at all. Sometimes, no obvious facial paralysis, only weakness of facial nerve function occurs. The clinical observation should be very thorough, otherwise it could be ignored. When the hypoglossal nerve is invaded by the carcinoma, the movement of the tongue is limited because of lingual paralysis. They are commonly seen in malignant tumors of the submandibular glands. The surface of mucoepidermoid carcinoma in the palate or retromolar region can be blue coloured. In this case, the tumor could be misdiagnosed as a cyst. Sometimes dilation of the capillary vessels can be seen on the surface of the adenoid cystic carcinoma. For parotid tumors, the parapharynx should be observed. If there is swelling, a deep lobe tumor should be considered.

Palpation: For a mass, its location, size, texture, movability and the relation between the tumor and surrounding tissues should be investigated. If the mass is hard, adhered to the surrounding tissues and immovable, a malignant tumor should be considered. The surface of pleomorphic adenoma is usually nodular (Fig. 6-5-1), while the surface of Warthin tumor is smooth, soft and compressible. Normally, there is a space between the mastoid and condyle of the mandible. It is significant

for the retromandibular tumors to show the presence of space on palpation. If the space has disappeared, the main trunk of facial nerve is usually close, even adhesive to the tumor. The dissection of the facial nerve will be very difficult.

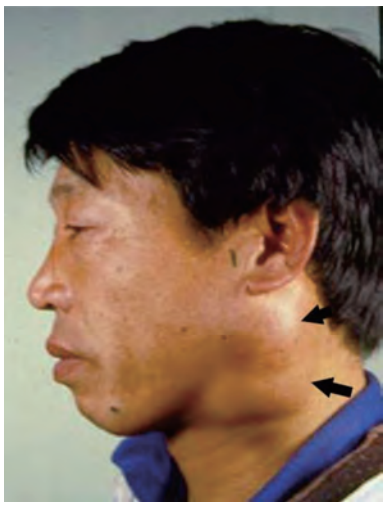

Fig. 6-5-1 Nodular pleomorphic adenoma

**Imaging diagnosis**

(1) Ultrasonography: It is a simple and harmless technique. Its effect for diagnosis are as follows: (a) to determine whether the mass is solid or cystic; (b) to determine whether there is a space-occupying lesion. We usually use it in the differential diagnosis of hypertrophy of the parotid gland and parotid gland tumor. On the echogram, benign tumors usually appear as well-defined, homogeneous hypoechoic lesions. Posterior echo is often enhanced (Fig. 6-5-2). While malignant tumors may appear as space occupying lesions with ill-defined borders and irregular shape. No posterior enhancement occurred on the echogram.

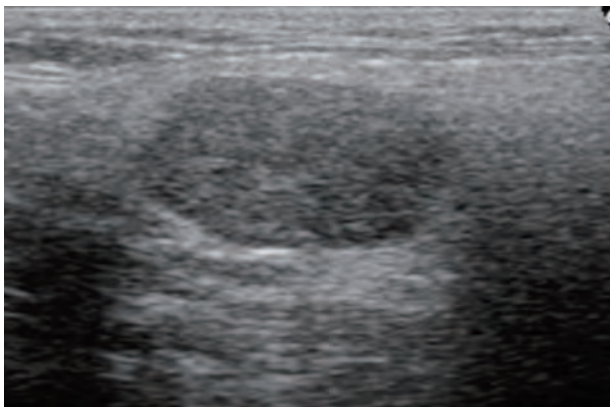

Fig. 6-5-2 Echogram of benign tumor

(2) CT scan: It can show the location and size of the tumor very clearly and differentiate the solid tumor from the cyst or lipoma according to the density of the mass or the CT values (Fig. 6-5-3). When the dynamic CT is used, the carotid artery and the internal jugular vein and the relation between these vessels and the tumor can be shown.

(3) MR imaging: Imaging in multiple planes is easy such as transection, coronal and sagittal plane. Both tumors and major blood vessels are shown clearly. We often use it in cases of extensive tumors.

(4) Scintigraphy: Warthin tumor uptakes 99m Tc. The uptake of radionuclide in the tumor is much more than that of the surrounding glandular tissues. Therefore, the tumor is shown as a "hot-like nodule" when 99m Tc scintigraphy is used (Fig. 6-5-4) . We often use it in cases suspected as Warthin tumor.

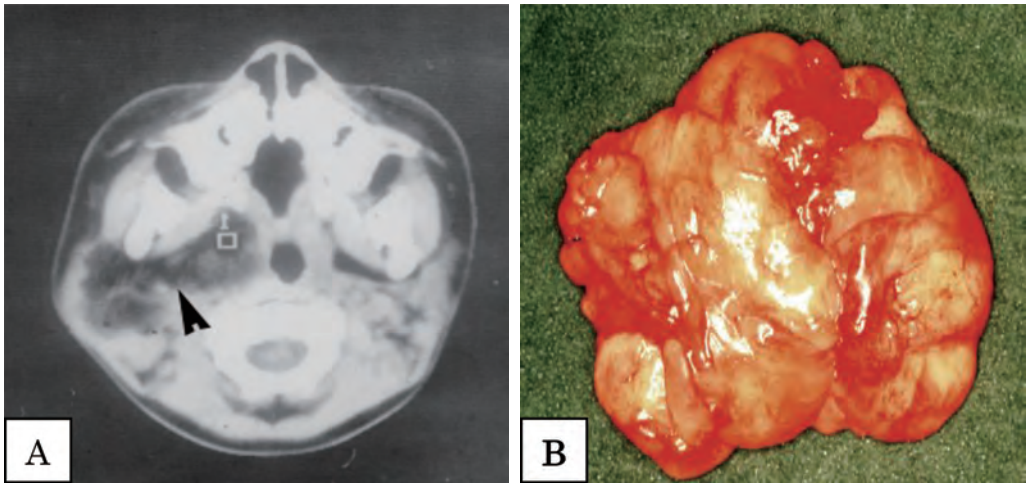


Fig. 6-5-3 CT of lipoma

Fig. 6-5-4 Scintigram of Warthin's tumor

**Fine needle aspiration cytology**

It is possible to differentiate the benign tumors from malignant tumors and adenitis from the tumor. Therefore, it is very significant to use it when the mass is difficult to be differentiated i.e. adenitis of lymph nodes from the tumor. There are some cytological features of several tumors, such as pleomorphic adenoma and adenoid cystic carcinoma. Sometimes it is possible to get the accurate diagnosis of histological type of tumor. However, sometimes it is very difficult because the histological appearances of salivary gland tumor very complicated. When the tumor is in a deep location, it is not easy to insert the needle into the tumor. Misdiagnosis is possible because no accurate specimen is taken. In this case, fine needle aspiration guided by the ultrasonography is suggested.

**Frozen section diagnosis**

It is possible to differentiate the benign tumor from the malignant one, but sometimes it is difficult to get the histological subclassification of the tumor because the section is thicker than the paraffin-embedded sections. If possible, the specimen for frozen section diagnosis should be an excised tumor or whole tumor to prevent the breakage of the tumor and seeding the tumor cells.

The frozen section examination is suitable to cases with invasive malignant tumors, such as adenoid cystic carcinoma and mucoepidermoid carcinoma without capsule. The main purpose is to determine whether there are residual tumor cells in the surrounding tissues, and whether the extension of the resection should be wider.

**Paraffin-embedded section diagnosis**

The accurate diagnosis of the salivary gland tumors depends on the paraffin-embedded section examination. For the parotid and submandibular gland tumors, it is forbidden to perform open biopsy before operation to avoid seeding the tumor cells. However, it could be considered in the following cases: (a) very extensive malignant tumors in the parotid or submandibular gland with destruction of the skull base which is inoperable because of the extent of the tumor or poor general condition of the patients. The biopsy is performed to offer a pathological diagnosis for radiotherapy or chemotherapy. (b) tumors of the palate or other minor salivary gland with superficial ulcers.

**Histological typing of salivary gland tumors**

Under microscopy, the morphology of salivary gland tumors is polymorphous. Therefore, the histological classification is complicated. In 2005, the World Health

Organization offered the 3rd classification. This new classification includes 10 types of benign tumors and 23 types of malignant tumors (Table 6-5-1). Its advantage is that it is very complete. Its disadvantage is that it is too complicated to be mastered by the surgeons.

Table 6-5-1 The WHO histological classification of salivary gland tumors (2005)

| |
|---|
| Adenoma |
| Pleomorphic adenoma |
| Myoepithelioma |
| Basal cell adenoma |
| Warthin tumor (adenolymphoma) |
| Oncocytoma |
| Canalicular adenoma |
| Sebaceous adenoma |
| Lymphadenoma |
| — sebaceous lymphadenoma |
| — non- sebaceous lymphadenoma |
| Ductal papilloma |
| — inverted ductal papilloma |
| — intraductal papilloma |
| — sialadenoma papilliferum |
| Cystadenoma |
| |
| Carcinoma |
| Acinic cell carcinoma |
| Mucoepidermoid carcinoma |
| — low-grade/well-differentiated |
| — high-grade/poorly differentiated |
| Adenoid cystic carcinoma |
| — glandular/tubular |
| — solid |
| Polymorphous low grade adenocarcinona, terminal duct carcinoma |
| Epithelial-myoepithelial carcinoma |
| Salivary duct carcinoma |
| Basal cell adenocarcinoma |
| Malignant sebaceous tumors |
| — sebaceous carcinoma |
| — sebaceous lymphadenocarcinoma |
| Oncocytic carcinoma |
| Cystadenocarcinoma |
| Low-grade cribriform |
| Mucinous adenocarcinoma |
| Clear cell carcinoma, not otherwise specified |
| Adenocarcinoma, not otherwise specified |
| Squamous cell carcinoma |
| Carcinoma ex pleomorphic adenoma |
| Carcinosarcoma |
| Metastasizing pleomorphic adenoma |
| Myoepithelial carcinoma |
| Malignant myoepithelioma |
| Small cell undifferentiated carcinoma |
| Large cell undifferentiated carcinoma |
| Lymphoepithelial carcinoma |
| Sialoblastoma |
| Other carcinomas |

According to the clinical biobehavior and malignancy, the carcinomas of salivary gland may be divided into three types: (a) high-grade malignant carcinoma: including less-differentiated mucoepidermoid carcinoma, adenoid cystic carcinoma, salivary duct carcinoma, adenocarcinoma not otherwise specified, squamous cell carcinoma, myoepithelial carcinoma, oncocytic carcinoma, and undifferentiated carcinoma. These carcinomas have high rates of cervical or distant metastasis, recurrence of the carcinoma, and poor prognosis of the patients. (b) low-grade malignant carcinoma: including acinic cell carcinoma, well-differentiated mucoepidermoid carcinoma, polymorphous low grade adenocarcinoma, and epithelial-myoepithelial carcinoma. These carcinomas have low rates of cervical or distant metastasis. The prognosis of the patients is relatively good although recurrence of the carcinoma may occur. (c) intermediate-grade malignant carcinoma: including basal cell adenocarcinoma, papillary cystadenocarcinoma, carcinoma in pleomorphic adenoma, mucinous adenocarcinoma, etc. The biobehavior of the carcinoma and the prognosis of the patients are between those of the above mentioned two types.

**Treatment**

Surgery is the main modality for management of salivary gland tumors. Radiotherapy, chemotherapy, etc, are the auxillary treatment modalities.

(1) Surgery

The basic principles of surgery: Most salivary gland tumors, including benign tumors, have no complete capsules. The recurrence rate is high if enucleation of tumor is performed. Therefore, the resection of the tumor with enough margin of normal surrounding glandular tissues is the basic principle of operation. During the operation, the integrity of the tumor bulk should be preserved, otherwise implantation of the tumor cells is very likely.

The dissection of the facial nerve: In most cases of parotidectomy, damage to the facial nerve should be avoided. Therefore, the dissection of facial nerve is very important. There are two basic techniques of the dissection of the facial nerve. First, the forward or anterograde dissection starts with the main trunk of the facial nerve. The dissection proceeds forward from the main trunk to the branches along the nerves. The alternative technique is retrograde dissection. The peripheral branches of the facial nerves are traced first. Further dissection of the nerve is meticulously carried out up to the bifurcation or main trunk of the facial nerve. It is easy to carry out forward dissection when a large tumor is located anteriorly. On the other hand, it is suitable to perform the retrograde

dissection when the tumor is located posteriorly.

Partial parotidectomy: It is a radical operation and it should be distinguished from simple enucleation of the tumor. It entails the resection of the parotid tumor with surrounding normal tissues. This procedure avoids breakage and implantation of the tumor.

This technique has the potential advantages as follows. First, it can preserve the function of most parts of the glands. Second, it reduces operation time because the surgical exposure is less and the procedure is easier to carry out. Third, if the tumor is located in the tail of parotid gland, there is a lower risk of damage to the facial nerve with partial parotidectomy because only the marginal mandibular branch and cervicofacial bifurcation of the facial nerve are exposed. Fourth, facial deformity is reduced because partial parotidectomy involves minimal loss of the gland itself. And finally, the incidence of Frey's syndrome is reduced.

The indications for partial parotidectomy include small pleomorphic adenoma which is less than 15 mm in diameter and Warthin tumor in the tail of parotid gland.

Sacrifice of the facial nerve: The facial nerve has to be sacrificed in the following cases: (a) when there is the symptom of facial paralysis before operation; (b) when the facial nerve is attached to the tumors and the histological typings of the tumor are of high-grade malignant carcinoma.

When the facial nerve is close to the tumor, but could be dissected from the tumor without breakage of the tumor and the histological types are low-grade malignant tumors, preservation of the facial nerve could be considered. However, post-operative radiotherapy is necessary. Cryosurgery during the operation is also a good choice to kill the residual tumor cells. Recently we applied 125I seed implant brachytherapy-assisted surgery with preservation of the facial nerve for treatment of malignant parotid gland tumors and got good results. The recurrence rate of the tumor was low and facial nerve function recovered to normal by 6 months postoperatively.

Reconstruction of the defect of facial nerve: When the facial nerve is sacrificed completely or partially, the defect should be reconstructed as soon as possible. Nerve grafting is most commonly used. The greater auricular nerve and the sural nerve are both suitable donor nerves. Generally speaking, the greater auricular nerve is the first choice if the defect is short. The sural nerve is used when the defect is longer.

The treatment of cervical lymph nodes: There is no doubt that it is necessary

to perform radical neck dissection for patients with clinically positive cervical lymph node metastasis. However, there are different opinions on whether elective neck dissection is necessary for patients with clinically negative cervical lymph node metastasis. According to our clinicopathological data of 405 cases with carcinoma of salivary glands, the rate of cervical metastasis was 14%. This indicated that elective neck dissection in principle was unnecessary for patients with carcinoma of salivary glands. However, the cervical metastasis rate was varied with different histological types of carcinoma. The metastasis rate for less-differentiated mucoepidermoid carcinoma, adenocarcinoma, squamous cell carcinoma, undifferentiated carcinoma and salivary duct carcinoma are over 35%. Therefore elective neck dissection should be considered for patients with these carcinomas.

(2) Radiotherapy

Salivary gland carcinomas are not highly sensitive to radiation. The carcinomas cannot be cured by radiotherapy alone. However, post-operative radiotherapy does reduce the recurrence rate of salivary gland carcinoma. In a clinical study of 405 cases with carcinoma of the salivary glands, we did not find obvious difference between the survival rates with surgery alone and combined surgery and postoperative radiotherapy. However, if only adenoid cystic carcinoma was considered, the survival rates of 5 and 10 years in patients with combined therapy were much higher than that of the patients with surgery alone. In our opinion, the indications for radiotherapy are as follows: (a) adenoid cystic carcinoma; (b) high-grade malignant tumors; (c) Post-operative residual tumors; (d) carcinoma to which the facial nerve is attached; (e) extensive tumors which have invaded skin, muscles and bone and (f) recurrent malignant tumors.

(3) Chemotherapy

The salivary gland carcinoma can be divided into two types for chemotherapy: (a) adenocarcinoma-like carcinoma: including adenoid cystic carcinoma, adenocarcinoma, carcinoma ex pleomorphic adenoma, papillary cystadenocarcinoma, and acinic cell carcinoma. They are relatively sensitive to cis-platinum, adriamycin (ADR), and 5-fluorouracil (5-Fu). (b) squamous cell carcinoma-like carcinoma: including mucoepidermoid carcinoma and squamous cell carcinoma. They are relatively sensitive to cis-platinum and methotrexate.

The distant metastasis rate of adenoid cystic carcinoma and salivary duct carcinoma is high (around 40%). Postoperative chemotherapy may be useful in preventing distant metastasis, but it is not clear about its effect.

**Prognosis**

The short –term survival rate of patients with salivary gland carcinoma is high. However, long- term survival rate drops constantly. We have analyzed 405 cases with salivary gland carcinoma, the 3 year survival rate was 78%; 5 year 70%, 10 year 56% and 15 year only 37%. Therefore, it is not enough for patients with salivary gland carcinoma to be followed up for 5 years. The period of their follow-up should be over 10 years.

**b. Pleomorphic adenoma**

Pleomorphic adenoma, or mixed tumor, is the most common salivary gland tumor. The terms pleomorphic adenoma and mixed tumor both represent attempts to describe this tumor's unusual histopathologic features, but neither term is entirely accurate.

**Clinical features**

Pleomorphic adenoma is most commonly seen in parotid gland, followed by submandibular gland, palate and other minor salivary glands, but very rarely in sublingual gland. Almost any age can be affected, but the peak incidence is in the fourth and fifth decades. There is a slight female predominance.

Growth of pleomorphic adenoma is slow and may take several years to reach 2 or 3 cm in diameter. The tumor is painless and the patient may be aware of the lesion for many months or years before seeking a diagnosis.

The tumors form rubbery, often lobulated swellings. Most pleomorphic adenomas of the parotid gland occur in the superficial lobe and present as a swelling in front of the ear. No facial paralysis and pain occur. If neglected, the tumor can grow to grotesque proportions. About 15% of parotid pleomorphic adenomas develop within the deep lobe of the gland beneath the facial nerve. Sometimes these lesions grow in a medial direction between the ascending ramus and stylomandibular ligament, resulting in a dumbbell-shaped tumor that appears as mass of the lateral pharyngeal wall or soft palate. Palatal tumors almost always are found on the posterior lateral aspect of the palate, presenting as smooth-surfaced, dome-shaped masses (Fig. 6-5-5). Most pleomorphic adenomas are movable, but the tumors in the hard palate are not movable because of the tightly bound nature of the hard palate mucosa. Initially, the tumors posterior to ascending ramus are movable, but become less movable as they grow larger.

**Treatment**

Pleomorphic adenomas are best treated by surgical excision. For lesions in the superficial lobe of the parotid gland, superficial or partial parotidectomy with identification and preservation of the facial nerve is recommended (Fig. 6-5-6). Local enucleation should be avoided to prevent seeding of the tumor bed. For tumors of the deep lobe of the parotid, total parotidectomy is usually necessary. Submandibular gland tumors are best treated by total removal of the gland with the tumor. Tumors of the hard palate usually are excised down to periosteum, including the overlying mucosa. In other oral sites of minor salivary glands, the lesion often enucleates easily through the incision site.

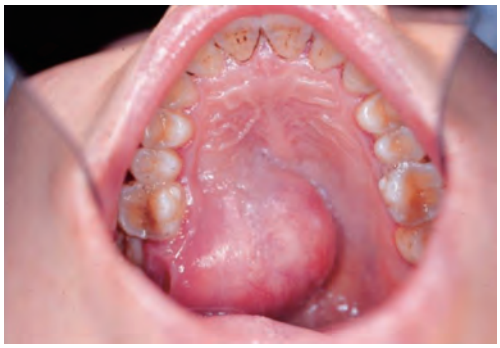

Fig. 6-5-5
Pleomorphic adenoma in the palate.

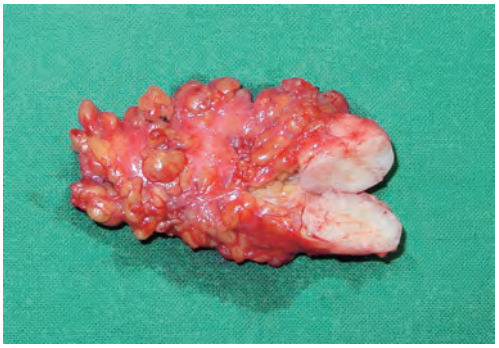

Fig. 6-5-6
Surgical specimen of pleomorphic adenoma.

**c. Warthin tumor**

Warthin tumor is also call as papillary cystadenoma lymphomatosum or adenolymphoma. It is the second most common benign parotid tumor, accounting for nearly 20% of all parotid neoplasms.

The pathogenesis of Warthin tumor may be related to the proliferation of heterotopic salivary gland tissue within parotid lymph nodes. Our previous study demonstrated a strong association between the development of this tumor and smoking. Smokers have a greater risk of Warthin tumor than nonsmokers.

**Clinical features**

Warthin tumor has a heavy predominance of males with a ratio of male to female of 6 to 1. It most often occurs in older adults, with a peak prevalence in the sixth and seventh decades of life. Almost all Warthin tumors occur in the parotid gland, and most frequently in the tail of the parotid near angle of the mandible. One

unique feature is the tendency of Warthin tumor to occur bilaterally, which has been noted in 13% of cases. Most of these bilateral tumors do not occur simultaneously but occur at different time. The tumors usually produce soft painless swellings but sometimes there can be pain or rapid expansion, probably as a result of the partly cystic nature of most of them.

Warthin tumor shows a hot-like nodule by scintigraphy with 99m Tc , which is very useful for diagnosis.

**Treatment**

Surgical removal is the treatment of choice for patients with Warthin tumor. The majority of Warthin tumors occur in the tail of parotid gland, which are indications of partial parotidectomy. About 12% Warthin tumors are multifocal which are related to the development of lymph nodes of parotid gland (Fig. 6-5-7). Several lymph nodes occur in the tail of the parotid gland and at the junction of the posterior border of the gland and anterior border of sternocleidomastoid muscle. In some of these lymph nodes, either microadenoma or tumors occupying the whole node may be found on microscopic examination. Therefore, the tail of the parotid gland and the lymph nodes at the glandular border should always be resected to prevent recurrence.

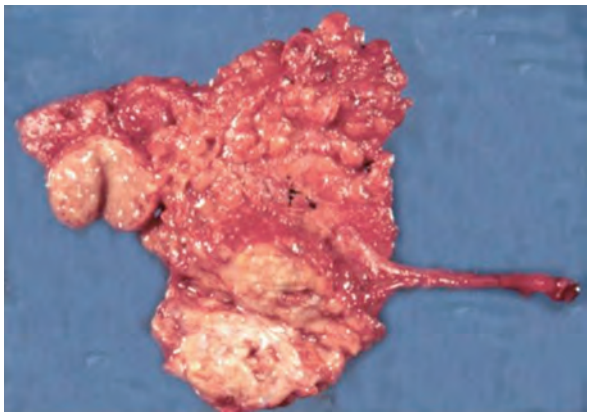

Fig. 6-5-7
Multifocal Warthin tumor.

**d. Mucoepidermoid carcinoma**

Mucoepidermoid carcinoma is one of the most common salivary gland malignancies. It was originally called as mucoepidermoid tumor because of its highly variable biologic potential. These tumors appear to behave in a benign fashion with favorable prognosis but may exhibit malignant behavior. Therefore, the term mucoepidermoid carcinoma is the preferred designation.

**Clinical features**

The tumor occurs fairly evenly over a wide age range, extending from the second to seventh decades of life. It is also the most common malignant salivary gland tumor in children. The tumor occurs slightly more in females than in males.

Mucoepidermoid carcinoma is most common in the parotid gland, followed by submandibular gland, palate, and other minor salivary glands. Retromolar region is one of the most common sites of mucoepidermoid carcinoma.

The clinical appearances of mucoepidermoid carcinoma depend on the differentiation of the carcinoma cells. Most carcinomas are well -differentiated and their clinical behavior seems like that of pleomorphic adenoma. They usually appear as an asymptomatic swelling. Most patients are aware of the lesion for a year or less. The tumor may be harder and irregular in shape, the boundary of the tumor is either clear or indistinct. The overlying mucosa of tumors in the palate or retromolar region may be blue colored. Symptoms of facial paralysis are very rare. The carcinoma may recur if surgery is not radical enough. However, rates of cervical and distant metastasis are very low and the prognosis of the patients is rather good.

The less-differentiated mucoepidermoid carcinoma grows rapidly. The boundary of the tumor is not clear. Pain and facial paralysis may develop. Rates of cervical, distant metastasis and recurrence of the carcinoma are high, and the prognosis of patients is poor.

**Treatment**

The treatment of mucoepidermoid carcinoma is predicated by the histopathologic grade, location, and clinical stage of the tumor. Surgery is the main modality for the treatment of mucoepidermoid carcinoma. For the well-differentiated mucoepidermoid carcinoma, facial nerve may be preserved except that the facial nerve penetrates into the tumor. If the surgery is radical, post-operative radiotherapy is unnecessary for the well-differentiated carcinoma, while it is necessary for the less-differentiated mucoepidermoid carcinoma. Elective neck dissection should be considered for the less-differentiated carcinoma, while it is unnecessary for the well-differentiated carcinoma.

**e. Adenoid cystic carcinoma**

Adenoid cystic carcinoma is one of the most common and best-recognized salivary gland malignancies. It was originally called as a cylindroma because of its distinctive histopathologic features.

**Clinical features**

Adenoid cystic carcinoma is most common in middle-aged adults and is rare in people younger than 20 years. There is a fairly equal sex distribution, although some studies have shown a slight female predilection.

Adenoid cystic carcinoma can occur in any salivary site, more than 50% develop within the minor salivary glands. The palate is the most common site for minor salivary gland tumors. The remaining tumors are found mostly in the parotid and submandibular glands. Adenoid cystic carcinoma is the most common tumor in the sublingual gland.

Adenoid cystic carcinoma usually appears as a slowly growing mass. Infiltration is the hallmark of this tumor, which often causes pain. Occasionally pain occurs early in the course of the disease before there is a noticeable swelling. Patients often complain of a constant, low-grade, dull ache, which gradually increases in intensity. Facial paralysis may develop with parotid tumors. Palate tumors can be smooth surfaced. Sometimes dilated capillary blood vessels may be seen on the overlying mucosa of adenoid cystic carcinoma. The tumor usually infiltrates along nerve sheaths. When they reach and spread along bony canals their extent is considerably greater than what radiographs show. The rate of cervical metastasis is low, but distant metastasis rate is very high. Metastatic spread most commonly occurs in the lungs and bones (Fig. 6-5-8).

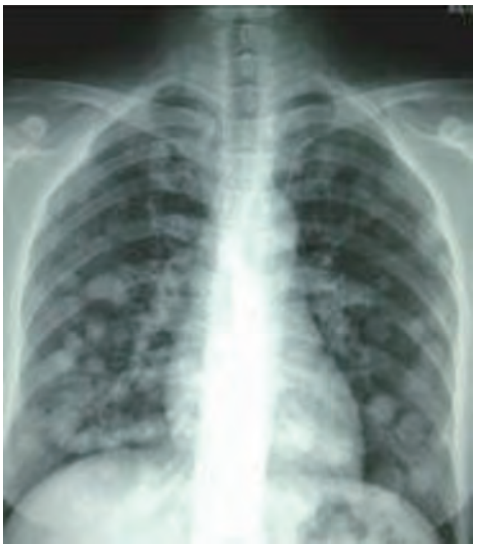

Fig. 6-5-8
Multifocal metastasis in the lung

**Treatment**

Adenoid cystic carcinoma is a relentless tumor that is prone to local recurrence and eventual distant metastasis. Surgical excision is usually the treatment of choice,

and postoperative radiotherapy may decrease the recurrence rate of the tumor and improve the survival rate of the patients. The first operation should be as extensive as possible, with a wide margin of healthy tissue. Selective neck dissection is not indicated because metastasis to regional lymph nodes is uncommon. For the patients with recurrent tumor, 125I seed implant brachytherapy may effectively control the tumor and is a treatment modality of choice.

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(Guang-yan Yu)

# 7

# *TMDs (Temporomandibular Joint Diseases)*

# 7-1. The anatomy structure and function of the temporomandibular joints

Temporomandibular joints (TMJs) are fine articulations with specific anatomic structures that make the most complicated movement of the body. This chapter focuses on the anatomy and function of the temporomandibular joints.

Temporomandibular joints are articulator structures between mandible and cranium base. The left and right temporomandibular joints are located on both sides of the cranium. They are linked together by the U shaped bony mandible, and the bilateral TMJs will move simultaneously and react to each other. The TMJ on one side cannot move without the reaction of the joint on the other side. This so-called ginglymoarthrodial joint is a unique characteristic of TMJs and it cannot be found in any other articulations in the body. Usually, other articulations always have muscles attached and the articulations are forced to move by the muscles while the movements are restricted by ligaments around the articulator structure. The movement of articulation is determined by structural factors such as muscle force, ligament limitation, and anatomic position of articulator surface. However, in addition to these factors, the TMJs are influenced by more complicated factors compared with other articulations because of the existence of occlusion between mandibular and maxillary teeth. The mandibular movement is somehow determined by occlusion. The occlusion can influence the direction and distance of mandibular movement and relative position of TMJ structure.

Therefore, some believe that certain clinical complaints relating to temporomandibular disorders and joint pain have a relationship with occlusal disorder or malocclusion. However up to now, there is no sufficient scientific evidence about epidemiology and etiology to approve the hypothesis that occlusion is the main cause of these clinical problems.

The bony structure of Temporomandibular joints include mandibular fossa of temporal bone, articular tubercle, and mandibular condyle; The soft fibrous tissue structure of TMJs include articular capsule that separate the joint space and surrounding tissue and extra-articular ligament that enhance the strength of articular capsule; the internal structure of TMJs include articular disc that lays in between the condyle and mandibular fossa and soft tissue attachment that connects with the disc.

(1) Mandibular condyle: Mandibular condyle is located at the top of the mandibular articular process. It looks like a long ovate bony structure from coronal view and finger shaped from lateral view. It's articulator surface is from anterior

surface to superior surface and is covered by fibrous cartilage tissue. The movement of the condyle is lubricated by synovial fluid.

(2) Mandibular fossa, articular tubercle (articular eminence): Mandibular fossa is a concave structure in the temporal bone opposite to the condyle in position. The anterior part of mandibular fossa extends forward and downward to form an articular eminence. The posterior part of mandibular fossa is adjacent to tympanic part and is bounded in tympanic crack. Articular eminence is a bony eminence located at the most lateral portion of articular process of cranium. The surface of articular eminence is covered by a layer of fibrous cartilage from posterior slope to anterior slope while the condyle is covered by a thin layer of fibrous membrane.

(3) Articular disc: The articular disc is made of extremely dense fibrous connective tissue and the disc attachment is rich in vascularity. Sagittal section of disc shows that its anterior and posterior parts are thick and the center part is thin. The thin center part shares the space between mandibular condyle and articular structure of temporal bone. The disc acts as a cushion for the articulation. The joint space is separated into two parts of superior space and inferior space by the disc. The superior space is formed by the disc and articular structure of temporal bone that allows the condyle-disc complex to glide along the posterior slope of the eminence. The inferior space is formed by the disc and mandibular condyle that allows rotational movements of the condyle.

(4) Articular capsule, articular ligaments: The articular capsule has an extra ligament on the lateral side that forms a distinct capsule with the soft tissue, but its inner and posterior side are unclear because the tissue structures there are thin. The lateral pterygoid muscle goes backwards attaching to the anterior part of the disc and condyle. Other ligaments of the articular capsule are sphenomandibular ligament and stylomandibular ligament.

(5) The muscles related to movement of temporomandibuar joint: The main muscles elevating the mandible are masseter muscles, temporal muscles, and medial pterygoid muscles. The inferior lateral pterygoid muscles assist in protruding the mandible, and the temporal muscles assist in retruding the mandible. All these muscles are called masticatory muscles. The muscles related to mouth opening are digastrics.

(6) The nerves and vascular supply of temporomandibular joints: The sensory nerve of TMJ is the third branch of trigeminal nerve (mandibular nerve). The vascular supply is predominantly by superficial temporal branch of the external carotid artery.

(Ting Jiang)

# 7-2. Congenital or developmental disorders of temporomandibular joint

Congenital or developmental disorders of temporomandibular joint include aplasia, hypoplasia, hyperplasia, and some associated with syndromes.

**a. Aplasia and hypoplasia**

Temporomandibular joint (TMJ) or condylar hypoplasia is failure of the condyle to attain normal size because of congenital and developmental abnormalities or acquired diseases that affect condylar growth. The condyle is small, but condylar morphology usually is normal.

The etiology can be congenital, developmental, or acquired. Congenital hypoplasia most frequently results from abnormal development of the first and second branchial arches. Most patients with congenital mandibular hypoplasia have associated syndromes. More than 60 syndromes having mandibular hypoplasia as a component have been described. The most common is oculo-auriculo-vertebral (OAV) spectrum, which includes hemifacial and bifacial microsomia. The second is Treacher Collins' syndrome. A retrospective analysis of all patients with planned surgical treatment of congenital mandibular hypoplasia at the Children's Hospital of Philadelphia between 1975 and 2003 was performed. The investigation revealed 266 patients with congenital mandibular hypoplasia. One hundred forty-eight presented with OAV spectrum, 52 with Treacher Collins' syndrome, 31 with Pierre Robin sequence, 17 with miscellaneous syndromes, and 18 were identified as having congenital mandibular hypoplasia without any known syndrome.

Developmental hypoplasia presents with a class II malocclusion due to underdevelopment of the mandible or presents with a mandibular deviation if there is hypoplasia on one side (Fig.7-2-1). Theses patients may or may not have joint dysfunction, and is accidently detected during routine X ray examination for dental therapy (Fig.7-2-2). The pathogenesis is unknown yet.

Case 1, a 12-years-old female patient presented with a mandibular deviation for 3-4 years duration. The panoramic radiograph showed condylar hypoplasia in the left side and mandibular body asymmetric as well (Fig.7-2-1). We reviewed the radiograph taken 3 years before, and found mandibular body was asymmetric but the ramus and the condyle developed normally, indicating the left condyle was underdeveloped in the recent 3 years. No medical history and no signs of TMD were found.

Case 2, a 42-years old-female patient. Show below is her the panoramic radiograph taken before her implant treatment. The left condyle was found to be hypoplasia, the first molar in the left mandible was missing (Fig. 7-2-2). The mandibular ramus and body were nomal on both sides. She denied any TMJ symptom, no signs of TMD were found.

Acquired hypoplasia includes oncologic defects, radiation damage, trauma, and hemifacial atrophy.

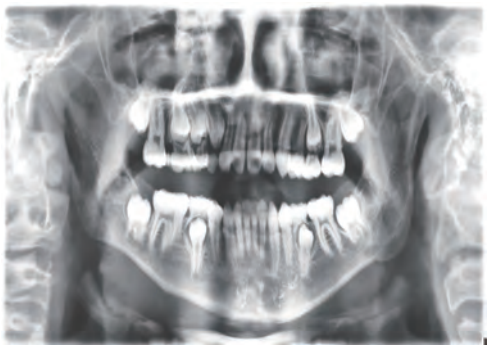

Fig. 7-2-1
Panoramic radiograph showing developmental condylar hypoplasia on the left side, with a mandibular deviation

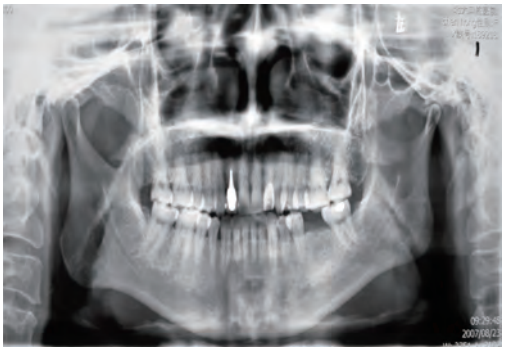

Fig. 7-2-2
Panoramic radiograph showing left condyle hypoplasia.

**b. Oculo-auriculo-vertebral spectrum**

Oculo-auriculo-vertebral spectrum (OAV) is also called as oculo-auriculo-vertebral syndrome, first and second branchial arch syndrome, hemifacial microsomia, or otomandibular dysostosis.

It is a congenital condition in which the lower half of the face is unilaterally underdeveloped and does not catch up with normal growth during childhood. The occurrence of oculo-auriculo-vertebral spectrum is between 1 in 3000 and 1 in 5600 births, and there is a slight male predominance.

Etiology of oculo-auriculo-vertebral spectrum is unknown, but is usually sporadic. It was thought to be caused by abnormal changes in blood vessels and the disruption of the blood supply during embryonic development (early vascular disruption) at about 30-45 days of gestation. However, a few cases have had a positive family history suggesting autosomal dominant, autosomal recessive, or multifactorial inheritance.

The clinical picture of oculo-auriculo-vertebral spectrum varies from a little asymmetry of the face to severe under-development of one facial half with orbital implications, a partially-formed ear or even a total absence of the ear (Fig,7-2-3A).

The chin and the facial midline are off-centered, and deviated to the affected side (Fig. 7-2-3B). Other asymmetric symptoms are the unilateral hypoplastic maxillary and temporal bones, a unilateral shorter zygomatic arch and malformations of the external and internal parts of the ear. Auditory problems (conduction deafness) as a result of malformations in the middle ear and facial nerve dysfunction (temporal and zygomatic branch of the facial nerve) are very common in these patients: 30–50% of the patients have auditory problems. The masseter, temporal and pterygoid muscles, and the muscles of facial expression are hypoplastic on the affected side. In most cases, there is an under-developed condyle (Fig. 7-2-3C), but aplasia of the mandibular ramus and/or condyle, with the absence of one glenoid fossa also sometimes occurs. In these cases, the maxilla is hypoplastic on the affected side.

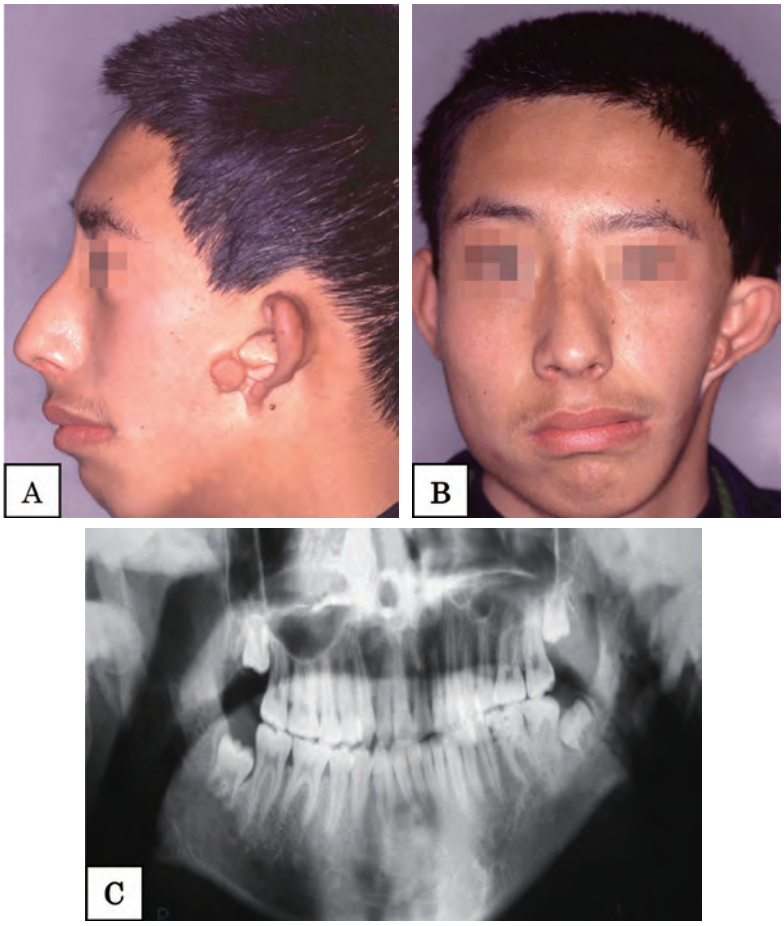


Fig. 7-2-3
A. Malformation of the external ear on the left side.
B. Asymmetry of the face, with the chin and the facial midline off-centered and deviated to the left side
C. Panoramic radiograph showing unilateral hypoplastic maxillary and mandibular bones with the under-developed condyle on the left side.

Deafness should be tested for at an early age, and speech therapy is often necessary.

Help may be required for feeding problems and encouraging weight gain in early infancy. Any congenital heart defects may require surgery. Plastic surgery may be used to reconstruct the ear, and bone distraction techniques are available to artificially lengthen the jaw bone to improve growth on the face. Children may also need ongoing orthodontic treatment.

**c. Condylar hyperplasia**

Condylar hyperplasia of the mandible is a state of overdevelopment that leads to facial asymmetry, mandibular deviation, malocclusion, and articular dysfunction. The condition was first described by Adams in 1836. Since then, there have been numerous reports in the literatures and it is now considered to be one of the more common conditions for which patients seek surgical attention. The cause of condylar hyperplasia has yet to be elucidated; trauma, infection (particularly in the TMJ), heredity, and intrauterine influences have been advanced as possible etiologic factors. It usually occurs in early adolescence or the mid-teens, with increasing deformity until growth is complete, usually by the end of the second decade.

Clinical features of condylar hyperplasia include an enlarged mandibular condyle, elongated condylar neck, outward bowing and downward growth of the mandibular body (Fig. 7-2-4), causing fullness of the affected side and flattening of

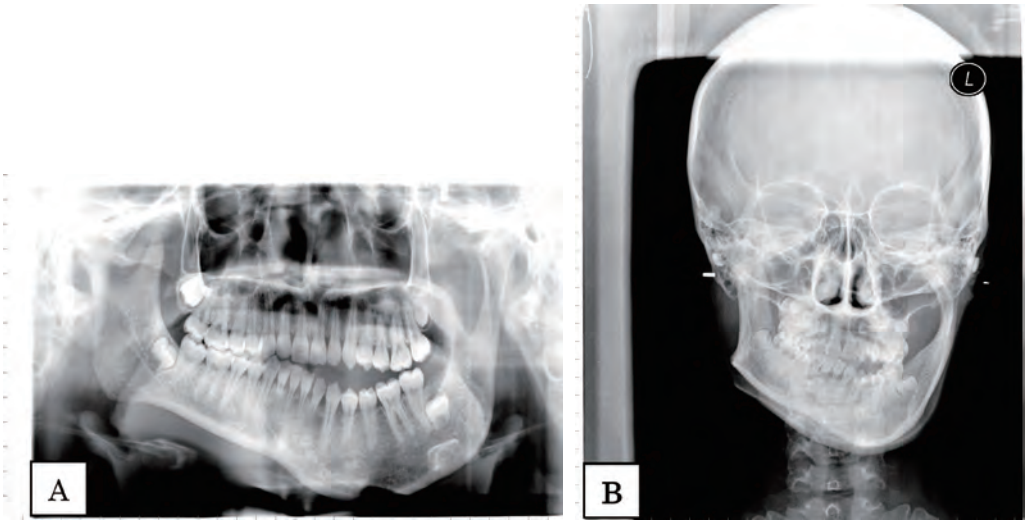


Fig. 7-2-4

A. Panoramic radiograph showing an enlarged mandibular condyle, elongated condylar neck, outward bowing and downward growth of the mandibular body on the left side.
B. Radiograph of the posterior-anterior projection showing facial asymmetry with fullness of the affected side

the contralateral side of the face. If the deformity occurred before growth is complete the occlusal plane is usually slanted because of dental compensation, whereas posterior open bite is usually apparent if the deformity occurred after completion of growth.

The basic consideration in the management of facial asymmetry secondary to condylar hyperplasia is to control the growth process to allow more balanced facial development. High condylectomy or condylar shave in actively growing cases can be performed in concert with other related mandibular surgery. Orthodontic treatment is essential afterward in patients treated by early condylar resection. Surgical methods are used for correcting asymmetry- mandibular sagittal split osteotomy, subcondylar ramus osteotomy, Le Fort I wedge osteotomy to re-level the tilted occlusal plane, and contouring of the lower mandibular margin can be selected depending on the degree of deformity.

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(Kai-yuan Fu)

# *7-3. Inflammatory diseases of temporomandibular joint*

**a. Septic arthritis of the temporomandibular joint**

It is a rare infectious disease that has been reported infrequently. Many organisms are capable of causing this problem, but the most likely include Neisseria gonococcus, Staphylococcus, Streptococcus, and Haemophilus influenzae. The pathogenesis of the infection is either local spread or hematogenous dissemination from a distant site secondary to a systemic process. The synovium, because it is highly vascular and has no limiting basement membrane, is particularly vulnerable to infection via this route.

This condition is usually associated with local or general predisposing factors. Local factors include blunt trauma, burn wounds, and iatrogenic causes; while general factors include systemic and autoimmune disease (i.e., rheumatoid arthritis, diabetes, immunosuppression, hypogammaglobulinemia), prolonged use of systemic steroids, and sexually transmitted diseases.

Bacterial infection of the TMJ promotes synovial hyperplasia, necrosis, granulation tissue, and abscess formation. The proteolytic enzymes released by granulocytes may cause irreversible changes within 7 days. Patients may present with pain, trismus, preauricular erythema, fever, malaise, malocclusion with ipsilateral posterior open-bite, regional lymphadenopathy, and contralateral mandibular deviation from increased joint fluid. The serum leukocyte count may be normal or increased. Erythrocyte sedimentation rate will typically be higher than in osteomyelitis and is more reliably elevated than a serum leukocyte count. C-reactive protein level may be used to follow disease severity and resolution. Blood cultures are mandatory for all joint infections, however, only 40% will be positive. Plain film such as Schüllar projection is very helpful for imaging diagnosis (Fig. 7-3-1). Increased intracapsular fluid caused by accumulation of inflammatory exudates and pus results in joint space widening and anterior/inferior displacement of the

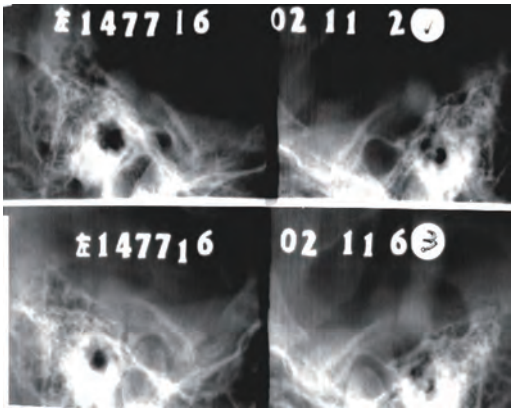

Fig. 7-3-1.
Plain film of Schüllar projection (upper) showing joint space widening and anterior/inferior displacement of the condylar head on both sides, but more severely on the right side (diseased side). The widened joint space was reduced (lower radiograph) 4 days after arthrocentesis treatment.

condylar head. Bony erosion may not be detected radiographically until several weeks. Computed tomography and magnetic resonance imaging may be required for further reevaluation and differentiation.

Timely diagnosis and treatment are essential to reduce the possibility of complications. Delayed treatment may cause destruction of the articular eminence or coronoid and condylar involvement, which could be seen at approximately 7 to 10 days after onset of symptoms. Ankylosis could be the result of undiagnosed septic arthritis of the TMJ. Different surgical methods have been proposed for joint drainage and decompression: needle aspiration, arthroscopy, and arthrotomy. If aspiration fails to decompress the joints and the effusion persists beyond 3 to 5 days, joint arthrotomy or arthroscopy should be considered. A controversy exists as to the use of daily joint antimicrobial irrigation. Several studies have shown that systemic antibiotics achieve adequate concentrations for the treatment of septic arthritis and antimicrobial joint irrigation may induce chemical synovitis with direct microbial inoculation.

Physical therapy is necessary to improve mandibular range of motion and deviation during mouth-opening. Moreover, early rehabilitation exercises are important to avoid complications such as fibrosis and ankylosis.

The complications of septic arthritis of the TMJ include intracranial abscess, destruction of the joint, ankylosis, and impaired growth of the condyle, so these patients should be followed up to monitor the growth of the mandible.

**b. Rheumatoid arthritis of the temporomandibular joint**

Rheumatoid arthritis (RA) is a chronic, systemic inflammatory disorder that may affect many tissues and organs, but principally attacks the joints producing an inflammatory synovitis that often progresses to destruction of the articular cartilage and ankylosis of the joints. Although the cause of rheumatoid arthritis is unknown, autoimmunity plays a pivotal role in its chronicity and progression.

The prevalence of TMJ involvement in patients with rheumatic disease has been found to vary greatly, depending on diagnostic criteria, the population studied, and the means of assessment of the TMJ. Lin et al (2007) reported that RA patients were found to have a very high prevalence of TMD (92.9%), but only 51.8% of them had experienced TMJ-related problems, while the others had remained clinically silent. Moreover, most of the patients (91.1%) had subjective TMD score < 6. Ardic et al also reported that nearly all of RA patients (93.9 per cent) had TMD symptoms, and

almost all of them had positive findings in high resolution computed tomography. The most common signs and symptoms of TMJ involvement are joint pain, edema, crepitation, and limited movement, all of which are associated with jaw stiffness on mouth opening. The most common radiographic findings are erosion and flattening of the head of the mandible and articular fossa and reduction of the joint spaces (Fig. 7-3-2), usually noticed 5 to 10 years after the onset of symptoms.

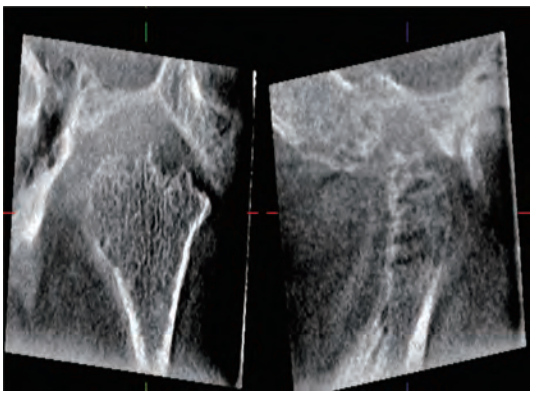

Fig. 7-3-2
Cone beam CT showing severely erosive changes of the codyle affected by rheumatoid arthritis of TMJ.

Rheumatoid arthritis is diagnosed chiefly on symptoms and signs, but also with blood tests and X-rays. Diagnosis and long-term management are typically performed by a rheumatologist.

Various treatments are available. Non-pharmacological treatment includes physical therapy and occupational therapy. Analgesia (painkillers) and anti-inflammatory drugs, as well as steroids, are used to suppress the symptoms, while disease-modifying antirheumatic drugs (DMARDs) are often required to inhibit or halt the underlying immune process and prevent long-term damage. In recent times, the newer group of biologics (biological agents) has increased treatment options.

**c. Osteoarthritis of the temporomandibular joint**

Osteoarthritis (OA, also known as osteoarthrosis, degenerative arthritis, degenerative joint disease), is a group of diseases and mechanical abnormalities entailing degradation of joints, including articular cartilage and the subchondral bone next to it. Rheumatoid arthritis is classified as either primary or secondary according to the etiology.

There is usually an underlying cause for rheumatoid arthritis, in which case it is described as secondary rheumatoid arthritis. If no underlying cause can be identified it is described as primary rheumatoid arthritis. Secondary rheumatoid arthritis involves the same process of articular breakdown with osseous remodeling, which occurs in the primary condition. Potential etiological factors include direct trauma to the TMJ, local TMJ infection, or history of active systemic arthritis. The most common known cause is TMJ disc displacement, there is clearly a close relationship between the two conditions.

Diagnosis is normally done through X rays. Radiographic evidence of structural bony changes include erosion, osteophytic formation, subchondral sclerosis, and joint space narrowing (Fig. 7-3-3, -4).

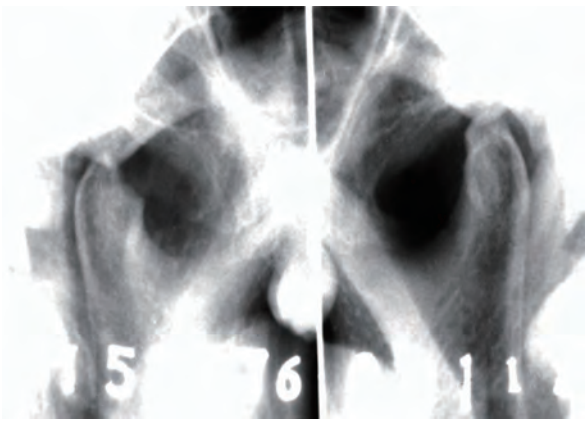


Fig. 7-3-3
Radiograph of transpharyngeal projection showing erosive change in the left condyle, and osteophytic formation on the right side.

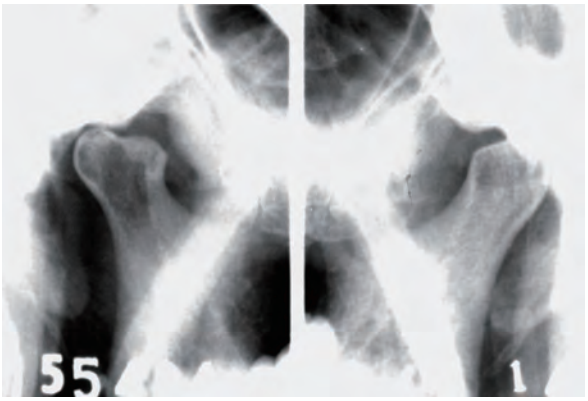


Fig. 7-3-4
Radiograph of transpharyngeal projection showing osteophytic formation and subchondral sclerosis of the left condyle.

Treatment of rheumatoid arthritis consists of lifestyle modification and medication and other interventions to alleviate pain. The chapter associated with temporomandibular disorders will introduce more details about the diagnosis and the treatment of TMJ rheumatoid arthritis.

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(Kai-yuan Fu)

# 8

# *Diseases of Nerve*

**a. Palsy of facial nerve (Bell's palsy)**

**Palsy of facial never (Bell's palsy)**

Bell's palsy is an idiopathic peripheral facial palsy which can be diagnosed if no specific cause can be identified by clinical examination. It was first described by Charles Bell in 1821 and named after him by neurologist William Growers. It is the most common cause of acute facial paralysis with an incidence rate of 25 per 100000 in America; 20 per 100000 in Europe; 30 per 100000 in Japan; 28 per 100000 in China according to statistic data in 1986 and 49.77 per 100000 according to new statistic data. The incidence is higher in north of the Yangtze River than south. It is more likely to strike older people, women and people living in rural areas.

**Etiology and pathology**

In traditional opinions, the causes of Bell's palsy are external factors such as cold stimulation, virus infection and the stress state. The spasm of small feeding arteries to the facial nerve would cause ischemia and swelling of nerve, and compression of the small blood vessels caused by the swollen nerve will increase the ischemia and result in facial paralysis. Some authors suggested that lesion of central nervous system or hereditary factors were possible causes.

The possible external etiological factors are as follows.

1. Environment factors. In traditional opinion, the disorder of blood supply to the facial nerve caused by cold stimulation would induce facial paralysis.
2. Viral infection. Viral infection is the highlighted factor of facial paralysis since McCormick suggested herpes simplex virus was a possible cause in 1972. Other viruses found until now including herpes simplex virus type 1, cytomegalovirus, herpes zoster virus, EB virus, coxsackie virus and human immunodeficiency virus. Herpes simplex virus is the most common cause of facial paralysis.
3. Anatomy factor. The facial nerve passes the internal ear in a narrow and zigzag canal. The labyrinthine segment which extends from the internal auditory canal to the geniculate ganglion is covered by a thin layer of glia without any epineurium, which make it quite vulnerable to any type of injury that results in edema.
4. The stress state of body. Most Bell's palsy happens when patients are fatigued or in a stress state, so some experts advocate it as another etiological factor.

   The pathological change of Bell's palsy is edema and swelling of facial nerve and degeneration of neuraxon and medullary sheath. The segment in facial nerve

canal and stylomastoid foramen is often seriously affected. Sometimes the osteocytes in mastoid and facial nerve canal are degenerated.

**Symptoms**

The palsy is often sudden in onset without any presage and evolves rapidly, with maximal facial weakness developing within two days. Most cases attack in the morning with unilateral involvement. Bilateral involvement is rare. Total hemifacial paresis is the typical symptom. Paralysis of orbicularis oris would cause drooping of corner of mouth and impaired closure of mouth. Orbicularis oculi paralysis would cause losing of the involuntary movement in levator palpebrae superioris which would result in palpebral fissure enlargement and exposure of conjunctiva which would cause conjunctivitis. Bell sign—upward diversion of the eye on attempted closure of the lid—is seen when eye closure is incomplete. Loss of wrinkles in forehead and frowning difficulty are the typical signs of Bell's palsy or peripheral facial paralysis which are the evidences to differentiate from central facial paralysis. The paralysis symptom will be more serious in motion so that the recovery and the effect of treatment should be evaluated in movement state. Associated symptoms may be hyperacusis, decreased production of tears, altered taste, otalgia and facial or retroauricular pain, depending on the location of lesion.

**Diagnosis**

It is easy to identify Bell's palsy by symptoms, medical history and clinical examinations. Many new techniques are developed to confirm the location of lesion, degree of injury, prognosis and surgical indications.

The examinations of peripheral facial nerve function include facial action test and electrodiagnosis. Nerve excitability test (NET), maximal stimulation test (MST), and electroneurography (ENoG) also called electromyography (EEMG) have the practical values for prognosis anticipation. Other tests to locate the location of injury are testing of taste, auditory and tearing.

Testing of taste: Hold the tongue and dry the saliva, put water with sugar or salt on the 2/3 of the front in the involved side. Patients could show whether there is taste by any motion without moving the tongue in case the water drops on the normal side to influence the result.

Auditory test: The purpose is to check the function of stapedial muscle by tuning fork tests. When stapedial muscle is paralyzed, the balance with tensor tympani muscle is lost which would result in hyperacusis.

Tearing test: Schirmer test is used to observe whether the geniculate ganglion is

involved. The details are given in chapter 6.

The location of nerve injury could be indicated based on the different symptoms.

(1) Distal to the stylomastoid foramen: facial nerve paresis.
(2) Chorda tympani nerve to stapedial nerve: facial paresis + loss of taste + salivary disorder
(3) Stapedial nerve to geniculate ganglion: facial paresis + loss of taste + salivary flow disorder + abnormal hearing.
(4) Geniculate ganglion: facial paresis + loss of taste + salivary and tearing flow disorder + abnormal hearing.
(5) Cerebellopontine angle to geniculate ganglion: facial paresis + mild disorder of sense and secretion + tinnitus and dizziness if auditory nerve is affected.
(6) Pontine nucleus: facial paresis + mild disorder of sense and secretion + abducens nucleus is involved sometimes + contralateral hemiparesis if corticospinal tracts are involved.

Radiologic evaluation is another option to diagnose lesions of labyrinth segment in internal auditory canal. The facial nerve could be observed in high resolution MRI especially when contrast agent Gd or carbohydrates is applied.

Bell' palsy should be differentiated from supranuclear paralysis, nuclear paralysis, cerebellopontine angle lesion, auditory nerve tumor, tympanitis, and traumatic facial paralysis. Some syndromes such as Ramsay Hunt syndrome and Melkersson syndrome will involve the facial nerve function.

**Treatment**

The natural development of Bell' palsy can be divided into acute phase, remission phase and sequelae phase.

The main aims of treatment in the acute phase (1~2 weeks) of Bell's palsy are improving circulation, inhibiting edema and inflammation to speed recovery.

1. Patients in the acute phase should be treated with high dose corticosteroids as soon as possible. Dexamethasone 10 mg per day should be prescribed by intravenous administration for the first 3 days followed by prednisone 10mg taken orally 3 times per day for another 3 days which is tapered over until the tenth day.
2. Sodium Salicylate 0.3~0.6 g should be taken orally 3 times per day for vasodilation.
3. Neurotrophic drugs Vitamin B1 100 mg and Vitamin B12 500 μg are administered by intramuscular injection per day. Acupoint-injection therapy with Vitamin B is another option after 7 days.

4. If obvious viral infection factors are present, antiviral agents such as ribavirin, adamantanamine, or radix isatidis infusion should be administered.
5. Physical therapy can be considered with ultrashort wave and ultrared ray. Hot pack and high stimulation physical therapy should be prohibited in the acute phase.

Eye care with eye drops or ointment should be emphasized during illness duration. Acupuncture treatment of strong stimulation is not recommended which would cause facial spasm. Surgical intervention should be performed with great care for there is no significant difference of recovery rate between surgery group and no surgery group as reported.

In the remission phase, the aim of treatment is to speed the recovery of facial nerve conduction and strengthen the function of expression muscles. The therapeutic methods were mentioned in the previous chapter of traumatic facial paralysis. Muscle stimulants, as Neostigmine, Fursutiamine, Galanthamine et.al can also be administrated.

In the sequelae phase, the aim is rehabilitation of facial anomalies because there is no prospect of further recovery of facial nerve function and synkinesis and/or facial spasm may persist in this phase.

**Prognosis**

Bell's palsy tends to carry a good prognosis. The severity of facial palsy, treatment protocol and age of patients are some of the influencing factors. Most patients would recover completely in 2~3 months. Mild patients without nerve degeneration would show first signs of recovery within 3 weeks after onset and recover to normal within 2 months. Patients with nerve degeneration would recover in 3~6 months. Severe cases would recover more slowly with poor prognosis. Proper treatment in the acute stage and functional muscle training in the remission phase are of great importance to alter the prognosis. Many researches have confirmed that ENOG is effective in differentiating patients with Bell's palsy into those who have an excellent prognosis from those who might have a poor return of facial movement if it is performed within 3 weeks.

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**b. The other diseases of facial nerve**

**Facial spasm**

Facial spasm also called hemifacial spasm (HFS) is characterized by paroxysmal bursts of involuntary tonic or clonic activity occurring in muscles innervated by the facial nerve. It can be divided to primary type and secondary type. The former is idiopathic hemifacial spasm (IHFS). The latter is also called symptomatic facial spasm.

**Etiology**

The cause of primary facial spasm is still controversial now. One possible cause is pathological factors in the central or periphery part along the conduction pathway of facial nerve. The central hypothesis also called nucleus hypothesis assumes that the cause is stimulation in the facial nucleus or supranuclear portion. The periphery hypothesis is more popular which attributes the etiology to the demyelination caused by pressure to the intercranial segment of facial nerve trunk.Arteriosclerosis and hypertension are possible reasons to hemifacial spasm. Some cases of facial spasm are sequelae of facial paralysis.

**Clinical symptom**

Facial spasm is more likely to happen in older people and females. It has a slow onset and no self-healing. The spasm, which is paroxysmal, intermittent, rhythmic and out of control, starts from the lower eye lid most of the time and spreads to the ipsilateral expression muscles gradually. The duration is several seconds to 10 minutes. Unilateral involvement is common. It would be serious when patients are nervous or tired and relieve during sleep. Pain can be observed in a few cases and headache, tinnitus, taste disorder in the front of the tongue are concomitant symptoms of some cases. No positive signs are found by neurologic examinations. Mild facial paralysis is the symptom in the late period. It progresses slowly without a remission phase. The frontalis involvement is rare and platysma muscle is affected sometimes.

**Diagnosis**

A diagnosis can be made according to the history and symptoms. EMG shows fibrillation potential and EEG has no abnormal signals. It should be differentiated from hysterical blepharospasm, habitual blepharospasm, the muscle spasm induced by trigeminal neuralgia, cerebellopontine angle tumor, inflammation or tumor of the facial nerve and brain injury. Sometimes it is differentiated with tarantism and athetosis. Hysterical spasm often affects females and accompanies with other hysterical symptoms. The EEG is normal. Children and adolescents are easily affected by habitual blepharospasm. It involves both sides of the face like tarantism. The latter has involuntary movements of extremities.

**Treatment**

There is no ideal treatment for primary facial spasm for the cause is still unclear. The treatment is the same as trigeminal neuralgia. Sedative drug, antiepileptic drug, neurotrophic drug, ultrasonic, iontophoresis of Calcium, Chinese herbal medicine and acupuncture all have been reported with unfavorable effect. Block therapy is another option. Radiofrequency thermo coagulation can be used when necessary. Because it would cause the degeneration of facial nerve and results in facial paralysis, strict indications for surgery and post surgery nursing are very important. Surgery treatment is still controversial now. Facial nerve squeezing, neurotomy and anastomosis to other cranial nerves are all abandoned already. The intracranial microvascular decompression with a high risk rate is not accepted by all patients. The long-term effect has not been confirmed yet.

Botulinum toxin is a neurotoxin protein produced by the bacterium clostridium

botulinum. There are seven serologically distinct toxin types. Local injection of botulinum toxin A is an effective measure for hemifacial spasm. By inhibiting the release of acetylcholine from the axon endings in peripheral motor nerves, the toxin causes flaccid (sagging) paralysis of muscles. Botulinum toxin A (Heng Li®) produced by Lanzhou Institute of Biological Products (LIBP) is widely used in China. The dosage used for hemifacial spasm is 2.5~5.0 U per point with total dosage less than 55 U each time and no more than 220 U per month. Mild facial paralysis is the main sequelae. It tends to relapse after an effective period of 3 to 6 months.

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(Zhi-gang Cai)

# 9

# Congenital Anomalies

# 9-1. Cleft Lip and/or Palate

**Epidemiology**

Cleft lip and palate is an external malformation that occurs about one in 600 births in Japan. The incidence ratio among Caucasians, Blacks and other races is 1:0. 34: 1.21, so it is highest in Asians. In a survey of 4209 cleft lip and/or palate patients at the Cleft Palate Center of Aichi-Gakuin University Hospital, cleft lip and palate was the most common (41.7%) followed by cleft lip/cleft lip and alvelous (32.6%) and cleft palate (25.4%) (Table 9-1-1)[1]. Cleft lip/cleft lip and alvelous occur more often in males than in females, but the difference is not significant. Cleft lip and palate is more prevalent in males and cleft palate is more prevalent in females (Table 9-1-2)[2]. A parent of 2 to 3% of the probands have cleft lip/cleft palate, which is about 10 times greater than 0.2% in the general population. The percentage of affected siblings is reported to be from about 8 to 18% in Japan.

Table 9-1-1 Cleft Type and Sex

| | CL+CLA | CLP | CP | Total |
|---|---|---|---|---|
| Male | 737 | 1069 | 418 | 2224 |
| Female | 637 | 689 | 649 | 1985 |

Table 9-1-2 Cleft Incidence

| Right side | Left side | Bilateral | Total |
|---|---|---|---|
| CL 63 (31.7%) | 110 (55.3%) | 26 (13.1%) | 199 (100%) |
| M. 34 F. 29 | M. 56 F. 56 | M. 17 F. 9 | M. 105 F. 94 |
| CLP 65 (21.8%) | 151 (50.7%) | 82 (27.5%) | 298 (100%) |
| M. 35 F. 30 | M. 91 F. 61 | M. 49 F. 33 | M. 175 F. 123 |

**Development**

The structures of the facial and oral area are formed at the facial primordium around the stomatodeum between the 4th and 5th week of fetal life. This facial primordium appears as the prominence. Five of the head side of the frontonasal prominence, a pair of maxillary prominence and tail side of a pair of mandibular

prominence of the side are distinguished at the embryonic 4 weeks. The incidence of the cleft lip appears to be due to disorders in fusion of facial primordium as per theory. Palatal formation starts with an elevation in bilateral palatine processes onto the tongue in the form of vertical shelves, followed by a downward migration (elevation stage). The elevated palatine processes then elongate and contact each other at the midline (contact stage). Adhesion and self-decomposition of the epithelium occur at the contact location, and mesenchymal tissues then fuse (fusion stage)(Fig. 9-1-1). Cleft palate must therefore be induced by a disruption during the developmental process of the palatal shelves. Cleft palate can occur due to a failure in the elevation of palatal shelves, failure in elevated palatal shelves to initiate contact, failure in proper fusion, or breakdown subsequent to fusion[3].

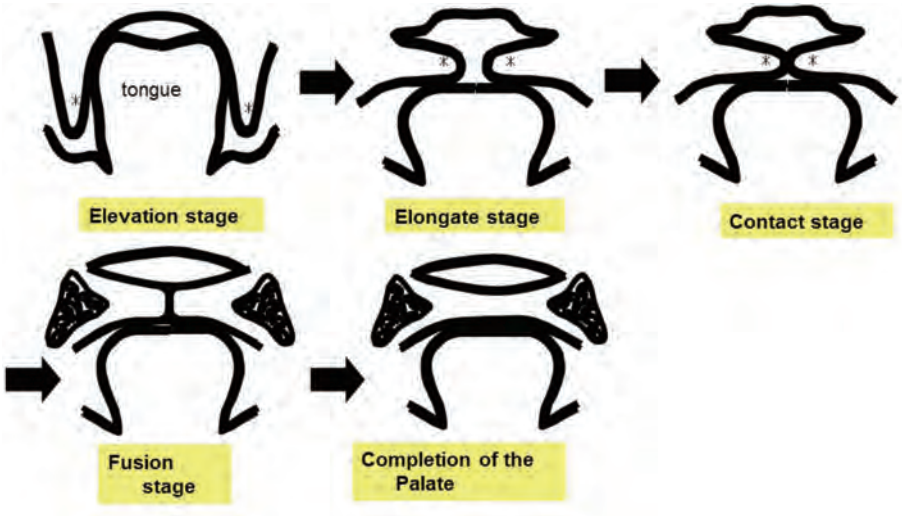


Fig . 9-1-1 Palatal formation stage

**Etiology**

The etiology of cleft palate can be explained by a multifactorial threshold mechanism involving both genetic and environmental factors. The genetic factors, such as the MSX1, TGFb3, TBX22, IRF6, PVRL 1 have been reported[4]. The environmental factors, vitamin A, estradiol, Dioxion (TCDD), and Alcohol have been reported[3]. Environmental factors that induce CL / CP in experimental animals are often found, but environmental factors that can be concluded as the cause of CL / CP in humans is small.

**Treatment**

**a. Pre-surgical treatment**

1) Mechanism of the normal sucking

Suckling movement develops as a reflection movement of swallowing and sucking in the embryonic stage. Basic ability of sucking movement has been already acquired before birth.

About fetal 10 weeks: the movement of swallowing and mandibular movements already begins.

Fetal 22 weeks: sucking motion begins.

Fetal 27 weeks: rhythmic movement of sucking and swallowing begin.

Fetal 37 weeks: fetus begins swallowing amniotic fluid- 700ml by effective suckling and also begins to discharge from the urine to the same degree.

In healthy infants sucking comprises of 4 searching reflex, lip reflex, sucking reflex and swallowing reflex, which occur as a chain reaction. In addition, suckling movement is divided into three movements of extrusion of milk, drinking and swallowing.

2) Feeding disorder

Feeding disorders refer to a state in which sufficient feeding amount cannot be secured. It is roughly classified into ones that cannot feed due to reduction or lack of feeding motivation, sucking difficulties and swallowing difficulties due to structural problems. Reduction or lack of feeding motivation occurs in diseases including cerebral palsy, congenital heart disease, chromosomal abnormality such as Down's syndrome and neonatal myasthenia gravis. On the other hand, structural problems include cleft palate, oral tumor, stomatitis and ankyloglossia in the infant side, and the inverted nipple, a giant nipple and mastitis in the maternal side. It would be left to the specialist if resolved when cause of the disease is improved. CLP patients have a problem due to the lack of negative pressure in the oral cavity when they suck the nipple, due to structural problems.

For nursing management of this disease, various contrivances have been made at each facility. In many facilities palatal plate (Hotz plate) (Fig. 9-1-2) has been used. Hotz plate performs a maxillary induction of abnormal morphology of the palate of CLP patients and the stabilization of the tongue. Further, it can also be expected to increase suckling amount. If CLP patients have a sucking problem, they may be advised special feeding bottles and nipples (Pigeon cleft palate nipple and bottle, KR nipple, (Pigeon Corp), special needs feeder nipple (Medela Corp), etc.

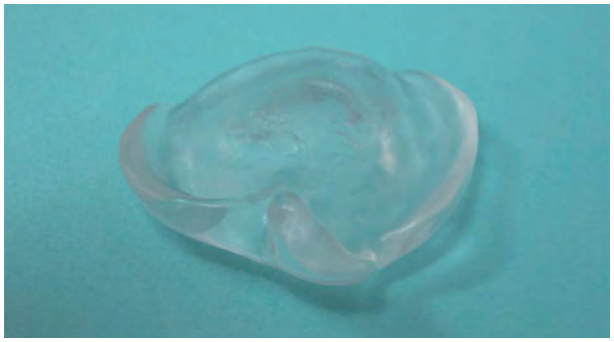

Fig. 9-1-2 Hotz plate

3) Presurgical Nasoalveolar Molding (PNAM)

PNAM treatment for patients with cleft lip and palate (CLP) is performed for the purpose of improving the deformed columella nasi and depressed nostril on the cleft side and is expected to reduce deformation during the operation. The bridge of the nose is raised with PNAM (Fig. 9-1-3).

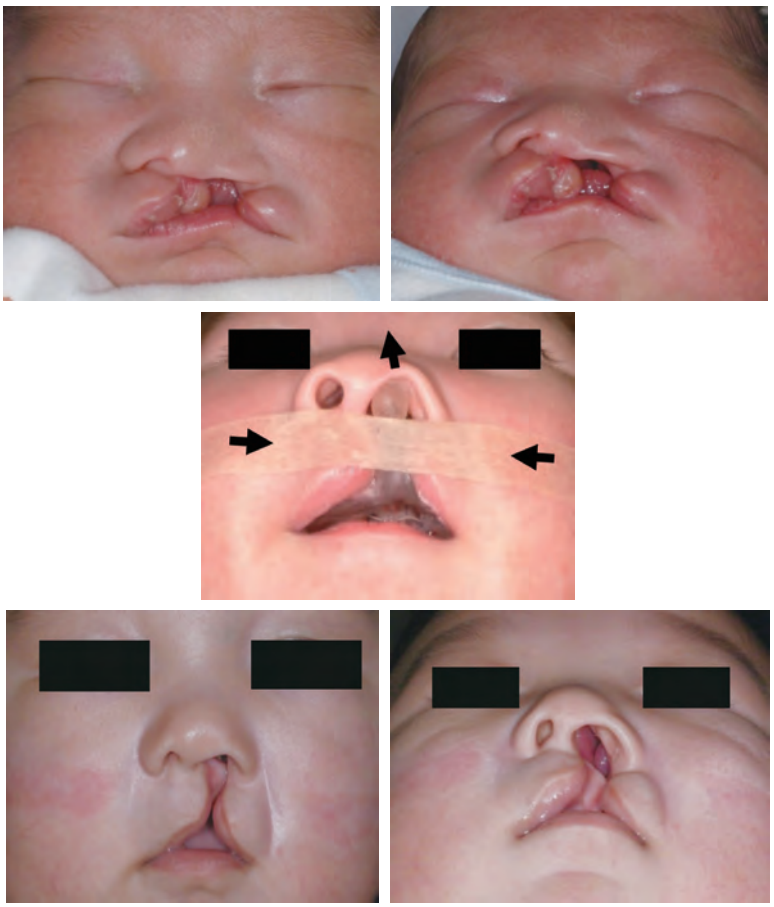

Fig. 9-1-3 Presurgical nasoalveolar molding (PNAM)

**b. Surgical treatment**

1) Unilateral Cleft Lip/Nose Repair after PNAM

Unilateral cleft lip is influenced by muscle imbalance, skeletal hypoplasia and asymmetry of the skeletal base. These patients have deformed columella nasi, depressed nostril on the affected side and enlarged nasal ala on the affected side, etc.

Muscle imbalance affects nasal symmetry in both complete and incomplete unilateral cleft lip/nose by distorting the position of the ala base and shape of the nostril. With a partial or complete discontinuation of the orbicularis oris muscle in unilateral cleft lip/nose, the extrinsic muscles of facial expression, which are attached to the orbicularis oris muscle on the cleft side, pull the ala base more laterally compared to the non-cleft side. The existing muscle imbalance also changes the position of the alar cartilage, as well as the orientation of the nostril from an oblique to a horizontal orientation. Because of the insertion of muscle on the base of septum and columella on the non-cleft side, contraction of the muscle pulls the septum and columella toward the non-cleft side. Surgery techniques of cleft lip are long-existing and a number of surgical procedures have been published. Earlier, the surgical method was simple surgery to suture only the bifida edge. However, various innovations have been made in order to obtain a good lip and outer nose forms. Surgery of unilateral cleft lip has been reported as stencil method of Tenison as triangle flap method. After that, Randal method and Cronin method improved the Tenison method and are still widely used. Design is extremely simple and it is possible to adjust the design during the surgery. It is possible to form the shape of a good nose and to decrease the extreme ablation amount of tissue. These techniques have a number of advantages, such as they can form a natural lip. However, the characteristic of Millard method is a surgical technique for removing the deformity of cleft lip. Accordingly it is not adaptation of Millard method in our surgery after PNAM. In general, authors operate when cleft lip patient gain a body weight of 6kg and at 6months of age.

a) Design (Fig. 9-1-4)

We are using a small triangular flap method in accordance with Cronin method. Triangle flap that it is easy to form the philtrum column is appropriate to give a natural feel in the case of after PNAM treatment. Key identifiable points are marked on the lip and nose. The base of each ala is identified and marked using methylene blue or appropriate marking pen. The alar base, on the cleft side, is usually elongated and distorted compared to the non-cleft side. The peak of the Cupid's bow is identified and marked on the normal side. The height of the lip, from the alar base to the peak of the Cupid's bows at rest and

without tension on the non-cleft side, is measured using a caliper or is just estimated. This is the height to be achieved on the cleft side. This is usually 6-11 mm and averages at 7mm in a 3-month old. The mid-line nadir, or lowest point, of Cupid's bow is identified and marked. An equal distance, from the height of Cupid's bow on the noncleft side to the mid-line of Cupid's bow, is used to identify the peak of the new Cupid's bow on the cleft side, and is marked on the vermilion-cutaneous junction. The exact point may have to be altered a millimeter or two in order to have a lip that is long enough. The lip height needs to be equal to the normal side when completely dissected and placed on tension with a skin hook.

The wet-line is marked with dots along its course on the vermilion on both sides of the cleft. Identification of this line provides symmetry and improved color match of the vermilion border. The peak of the Cupid's bow and height of the lip on the lateral lip segment is determined by the height of the lip on the normal side, based on the initial measurement. The distance along the vermilion, and down the lateral lip segment, may be altered according to the height of the lip desired. It may be necessary to go along the vermilion cutaneous border, down the lateral lip segment, a few millimeters more in order to create lip, which is equal to the normal side. This may result in a shorter distance from the new peak of Cupid's bow on the medial cleft side, to the commissure of the lateral lip segment, as compared to the peak of the Cupid's bow to the commissure on the normal side. In the nasal floor of cleft side, it marks the midpoint of the columellar base and the alar base.

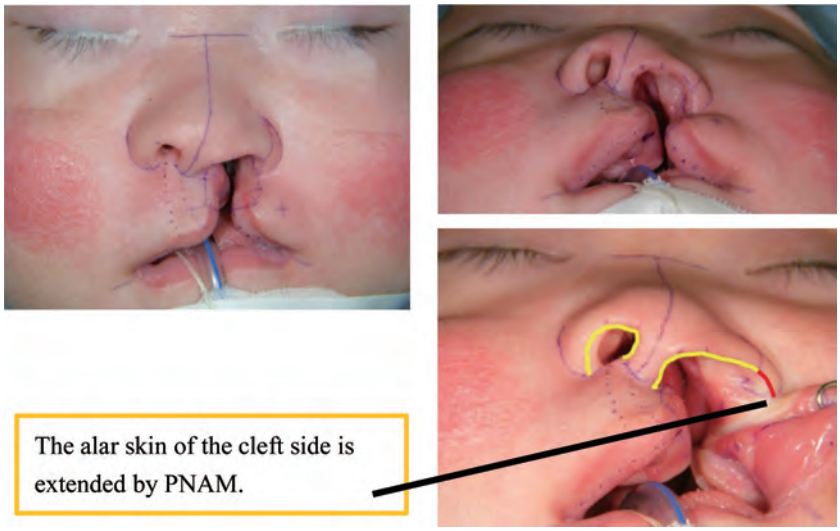


Fig. 9-1-4 Design

It is necessary for the design to consider the fact that the alar skin of the cleft side is extended and elevated by PNAM. The distance is measured to reach from the columellar base of the non-cleft side to the alar base through the nostril edge. After that, it is taken as the same distance on the cleft side. The alar of cleft side is extended as indicated in this point by the dotted line in Fig.4C. We mark a point at the same distance from the alar base of the non-cleft side to the midpoint from this point. In this way, post-operatively, cleft side nostril can be the same size as that of the non-cleft side. Measure the length of white lip of the non-cleft side. Measure the length of the white lip of cleft side. The point of the base of the triangle flap is taken by < (The length of the non-cleft side of the white lips) - (length of cleft side of the white lips) -1mm >. This way is designed to prevent the drooping of the cleft side postoperatively.

b). Incision

After local anesthesia, the incision is made for the cleft margin flap. Detachment is done from the alar base to a height of alar on the periosteum of the maxilla. You can get the mobility from alar side to the lip's median side. Then it is released of the tension for the inside of cleft side nostril to detach from under the periosteum to the Piriform aperture at the height of the gingival cheek transition (Fig. 9-1-5). Insert the dissecting scissors from the columellar base and alar, to sufficiently detach between the alar cartilage and skin (Fig. 9-1-6). It is confirmed that the dissecting scissors passes from the columellar base to alar base and, the space is made between the large alar cartilage and skin (Fig. 9-1-7). Next, release between the skin and the orbicularis oris muscle using the scalpel.

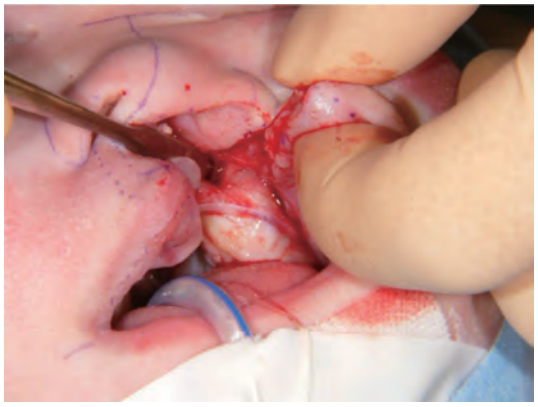

Fig. 9-1-5
Release of the tension for the inside of cleft side nostril

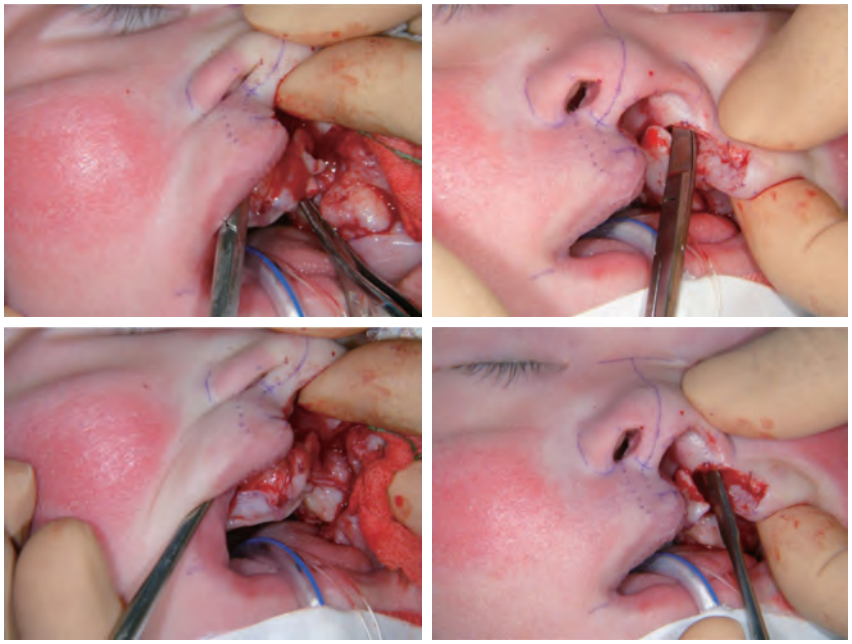

Fig. 9-1-6 Detachment between the alar cartilage and skin

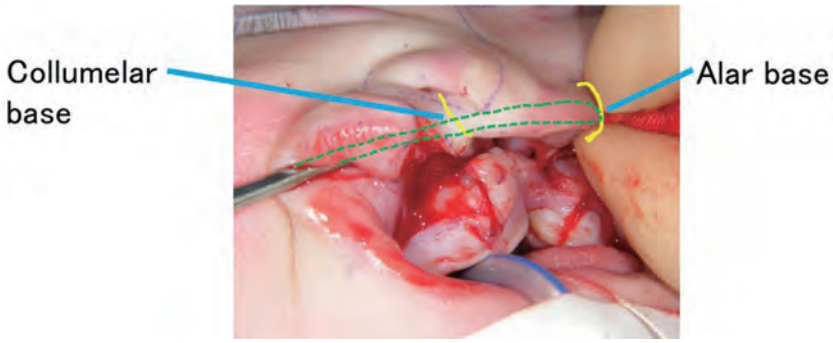


Fig. 9-1-7
Space made between the large alar cartilage and skin

c). Muscle sling formation (Fig. 9-1-8)

It is possible to form the philtrum column by overlapping the muscle of non-cleft side and the muscle of cleft side since it has released the orbicularis oris. Moreover, since it is possible to make the volume of the red lip less susceptible to the formation of the notches. This site is sutured using absorbing yarn. 4-0 nylon thread may be used if necessary.

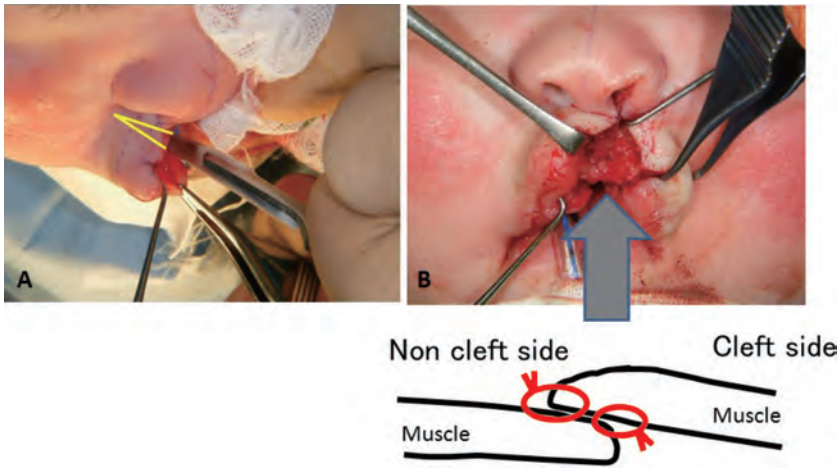


Fig. 9-1-8 Muscle sling formation

d). Nasal floor after provisional suture (Fig. 9-1-9)

Excise the excess tissue if present after provisional suture.

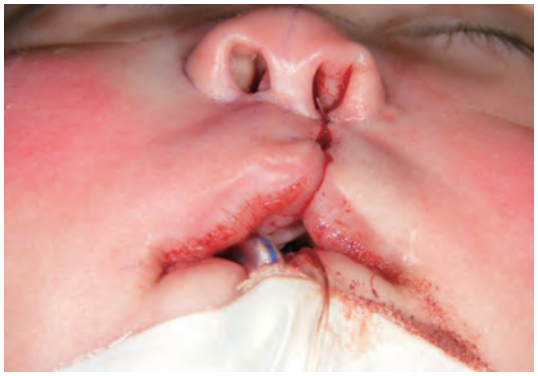

Fig. 9-1-9 Nasal floor after provisional suture

e). Rhinoplasty by the lifting of nylon threads (Fig. 9-1-10)

Prepare the nostrils form after the dermis and the skin suture. Authors do not use the open method by Reverse U incision for the decline of the nostril edge of cleft side. Fix the skin of the nose in several yarns of nylon in a part that can maintain a good nasal form because of the already detached border between the large alar cartilage and skin, as shown in Fig. 9-1-9. Secure the nylon thread without suture infections after one month and remove the stitches after that. It is sutured using 5-0 nylon for the dermis layer. In addition, it is sutured with 7-0 nylon for the skin layer.

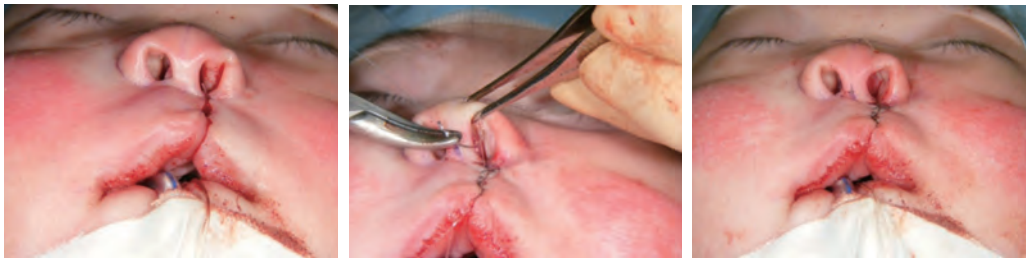

Fig. 9-1-10 Rhinoplasty by the lifting of nylon threads

f) Red lip formation (Fig. 9-1-11)

Finally excess tissue beyond markings are cut. After that, it will be sutured with 5-0 nylon and 7-0 nylon. Buccal cavity is sutured with absorbing yarn.

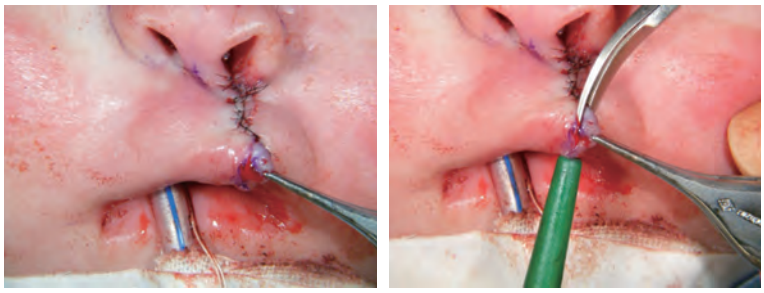

Fig. 9-1-11 Red lip formation

g) Completed (Fig. 9-1-12)

In this case, the nostril is lifted with nylon thread.

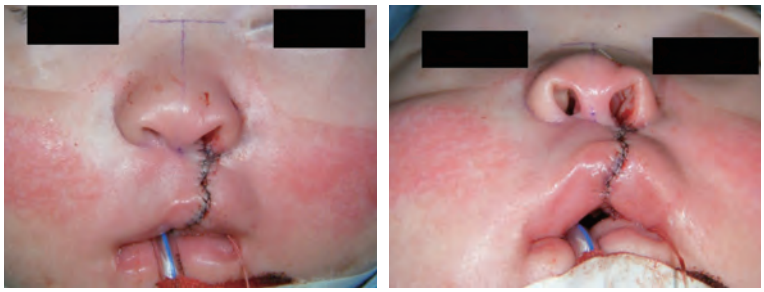

Fig. 9-1-12 Completed

**c. Bilateral cleft lip/nose repair after PNAM**

Bilateral cleft lip patients have a short columellar and protrusion and displacement of premaxilla (Fig. 9-1-13). For these, a sufficient improvement by only surgery was not possible. We have been using the Hotz plate since 1984, and it leads to form induction at the time of development. In addition, it performs a columellar extension and adjusts the position of the premaxilla, thereby achieving the external nose form correction and the decrease of the nose deformation in the pre-surgical phase by PNAM + taping as Fig. 9-1-14. Correction of bilateral cleft lip is divided into two stages - first a preliminary stage treatment done for a certain period and later a one stage operation to carry out on both sides at the same time. This performs an operation on unilateral cleft at one time and performs an operation on the opposite side in two times, and it is possible to compensate for tissue deficiency to be a problem in one stage surgery, reducing the whistling deformity.

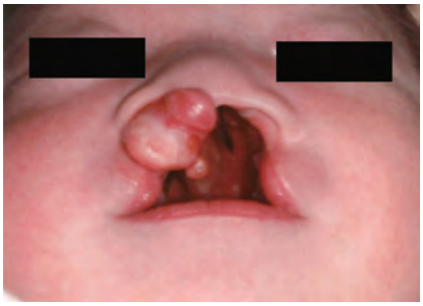

Fig. 9-1-13 Bilateral cleft lip patient

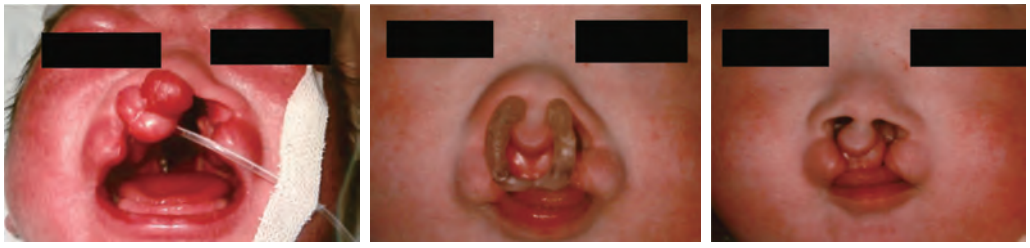

Fig. 9-1-14 Pre-surgical phase with PNAM + taping

**d. Palatoplasty**

The purpose of palatoplasty is to repair the function of speech, breathing and swallowing by correcting the structural disorder. In general, we operate when cleft palate patients gain body weight of 10kg and at about 18 months to 24months of age.

Cleft palate repair of Two-Flap repair procedures

The two-flap repair is widely used. The technique involves raising two long flaps

that extend to the alveolar margin anteriorly, based posteriorly on the greater palatine neurovascular bundle. Many of the surgeons who use this technique advocate resuturing of the flaps to their original position such that they are not using the flaps to achieve “push-back”. Adovocates of this technique argue that raising the flaps facilitates exposure of the soft palate musculature. Further study will be necessary to determine if elevation of these flaps impairs maxillary growth and dental occlusion.

a) Design

It is determined at the beginning of the procedure that lateral releasing incisions will be necessary, incisions are made at the junction of oral and nasal mucosa. This junction is usually clearly seen as the nasal mucosa is more pink and telangiectanic and is usually clearly seen on the oral side of the cleft. If the residual cleft extends into the hard palate, the oral flap then needs to be elevated to the edge of the bony palatal cleft. With an appropriate dental scaler, the mucoperiosteal flaps are lifted from the hard palate.

b) The incision and the elevation of the mucoperiosteal flaps

The incision is along depth of the muscle approximately from a subsequent section of hard and soft palate using a No.11 scalpel, to the tip of uvla along the cleft’s edges. It is subjected to submucosal dissection leading from the canine to the maxillary tuberosity along inside of the alveolar arch at 5mm with No.12 scalpel. Separation of the mucoperiosteal flaps is carried out slowly under the periosteum from the front.

c) Technique for the pterygoid hamulus and the greater palatine neurovascular bundle

The oral mucoperiosteal flap is then elevated laterally to expose the greater palatine neurovascular bundle and, if necessary to achieve mobilization, the periosteal sleeve around greater palatine neurovascular bundle is incised, a probe passed between the greater palatine bundle and the alveolus, and the neurovascular pedicle is elevated out of the foramen. Just behind and lateral to the foramen, a firm structure can be felt, and this is partly composed of the oral component of the tensor palati tendon described above. Lesser palatine neurovascular branches are also present at this point. The dissection is continued back into the soft palate, separating the oral mucosa and underlying mucous glands from the underlying musculature, palatopharyngeus and palatoglossus muscles. This is done by a combination of knife and blunt dissection and extends to the posterior border of the velum and laterally to the pterygoid hamulus. The pterygoid hamulus is folded to reduce the tension of the palatine tensor muscle.

d) Suturing

The nasal mucosa, with its attached muscle, is then sutured. Closure of the nasal layer at this stage facilitates the later muscle dissection by placing it under some tension. Sutures (the author uses 4-0 Opeporics) are placed in the nasal mucosa close to the edge, but then picking up more of the mucous glands (and a little muscle anteriorly). The aim is a suture, which will evert the nasal layer toward the nasal surface. Closure is continued to a point where it is possible without tension.

An incision is then made on each side of the mid line, beginning 3-5mm from the midline posteriorly, and closer to nasal layer sutures. This knife dissection extends deep to the nasal mucosa, leaving mucosa glands medially. If the soft palate is short, Z-plasty of nasal mucosa is carried out to extend the nasal mucosa of the soft palate. It is sequentially sutured toward from tip of the uvula to the anterior of the nasal mucosa with absorbent thread. Muscle layer is sutured with 4-0 nylon. Oral mucosa is also successively sutured from lateral side.

e) Protection of the raw surface

The artificial dermis of the biomaterials is attached to the raw surface to facilitate formation of the granulation of the palate. The splint is mounted on the hard palate and is sutured to the silk. The splint is removed in one week.

**References**

1) Ono M, Kurita K, Yoshida K, Nagase Y, Hayakawa T Kato T, Natsume N, Epidemiological research on Van der Woude syndrome among Japanese. Aichi-Gakuin Dental Science, 27:, 9-15, 2014.

2) Nagase Y, Natsume N, Kato T, Hayakawa T, Epidemiological Analysis of Cleft Lip and/or Palate by Cleft Pattern. J Maxillofac Oral Surg. 2010 Dec; 9(4): 389-95.

3) Imura H, Yamada T, Mishima K, Fujiwara K, Kawaki H, Hirata A, Sogawa N, Ueno T, Sugahara T, Effect of 2,3,7,8-tetrachlorodibenzo-p-dioxin suggests abnormal palate development after palatal fusion. Congenit Anom. 2010 ; 50(2): 77-84

4) Butali A, Suzuki S, Cooper ME, Mansilla AM, Cuenco K, Leslie EJ, Suzuki Y, Niimi T, Yamamoto M, Ayanga G, Erkhembaatar T, Furukawa H, Fujiwawa K, Imura H, Petrin AL, Natsume N, Beaty TH, Marazita ML, Murray JC.: Replication of genome wide association identified candidate genes confirm the role of common and rare variants in PAX7 and VAX1 in the etiology of nonsyndromic CL(P). Am J Med Genet A. 2013 May; 161A(5): 965-72.

(Hideto Imura, Nagato Nasume)

## *9-2. Syndrome*

**a. Treacher Collins syndrome**

Treacher Collins syndrome, also known as mandibulofacial dysostosis, is a rare genetic disorder characterized by craniofacial deformities. Treacher Collins syndrome is found in 1 in 25,000~50,000 births. The typical physical features include downward slanting eyes, micrognathia (a small lower jaw), conductive hearing loss, underdeveloped zygoma, drooping part of the lateral lower eyelids, and malformed or absent ears. This condition is a result of a defect of the first arch during development.

One known cause of this syndrome is a mutation in the TCOF1 gene, at chromosome 5q32-q33.1. The protein coded by this gene is called treacle and has been hypothesized to assist in protein sorting during particular stages in embryonic development, particularly that of the structures of the head and face. The disorder is inherited in an autosomal-dominant pattern.

The symptoms of this disorder vary greatly, ranging from almost unnoticeable to severe. Most affected patients have underdeveloped facial bones, which result in a sunken appearance in the middle of the face, a prominent nose, and a very small jaw and chin (micrognathia). Some people with this condition are also born with a cleft palate. In severe cases, the micrognathia may displace the tongue of an affected neonate (new-born) sufficiently to cause obstruction of the oropharynx and potentially life-threatening respiratory problems, but it has been known that epiglottis can be surgically removed to help in airway obstruction. The neonate will asphyxiate unless a proper airway is established.

People with Treacher Collins syndrome often have eyes that slant downward, sparse eyelashes, and a notch in the lower eyelids called a coloboma. People with Treacher Collins Syndrome may also need a feeding tube because some cases are so severe that they cannot swallow. This condition is also characterized by absent, small, or unusually formed ears (pinnae), called microtia. Defects in the middle ear (which contains three small bones that transmit sound) cause hearing loss in about half of the cases. People with Treacher Collins syndrome usually have normal intelligence.

People with the syndrome can undergo surgeries on the face to improve appearance, get hearing aids, and can also undergo surgery on a cleft palate.

**b. Goldenhar syndrome**

Also known as Oculo-auriculo-vertebral spectrum, the term Goldenhar syndrome was used when the spine and the eye are involved. Goldenhar syndrome was originally recognized as a clinical entity by Goldenhar in 1952 (Heffez L et al., 1984). The clinical manifestations closely resemble those of hemifacial microsomia (first and second branchial arch syndrome). In the Goldenhar patient, however, the clinical findings are more varied and classically include the triad of ① epibulbar dermoids and/or lipodermoids; ② auricular appendices and pretragal blind-ended fistulas and ③ vertebral anomalies.

Causes of Goldenhar syndrome are unknown, and it has been suggested that there is a brachial arch development issue late in the first trimester, also there is anecdotal evidence linking it to exposure to certain toxins (e.g. dioxin) before or during pregnancy.

Chief complaints of Goldenhar syndrome are incomplete development of the ear, nose, soft palate, lip, and mandible on usually one side of the body. Other problems can include severe scoliosis (twisting of the vertebrae), lipodermoids (fat in the eye), and hearing loss. As patients get older, there is an increase in health problems with the heart and lungs. Inability to function normally on a daily basis increases and 90% of patients with this syndrome will not be able to perform work related duties.

Surgical treatment may be necessary to help the child to develop e.g. jaw distraction/bone grafts, occular dermoid debulking, repairing cleft palate/lip, repairing heart malformations, spinal surgery. 90% of patients with Goldenhar syndrome will require assistance as the syndrome progresses by means of hearing aides, glasses, wheelchair, cane, walker, nurses' aide and generalized care to function on a daily basis.

(Kai-yuan Fu)

# 10

# *Soft Tissue and Mucosal Disease*

# 10-1. Labial lesions

**a. Chronic cheilitis**

Chronic cheilitis is a chronic inflammation on the vermillion portion of the lip. Although the cause is unclear, it is thought to be associated with predisposing factors, such as cold, dryness, spicy food, lip biting and even stress.

**Clinical manifestations**

Patients with chronic cheilitis usually presents with dryness, exfoliation and rhagades of vermillion lip mucosa. Patients can complain about itchiness and slight swelling of the lip.

**Diagnosis**

The diagnosis of chronic cheilitis is based on the clinical characteristics.

**Treatment**

Topical treatments are recommended to the cheilitis patients, such as corticosteroids, moisture ointments as well as the avoidance of various irritations.

(Hong Hua)

**b. Granulomatous cheilitis (GC)**

Granulomatous cheilitis belongs to the larger group of orofacial granulomatosis (OFG). The underlying mechanisms remain unclear.

**Clinical manifestations**

Clinically, GC is characterized by a persistent diffuse swelling of either or both lips. The swelling is described as a painless, nonpruritic, firm edema, and is usually asymmetric.

**Diagnosis**

The diagnosis of GC is based on the clinical and histopathological manifestations both. It presents the painless swelling of one or both lips, with histologic evidence of non-caseating granulomatous inflammation.

GC should be distinguished from other OFG disorders, such as sarcoidosis, tuberculosis, Crohn's disease and Melkersson–Rosenthal syndrome.

Melkersson–Rosenthal syndrome is a triad of symptoms including swelling of the lip, facial nerve paralysis and fissured tongue.

**Treatment**

The treatment of granulomatous cheilitis is very challenging. Corticosteroids can be applied to GC incuding local injection or systemic usage. Other treatment regimens include clofazimine, minocycline, and immunomodulatory agents (infliximab, thalidomide et al ). Surgical management is the last resort for GC patients.

(Hong Hua)

**c. Angular stomatitis**

Angular stomatitis is an eczematous eruption of the skin and contiguous labial mucous membrane at the angle of the mouth. A variety of etiological factors have been described, including candidiasis, bacterial infections, mechanical irritation, nutritional deficiencies and conditions associated with hypersalivation, which causes maceration and inflammation[1)].

**Signs and symptoms**

Angular stomatitis occurs in all age groups and is characterized symptomatically by a feeling of dryness and a burning sensation at the corners of the mouth. Clinically, the epithelium at the commissures appears wrinkled and somewhat macerated (Fig. 10-1-1). Predisposing factors include micro-biological changes, nutritional deficiencies, mechanical irritation and allergic causes. Angular stomatitis has been associated with various microbiological species, including *Candida, Streptococci* and *Staphylococci*.

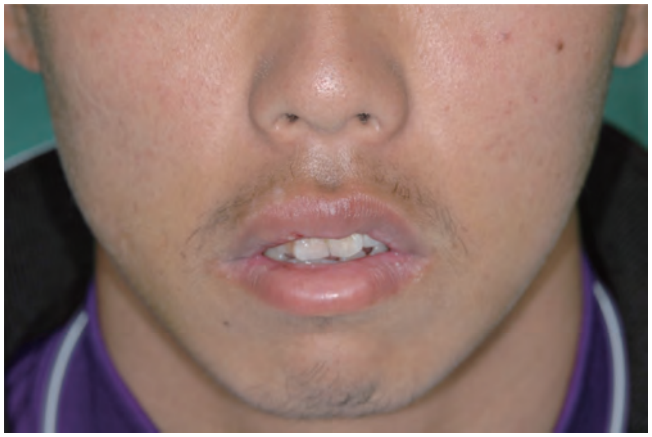

Fig. 10-1-1 Angular stomatitis caused by *Candida* infection

**Diagnosis**

Angular stomatitis may also be a part of symptoms defining the condition called Plummer-Vinson syndrome. Moreover, this disease may be associated with nutritional deficiencies, namely riboflavin (vitamin $B_2$) and zinc deficiency.

**Treatment**

The treatment is empirical at best because of the apparently varied etiology. It should be remembered that the infection present is secondary and that, unless the primary cause is corrected, treatment of the infection will not produce a permanent cure.

**Reference:**

1) Akpan A., Morgan R. Oral candidiasis. Postgrad Med J 78: 455–459, 2002.

(Izumi Yoshioka, Masataka Uehara, Kazuhiro Tominaga)

**d. Hemangioma and vascular malformation of the lip**

Vascular anomalies are congenital lesions of abnormal vascular development. Vascular anomalies are broadly classified into two groups: hemangioma and vascular malformation[1]. Vascular malformation is characterized by blood vessels defined by a mature endothelium and a normal cellular cycle and can be subdivided into low-flow, intermediate and high-flow types. The low-flow type vascular malformation is composed of a venous component. The high-flow type vascular

malformation corresponds to arteriovenous malformations, and the intermediate type vascular malformation is mixed with a venous and arterial component. Sixty percent are localized to head and neck region[2]. Lip may be one of the common sites to be affected.

**Signs and symptoms**

Ecstatic blood vessels and the reddish-blue surface are characteristically found in vascular anomalies. Change on pressure is a common finding with return to original color on withdrawal of pressure. Hemangioma and vascular malformation can distort lip anatomy and are at increased risk of ulceration and/or bleeding, which lead to impaired function and disfigurement. Intervention of hemangioma of the lip is warranted for associated complications, including facial disfigurement, feeding difficulties, speech impairment, and psychosocial manifestations.

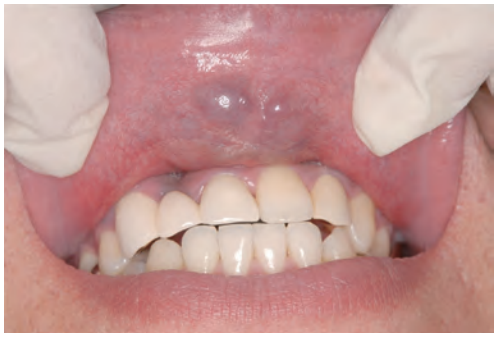

Fig. 10-1-2
Vascular malformations of the labial mucosa

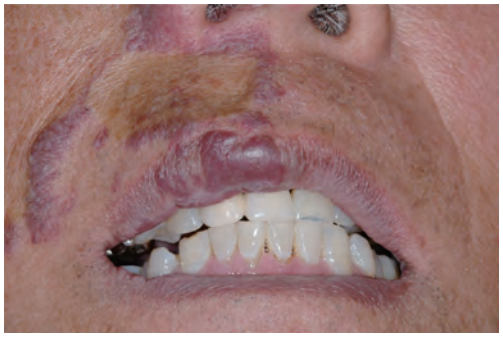

Fig. 10-1-3
Vascular malformations of the upper lip

**Diagnosis**

The diagnosis of vascular anomalies of the lip is based on the patient's medical history and a physical examination.

Ultrasound scanning is the first choice for noninvasive evaluation of patients with vascular malformations, doppler mode to assess flow characteristics. Magnetic resonance appears to be the ideal technique to define the site, extension and origin of vascular malformations. Magnetic resonance angiography (MRA) and magnetic resonance venography (MRV) are useful to confirm the extent and type of venous malformations, delineates feeding and draining vessels, distinguishes between different soft tissues (muscle, fat) and the vascular structures. Angiography is the most detailed test and the best way to diagnose arteriovenous malformations.

**Treatment**

Before choosing the adequate type of treatment for a hemangioma, a number of characteristics should be considered, such as duration, size, location and number of tumors, patient age, and the hemodynamics of the tumor.

Hemangioma usually grows during the first year of life, and then slowly involutes. More than 50% involute completely by the age of 10 years[3]. Wait and see policy tends to be chosen in the first years of life, rather than treating hemangioma surgically. Intervention is necessary in up to 20% of cases, high-dose systemic or intralesional steroids being the first-line treatment.

The main types of treatments of the vascular anomalies of the lip are surgical removal and intralesional injection of sclerosant agents. Surgical removal is possible for small anomalies but is considered to be problematic because vermilion tissue is difficult to reconstruct for a satisfactory cosmetic result.

Sclerotherapy is an effective and conservative technique for the treatment of vascular anomalies of the lip. Sclerotherapy is commonly limited to a low-flow and a partial intermediate flow type. The sclerosant agents used are 5% sodium morrhuate, sodium psylliate, quinine urethrone, 5% ethanolamine oleate (EO), 1% polidocanol, sodium tetradecyl sulfate, and hypertonic saline. A sclerosant agent in the connective tissue induces an inflammatory reaction and scars that may lead to cosmetic problems. Ulceration and necrosis may appear as local adverse effects stemming from sclerotherapy. Five percent EO can also cause a renal toxicity associated with marked intravascular hemolysis and hemoglobinuria.

Although Laser therapy and cryotherapy have been shown to be effective for superficial lesions, they may result in scarring and hyperpigmentation.

**References:**

1) Mulliken JB, Glowacki J.: Hemangiomas and vascular malformations in infants and children: a classification based on endothelial characteristics. Plast Reconstr Surg 69: 412-420, 1982.
2) Zide BM, Glat PM, et al.: Vascular lip enlargement: Part IHemangiomas—Tenets of therapy. Plast Reconstr Surg 100: 1664-1673, 1997.
3) Simpson JR: Natural history of cavernous hemangiomas. Lancet 2: 1057-1059, 1959.

(Izumi Yoshioka, Manabu Habu, Kazuhiro Tominaga)

## *10-2. Tongue lesions*

**a. Median rhomboid glossitis**

Median rhomboid glossitis is defined as the central papillary atrophy of the tongue and it affects 0.01%–1.0% of the population[1]. It is typically located around the midline of the dorsum of the tongue. It occurs as a well-demarcated, symmetric, depapillated area arising anterior to the circumvallate papillae. There are several predisposing factors associated with median rhomboid glossitis such as smoking, denture wearing, diabetes mellitus, as well as *Candida* infections. Treatment is generally unnecessary, but antifungal medications may be used for symptomatic cases.

**Signs and symptoms**

Median rhomboid glossitis is a condition characterized by symmetric, well demarcated, erythematous and depapillated area on the top part (dorsum) of the middle or back of the tongue, which may be smooth or nodular (Fig. 10-2-1). The lesion is typically 2-3 cm in its longest dimension. Apart from the appearance of the lesion, there are usually no other signs or symptoms. Rarely is any soreness associated with the condition. There may be *Candida* lesions at other sites in the mouth, which may lead to a diagnosis of chronic multifocal oral Candidiasis.

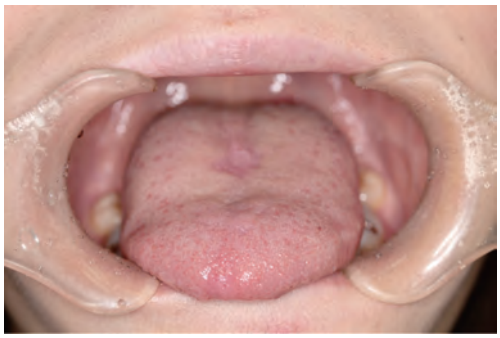

Fig. 10-2-1 Median rhomboid glossitis

**Diagnosis**

Median rhomboid glossitis is clinically evident, and it is usually diagnosed empirically. However, several other entities may be considered in the differential diagnosis: irritation fibroma, mucocele, granular cell tumor, tertiary syphilis, lingual thyroid and, in rare cases, carcinoma[2]. Most of these conditions can be easily ruled out on the basis of clinical appearance.

**Treatment**

No treatment is necessary for median rhomboid glossitis, but nodular cases are often removed for microscopic evaluation. Antifungal therapy will reduce clinical erythema and inflammation due to *Candida* infection.

**References:**

1) Joseph BK, Savage NW: Tongue pathology. Clin Dermatol 18: 613–618, 2000.
2) Van der Wal N, van der Kwast WA, et al.: Median rhomboid glossitis: A follow-up study of 16 patients. J Oral Med 41: 117–120, 1986.

(Izumi Yoshioka, Masataka Uehara, Kazuhiro Tominaga)

**b. Geographic tongue**

Geographic tongue is a benign disorder involving dorsal surface of the tongue which appears as depapillated areas with leading and folded edges in yellowish or grayish white color and sometimes with unclear borders. The lesion occurs in up to 3% of the general population. Most often, patients are asymptomatic; however, some patients report increased sensitivity to hot and spicy foods. The etiology and pathogenesis of geographic tongue are still unknown[1)]. There may be a relationship between the geographic tongue and psoriasis, diabetes mellitus, Reiter's syndrome, pregnancy and psychological factors[1)]. Geographic tongue affects males and females and is noted to be more prominent in adults than in children. No treatment is normally needed, but antifungal and antibacterial medications may be used for symptomatic cases. There is no malignant potential.

**Signs and symptoms**

Geographic tongue has a bald, red area of varying sizes that is surrounded, at least in part, by an irregular white border. The appearance of the affected portion of the tongue results from loss of the papilla (Fig. 10-2-2). The histopathological findings are parakeratosis and psoriasiform hyperplasia with neutrophilic infiltration into the epithelium. It is usually without symptoms, but some may complain of a burning or tingling sensation, often from secondary fungus or bacterial infection.

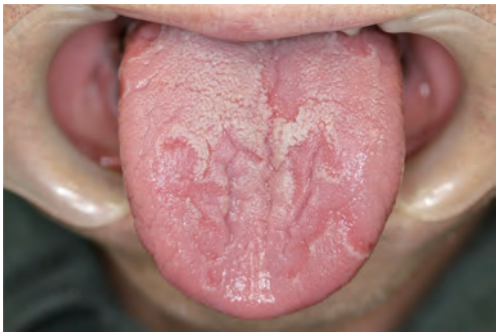

Fig. 10-2-2 Geographic tongue

**Diagnosis**

Several other entities may be considered in the differential diagnosis: carcinoma, candidiasis and lichen planus.

**Treatment**

Treatment is generally unnecessary and the condition will usually fade away on its own, but may recur and may migrate to other areas of the tongue. While there is no known cure or commonly prescribed treatment for geographic tongue, there are several ways to suppress the condition, including avoiding foods that exacerbate the problem. Symptomatic lesions can be treated;a topical or systemic antifungal medication can be tried if secondary *Candidiasis* is suspected.

**Reference:**

1) Greenbreg M., Glick M., et al: Oral Medicine. 12th Ed, BC Deker, London, 2008, p103-104.

(Izumi Yoshioka, Masataka Uehara, Kazuhiro Tominaga)

**c. Fissured tongue**

Fissured tongue is a condition characterized by multiple small furrows or grooves on the dorsal surface of the tongue (Fig. 10-2-3). Typically most fissures are found on the middle one-third of the tongue. Although these grooves may look unsettling, the condition is usually painless. Some individuals may complain of an associated burning sensation. No treatment is necessary except to encourage good oral hygiene including brushing the top surface of the tongue to remove any food debris from the fissures.

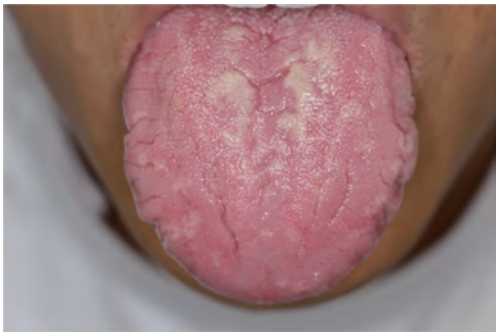

Fig. 10-2-3 Fissured tongue

**Signs and symptoms**

Upon clinical examination, fissured tongue affects the dorsum and often extends to the lateral borders of the tongue. The depth of the fissures varies but has been noted to be up to 6 mm in diameter. When particularly prominent, the fissures or grooves may be interconnected, separating the tongue dorsum into what may appear to be several lobules.

**Diagnosis**

Fissured tongue affects only the tongue and is a finding in Melkersson-Rosenthal syndrome, which consists of a triad of fissured tongue, granulomatous cheilitis, and facial nerve paralysis[1, 2]. Moreover, it is seen in most patients with Downs syndrome, acromegaly, and Sjogren's syndrome[1, 2].

**Treatment**

If the fissures are causing halitosis, then mechanical tongue cleansing should be introduced in the patients' oral hygiene routine. As the condition is otherwise entirely benign, no treatment is indicated and the patient should be reassured that it is a common variance of the normal appearance of the tongue.

**References:**

1) Rogers RS, Bruce AJ: The tongue in clinical diagnosis. J Eur Acad Dermatol Venereol 18: 254–259, 2004.
2) Zargari O: The prevalence and significance of fissured tongue and geographical tongue in psoriatic patients. Clin Exp Dermatol 31: 192–195, 2006.

(Izumi Yoshioka, Masataka Uehara, Kazuhiro Tominaga)

**d. Black hairy tongue**

Black hairy tongue is a benign disorder characterized by hypertrophy and discoloration of the filiform papillae of the tongue (Fig. 10-2-4). This disorder has been associated with numerous medications and predisposing conditions. The first therapeutic action consists of eradicating predisposing factors, because black hairy tongue is a benign and self-limiting disorder. Mechanical removal of the lesions, by brushing or scraping, can be very effective.

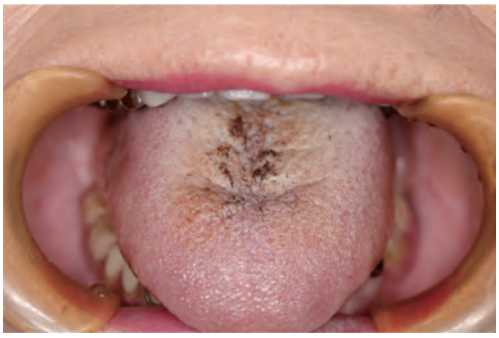

Fig. 10-2-4
Black hairy tongue due to extensive use of antibiotics.

**Signs and symptoms**

Black hairy tongue is a benign disorder characterized by hypertrophy of the filiform papillae of the tongue and is usually asymptomatic. A common clinical feature of a black hairy tongue is brownish appearance caused by variety of precipitating factors, such as chronic smoking, poor oral hygiene, tooth loss, chronic or extensive use of antibiotics, and radiation therapy to the head and neck[1]. Although the etiology of black hairy tongue is not well understood, secondary infection of *Candida albicans* and and/or bacillus subtilis varietas niger can frequently be involved.

**Diagnosis**

The main differential diagnosis of hairy tongue consists of some forms of acanthosis nigricans (which usually involves the lips), hairy oral leukoplakia (white lesions), and black staining over a normal tongue (bismuth, food colorings). Diagnosis is usually made on the clinical appearance without the need for a tissue biopsy. However, when biopsies have been taken, the histologic appearance is one of marked elongation and hyperparakeratosis of the filiform papillae and numerous bacteria growing on the epithelial surface[2].

**Treatment**

Black hairy tongue is a temporary condition which resolves on its own once the incriminating factor is removed. In many cases, simply brushing the tongue with a toothbrush or using a commercially available tongue scraper is sufficient to remove elongated filiform papillae. In most cases, the treatment of hairy tongue does not require pharmacologic intervention. If *Candida infection* is present, topical antifungal medications can be used when the condition is symptomatic (eg, glossopyrosis).

**References:**

1) Nisa L, Giger R: Black hairy tongue. Am J Med 124:816-817,2011
2) Bouquot B.W, Neville DD et al. Oral & maxillofacial pathology 2nd Ed, W.B. Saunders. Philadelphia, 2002, p. 13–14.

(Izumi Yoshioka, Masataka Uehara, Kazuhiro Tominaga)

**e. Tongue coating**

Tongue coating is the presence of a whitish layer on the upper surface of the tongue (Fig. 10-2-5). Tongue coating comprises of bacteria, large amounts of desquamated epithelial cells released from the oral mucosa, leukocytes from periodontal pockets, blood metabolites and various nutrients.

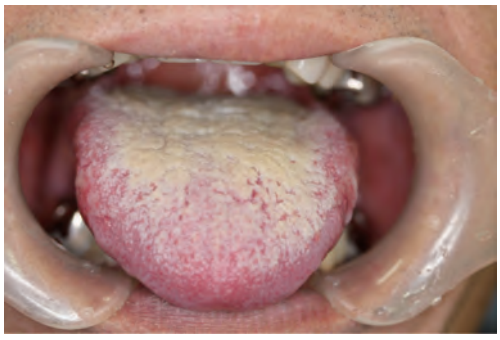

Fig. 10-2-5 Tongue coating

**Signs and symptoms**

The color of a normal tongue is pink-to-slightly white, and is very often covered with a coating. Tongue coating is a ‘moss-like’ deposit which forms over the tongue

surface. Factors of tongue coating include oral hygiene, salivary flow, periodontal status, dietary habits, motor function of the tongue, smoking and age[1]. Tongue coating may occur with other symptoms including halitosis and burning sensation.

**Diagnosis**

The differential diagnosis of tongue coating includes hairy leukoplakia, lichen planus, *Candida infection and graft versus host disease*.

**Treatment**

Mechanical cleaning such as brushing or tongue scraping is recommended. If *Candida infection* is present, antifungal agents are used.

**Reference:**

1) van den Broek AM, Feenstra L, et al.: A review of the current literature on management of halitosis. Oral Dis 14: 30-39, 2008.

(Izumi Yoshioka, Manabu Habu, Kazuhiro Tominaga)

**f. Hemangioma and vascular malformations of the tongue**

Vascular anomalies occur commonly in the head and neck and represent generally only an aesthetic problem. However, when localized in the tongue, these lesions can create clinical problems consisting, in the majority of cases, of spontaneous haemorrhage from the mouth. Although uncommon, progressive asymmetric growth of the tongue (macroglossia) can be also observed.

**Signs and symptoms**

Hemangioma and vascular malformations of the tongue appear as a soft mass, smooth or lobulated, and sessile or pedunculated and may vary in size from a few mms to several cms. They are usually deep red and may blanch on the application of pressure (Fig. 10-2-6, -8). These lesions of the tongue may cause peculiar problems, such as susceptibility to trauma and bleeding (due to biting), obstructive symptoms (difficulties with breathing, chewing, swallowing, speech), delay in linguistic development and compromised airway.

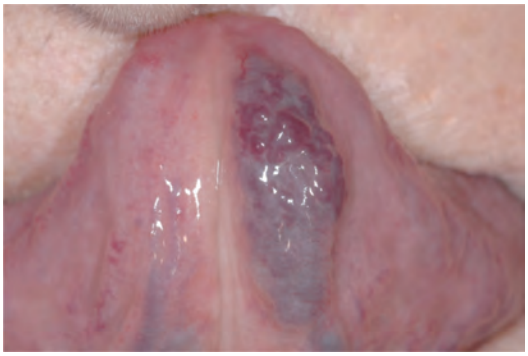

Fig. 10-2-6 Vascular malformation of the tongue.

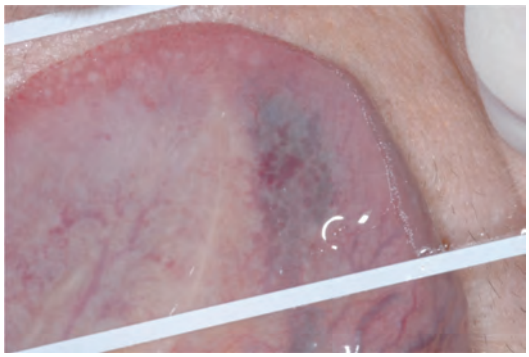

Fig. 10-2-7
Placing a microscope glass slide under pressure.

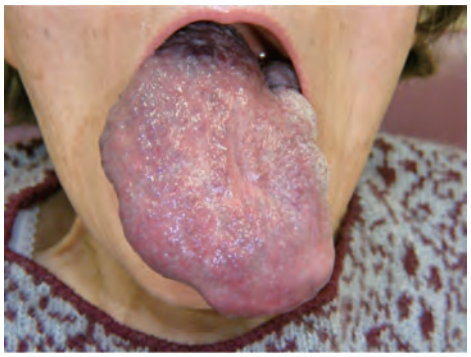

Fig. 10-2-8
Vascular malformation of the tongue.

**Diagnosis**

A variety of other lesions can resemble hemangioma and vascular malformation of the tongue. The differential diagnosis includes pyogenic granuloma, telangiectasia, angiosarcoma, squamous cell carcinoma, and other vascular appearing lesions of face & oral cavity such as Sturge Weber syndrome. Pre-treatment histological diagnostics are not performed, as haemangioma and vascular malformation are as a rule benign, and tissue sampling would cause unnecessary bleeding.

For imaging diagnosis, refer to “Hemangioma and vascular malformation of the lip” section.

**Treatment**

The strategy for treating hemangioma and vascular malformation of the tongue should be based on personalized medicine. Various therapeutic approaches include surgical removal, sclerotherapy, systemic corticosteroids, interferon-α, intratumoral ligation, radiation, or a combination of these modalities. Hemangioma usually regresses spontaneously therefore clinical observation alone is recommended[1]. However, therapeutic intervention for hemangioma of the tongue may be indicated

in children with compromised airway, bleeding or ulceration. Therapeutic modalities may include steroid, cryotherapy, embolization, sclerotherapy, surgical removal and laser therapy.

For smaller vascular malformations of the tongue, surgical excision is the best curative option where possible. For very large lesions of the tongue, complete surgical excision is impossible without causing significant functional impairment and disfigurement. Therefore, the goal of therapy for symptomatic large vascular malformations of the tongue is to eliminate the malformation and conserve as much lingual tissue as possible.

Sclerotherapy is the therapy of choice for low-flow lesions such as venous malformations and symptomatic hemangiomas. Although high-flow vascular lesions do not respond to sclerotherapy alone, sclerotherapy may be utilized to decrease the size of the lesion. Sclerotherapy, systemic corticosteroids, interferon-α and intratumoral ligation are used as preoperative adjuncts to surgery[2]. Intravascular embolization of arteriovenous malformations can be used alone or in combination with surgical excision[2].

**References:**

1) Werner JA, Dunne AA, et al.: Current concepts in the classification, diagnosis and treatment of hemangiomas and vascular malformations of the head and neck. Eur Arch Otorhinolaryngol. 258: 141-149, 2001.
2) Richter GT, Friedman AB: Hemangiomas and Vascular Malformations: Current Theory and Management. International Journal of Pediatrics 2012: Article ID 645678, 10, 2012.

(Izumi Yoshioka, Manabu Habu, Kazuhiro Tominaga)

**g. Hunter's glossitis**

Pernicious anemia is an autoimmune atrophic gastritis that causes a deficiency in vitamin $B_{12}$ due to its malabsorption. This disease is often characterized by the presence of a triad of symptoms: generalized weakness, a sore, painful tongue, and numbness or tingling of extremities. In some cases the lingual manifestations are the first sign of the disease. Hunter's glossitis is one of the more common symptoms of pernicious anemia.

**Signs and symptoms**

Smooth tongue is a condition characterized by a smooth glossy tongue. The tongue is generally inflamed, often described as “beefy red” in color, either in entirety or in patches scattered over the dorsum and lateral borders (Fig. 10-2-9). Characteristically, with the glossitis, glossodynia and glossopyrosis, there is gradual atrophy of the papillae of the tongue that eventuates in a smooth or bald tongue. The pain and burning sensation are usually confined to the tongue, but may also extend to other parts of the oral mucosa.

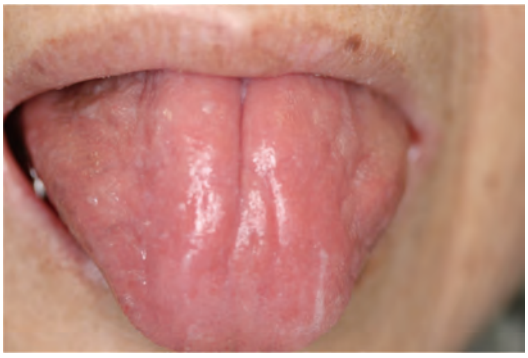

Fig. 10-2-9 Hunter’s glossitis

**Diagnosis**

Smooth tongue may be associated with pernicious anemia, iron deficiency anemia, pellagra, syphilis, or xerostomia[1)]. The diagnosis should be considered when faced with any hematological and neurological manifestations.

**Treatment**

Treatment is based on the administration of parenteral vitamin $B_{12}$.

**Reference:**

1) Powell FC: Glossodynia and other disorders of the tongue. Dermatol Clin 5: 687-693, 1987.

(Izumi Yoshioka, Manabu Habu, Kazuhiro Tominaga)

# *10-3. Potential malignant oral lesions*

**a. Oral leukoplakia**

Leukoplakia has been defined as a clinical term for predominantly white lesions of the oral mucosa, which cannot be rubbed off and cannot be characterized as any other definable lesion (Fig. 10-3-1, -3). It may affect any site of the oral cavity[1-3]. Leukoplakia is the most common premalignant, potentially malignant, or precancerous lesion of the oral mucosa[4, 5]. Therefore, when epithelial dysplasia is observed on histopathological examination, malignant transformation may be highly predictable, and when carcinoma *in situ* or invasive carcinoma is detected, the clinical diagnosis of leukoplakia should be superseded by a histopathological diagnosis[4, 5]. Studies have demonstrated that oral leukoplakia shows a significant tendency of malignant transformation, ranging from 0.13% to 6%[3-5]. Histopathologically, leukoplakia is characterized by atrophy of the epithelium to hyperplasia with or without hyperkeratosis (Fig. 10-3-4)[1].

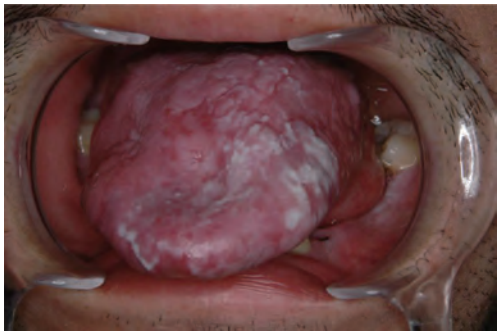

Fig. 10-3-1
Leukoplakia on the dorsum of the tongue

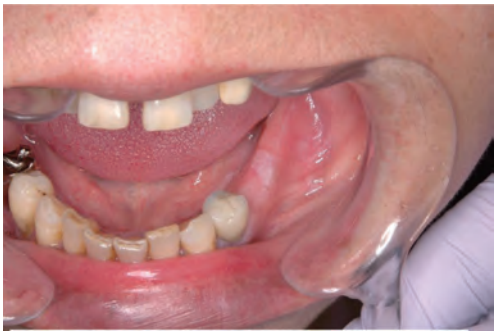

Fig. 10-3-2
Leukoplakia on the left mandibular gingiva

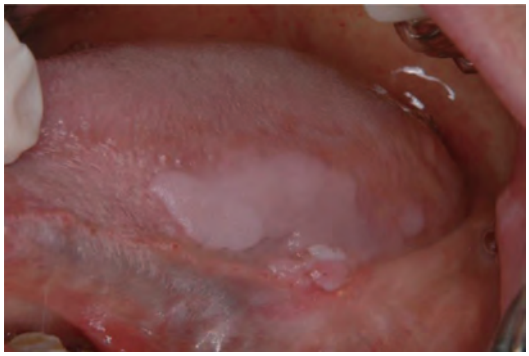

Fig. 10-3-3
Leukoplakia on the left side of the tongue

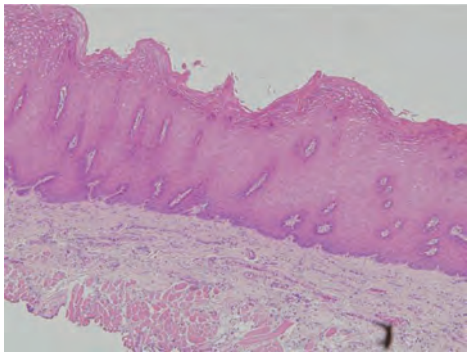

Fig. 10-3-4
Histopathologic features of leukoplakia showing squamous hyperplasia without cytological atypia

Clinically, two different subtypes have been recognized: homogeneous and nonhomogeneous[3]. Homogeneous leukoplakia has been defined as a predominantly white lesion of a uniform flat, thin appearance that may exhibit shallow cracks and that has a smooth, wrinkled, or corrugated surface with a consistent texture. Nonhomogeneous leukoplakia has been defined as a predominant white-and-red lesion ("erosive leukoplakia," "erythroleukoplakia") that may be either irregularly flat, nodular ("speckled"), or verrucous. Several risk factors have been described, e.g., tobacco & alcohol use, presence of *C. albicans*, and trauma[3, 4]. Various treatment modalities have been suggested, such as careful observation, removal of risk factors, medical therapies (including anti-inflammatory and antimycotic agents, topical chemotherapeutic drugs, and retinoids), and surgeries (including cryosurgery and laser surgery), although there is currently no consensus on the most appropriate management[6, 7].

**References:**

1) WHO. Collaborating Centre for Oral Precancerous Lesions. Definition of leukoplakia and related lesions: an aid to studies on oral precancer. Oral Surgery, 1978; 46: 518-539.
2) Waal van der I, Schepman KP, Meij van EH. A modified classification and staging system for oral leukoplakia. Oral Oncol 2000; 36: 264-246.
3) Sciubba JJ. Oral leukoplakia. Critical Reviews or Oral Biology and Medicine, 1995; 6: 147-160.
4) Shiu MN, Chen TH, Chang SH, Hahn JL. Risk factor for leukoplakia and malignant transformation to oral carcinoma. Br J Cancer 2000; 82: 1871-1874.
5) Thomas G, Hashibe M, Jacob BJ, Ramadas K, Mathew B, Sankaranarayanan R, et al. Risk factors for multiple oral premalignant lesions. Int J Cancer 2003; 107: 285-291.
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7) Vedtofte P, Holmstrup P, Hjorting-Hansen E, Pindborg JJ. Surgical treatment of premalignant lesions of the oral mucosa. Int J Oral Maxillofac Surg 1987; 16: 656-664.

(Kei Tomihara, Makoto Noguchi)

**b. Oral erythroplakia**

Erythroplakia is defined as "A fiery red patch that cannot be characterized clinically or pathologically as any other definable disease," and has been described as a potentially premalignant oral lesion[1]. Clinically, the lesions may appear smooth or granular with a well-defined margin often adjacent to normal mucosa (Fig. 10-3-5, -6)[1]. Erythroplakia may be found in association with or adjacent to areas of leukoplakia. In fact, when a mixture of red and white changes is observed, it is usually categorized as nonhomogeneous leukoplakia ("erythroleukoplakia")[2]. Erythroplakia shows the highest risk of malignant transformation compared with other oral premalignant lesions, including oral leukoplakia and oral lichen planus, ranging from 14% to 50%, including those with pre-existing invasive carcinoma[3, 4]. Erythroplakia primarily affects the middle-aged and elderly; there is no gender prevalence[5]. The soft palate, floor of the mouth, and buccal mucosa are commonly affected[5]. Histopathologically, erythroplakia often shows epithelial dysplasia, carcinoma in situ, or microinvasive carcinoma[5]. Etiologically, tobacco consumption and alcohol abuse are considered to be important risk factors[3-5]. Because of the high risk of malignant transformation, erythroplakia should be treated effectively. Surgical excision of the lesion has been recommended[6, 7]. Several nonsurgical interventions, including vitamin A, retinoids, or bleomycin, have also been suggested, although there is no direct evidence for their effectiveness in preventing malignant transformation[5].

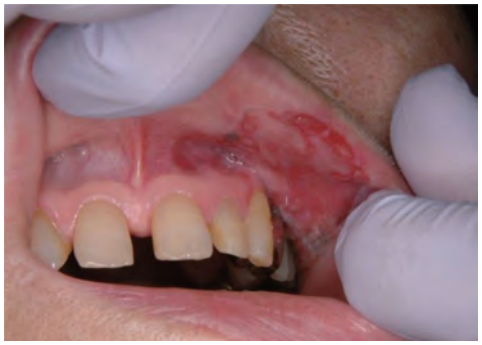

Fig. 10-3-5
Erythroplakic patch with well-defined margins, adjacent to normal-appearing mucosa on the upper labial mucosa. Histopathologically, the lesion contains carcinoma *in situ.*

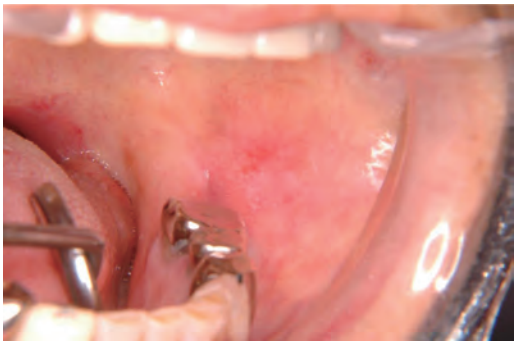

Fig. 10-3-6
Erythroplakic lesion on the buccal mucosa. Histopathologically, the lesion contains invasive carcinoma.

**References:**

1) Shafer WG, Waldron CA. Erythroplakia of the oral cavity. Cancer 1975; 36: 1021-1028.
2) Pindborg JJ, Reichart PA, Smith CJ, van der Waal I. Histological typing of cancer and precancer of the oral mucosa. International histological classification of tumors. World Health Organization: 1997.
3) Bouquot JE, Ephros H. Erythroplakia: the dangerous red mucosa. Pract Periodontics Aesthet Dent 1995; 7: 59-67.
4) Thomas G, Hashibe M, Jacob BJ, Ramadas K, Mathew B, Sankaranarayanan R, et al. Risk factors for multiple oral premalignant lesions. Int J Cancer 2003; 107: 285-291.
5) Reichart PA, Pholipsem HP. Oral erythroplakia-a review. Oral Oncol 2005; 41: 551-561.
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7) Amagasa T, Yokoo E, Sato K, Tanaka N, Shinoda S, Takagi M. A study of the clinical characteristics and treatment of oral carcinoma in situ. Oral Surg Oral Med Oral Med Oral Pathol 1985; 60: 50-55

(Kei Tomihara, Makoto Noguchi)

**c. Oral lichen planus**

Oral lichen planus (OLP) is a chronic inflammatory disease demonstrating a wide range of clinical manifestations[1]. It affects primarily the middle-aged, with a higher prevalence in females[2]. The buccal mucosa, tongue, and gingiva are usually affected. OLP usually occurs bilaterally. Clinically, there are six types of OLP. The reticular form is the most common type and can present as an interlacing white, linear, annular, lacy pattern with an erythematous border. Erosive, plaque-like, papular, atrophic, and bullous forms have also been described. OLP is diagnosed on the basis of clinical and histologic findings. The classic histopathologic features of OLP include hyperkeratosis, liquefaction of the basal epithelial cells, and eosinophilic colloid bodies (Civatte bodies) seen at the basal epithelial level[3]. Acanthosis and saw-tooth rete ridge formation may also be seen[3]. A dense, band-like inflammatory infiltrate consisting of lymphocytes is seen at the subepithelial

region[3]. Various causative factors have been described, such as dental materials, systemic medications, chronic liver disease and hepatitis C virus (HCV) infection, stress, genetics, tobacco chewing, and graft-versus-host disease[4-8]. Removal of such factors may be important for the management of OLP; however, topical or systemic corticosteroids or retinoids have been widely used (Fig. 10-3-7, -10)[6-8].

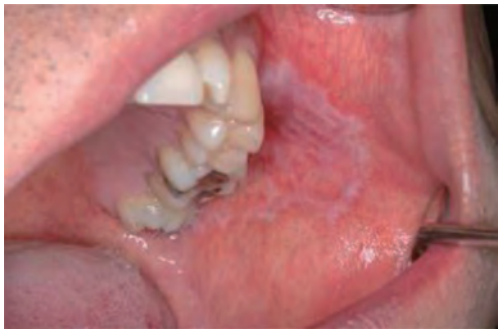

Fig. 10-3-7
Reticular oral lichen planus affecting the buccal mucosa. An erythematous mucosa with white striations can be observed.

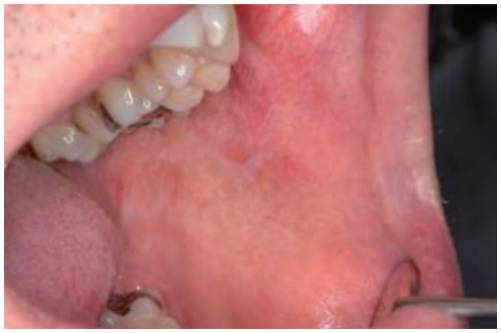

Fig. 10-3-8
The application of a topical corticosteroid reduced the severity of symptoms.

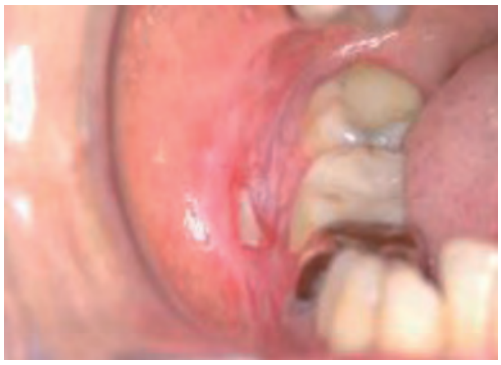

Fig. 10-3-9
Erosive oral lichen planus affecting the unattached gingiva. An ulceration surrounded by erythematous mucosa with white striae.

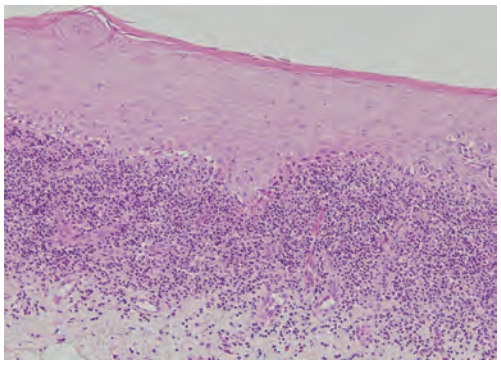

Fig. 10-3-10
Histopathologic features of oral lichen planus showing hyperkeratosis of basal epithelial cells with a dense band-like lymphocytic infiltrate at the subepithelial region with white striae.

**References:**


1) Scully C, Beyli M, Ferreiro MC, et al. Update on oral lichen planus: etiopathogenesis and management. Crit Rev Oral Biol Med 1998; 9: 86-122
2) Eisen D. The clinical features, malignant potential, and systemic associations of oral lichen planus: a study of 723 patients. J Am Acad Dermatol. 2002; 46: 207-214
3) Villarroel Dorrego M, Correnti M, Delgado R, et al. Oral lichen planus: immunohistology of mucosal lesions. J Oral Pathol Med. 2002; 31: 410-414

4) Sugerman PB, Savage NW, Walsh LJ, et al. The pathogenesis of oral lichen planus. Crit Rev Oral Biol Med 2002; 13: 350-365
5) Roopashree MR, Gondhalekar RV, Shashikanth MC et al. Pathogenesis of oral lichen planus--a review. J Oral Pathol Med. 2010; 39: 729-734
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(Kei Tomihara, Makoto Noguchi)

**d. Discoid lupus erythematosus**

Discoid lupus erythematosus (DLE) is an autoimmmine disease which affects the skin and mucosa causing atrophy, scarring and photosensitivity. Few patients (<5%) with DLE could progress to SLE.

The development of squamous cell carcinoma has also been described in lesions of DLE involving the vermilion border of the lip, and actinic radiation has shown to be an important adjunct role.

**Clinical manifestations**

Women are more affected than men. The male-to-female ratio is 1:2. The usual age of onset is between 20 and 40 years old. Patients may complain of occasional pain with lesions.

The primary lesion of skin is an erythematous papule or plaque with scaling and crusty appearance. As the lesion progresses, the scale may thicken and pigmentary changes may develop. The center areas may appear lighter in color with a rim darker than the normal skin.

Oral musosa also can be affected and lips are the most common affected site. The lesions appear identical to the lesions of the skin or may similar as oral lichen planus on the lips

**Diagnosis**

The diagnosis of DLE is based on the clinical and histological manifestations.

The characteristic histopathologic alterations observed in discoid lupus erythematosus include vacuolar alteration of the basal cell layer, thickening of the basement membrane, follicular plugging, hyperkeratosis, atrophy of the epidermis, and inflammatory cell infiltrate (usually lymphocytic) in a perivascular, periappendiceal, and subepidermal location. Immunopathological examinations show deposition of immunoglobulin and/or complement at the dermal-epidermal junction.

Serologic testing can be taken for DLE patients. Antinuclear antibody (ANA) positive is found in 20% DLE patients. In addition, Double-stranded DNA or anti-Sm antibodies usually reflect SLE, and they may also occur in some DLE patients (<5%).

**Treatment**

Sun-protective measures should be taken in these patients, including sunscreens, protective clothing, and behavior alteration.

Standard medical therapy includes topical corticosteroids. Intralesional injection of corticosteroids is useful therapy for individual lesions. Alternative therapies include thalidomide, oral or topical retinoids, and other immunosuppressive agents.

(Hong Hua)

# 10-4. Ulcerative and bullous disorders

**a. Apthous stomatitis**

Recurrent aphthous stomatitis (RAS) is one of the most common oral diseases worldwide[1-3]. It is characterized by variably sized multiple, recurrent, small, round or ovoid ulcers with circumscribed margins and erythematous borders (Fig. 10-4-1, -2)[1-3]. The etiology of RAS remains unclear, but there may be involvement of underlying genetic predisposition, cell-mediated immunological mechanisms, or an interleukin genotype. Physical injury has been suggested to be a local predisposing factor or systemic diseases such as Behçet's disease, cyclic neutropenia, periodic fever with aphthous pharyngitis and adenitis, Sweet's syndrome, various nutritional deficiencies with or without underlying gastrointestinal disorders, and HIV infection have been suggested as systemic predisposing factors for RAS[4-6]. There is no curative treatment for RAS; however, it is important to recognize the systemic cause for appropriate RAS management[7, 8]. Topical or systemic administration of various therapeutic agents (e.g., glucocorticoids, anti-inflammatory agents, antimicrobial agents) has been suggested to reduce the severity of ulceration[7, 8]. Topical therapy is the first choice, particularly for small RAS; however, in severe cases, systemic therapies may be necessary[8].

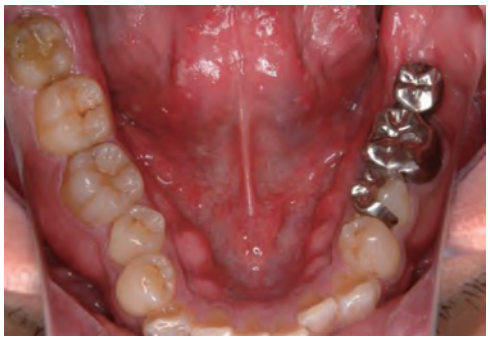

Fig. 10-4-1
Minor aphthous ulceration on the floor of the mouth

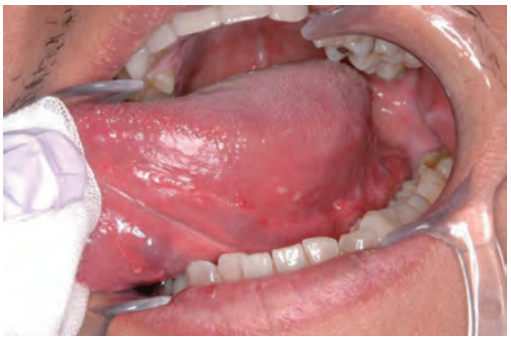

Fig. 10-4-2
Minor aphthous ulceration on the lateral border of the tongue

**References:**

1) Bruce AJ, Rogers RS, 3rd. Acute oral ulcers. Dermatol Clin 2003; 21: 1-15.
2) Rees TD, Binnie WH. Recurrent aphthous stomatitis. Dermatol Clin 1996; 14: 243-56.
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6) Sakane T, Takeno M, Suzuki N, Inaba G. Behc¸et's disease. N Engl J Med 1999; 341: 1284-91.
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(Kei Tomihara, Makoto Noguchi)

**b. Traumatic ulcers**

Traumatic ulceration of oral mucosa may be physical or chemical. Physical damage to the oral mucosa may be caused by sharp surfaces within the mouth, such as components of dentures, orthodontic appliances, dental restorations, or prominent tooth cusps. In addition, some patients suffer traumatic ulceration as a result of cheek chewing. Chemical irritation cause is placement of some tablets such as aspirin or caustic toothache remedies on the mucosa adjacent to painful teeth or under dentures.

**Clinical manifestations**

Traumatic ulceration characteristically presents as a single localized irregular type of ulcer. The individual lesions present as areas of erythema surrounding a central removable, yellowish membrane Or a rolled white border of hyperkeratosis adjacent to the area of ulceration. Chemical irritation may present as a more widespread superficial area of erosion or ulceration often with a slough of fibrinous exudate.

**Diagnosis**

Traumatic ulceration characteristically presents as a single irregular ulcer. Often, the cause of trauma becomes obvious from the history or clinical examination. Traumatic ulcers must be differentiated from squamous carcinoma and other mucosal ulcerative diseases. An ulcer which does not heal within two to three weeks should be biopsied to rule out rule out infection or neoplasma.

**Treatment**

The treatment is to remove the cause if it is known. Relief of pain can be achieved with topical anesthetics.

**Prognosis**

The ulcer should heal if the cause is removed.

(Hong Hua)

**c. Behcet's disease**

Behcet's disease (BD) is an inflammatory, multiple systemic autoimmune diseases. It is particularly prevalent in the 'Silk Route' populations. The disease can affect any age. Males are slightly more commonly affected than females.

The etiopathogenesis of the disease remains unknown. However, studies have demonstrated excessive thrombin formation and the potential role of impaired fibrinolytic kinetics in the generation of the hypercoagulable state in BD.

**Clinical manifestations**

Oral and genital mucous ulcers, uveitis and reactivity of the skin to needle prick or injection (pathergy test) constitute common clinical hallmarks of BD. It can also affect other systems including the vascular, gastrointestinal and neurological systems as well as ocular involvement and arthritis.

The most common lesions in BD are recurrent and painful ulcerations of the oral and genital mucosa. The Oral ulcers appear punched out and are surrounded by an inflamed rim. Genital ulcers are particularly painful in the females and may form scars with healing.

Recurrent eye involvement occurs in about 90% of BD patients. Both eye are eventually involved and may result in blindness.

The skin lesions with pustules may develop at sites of needle pricks for blood taking. Other skin lesions include papules, vesicles, folliculitis, necrotizing vasculitis, pyoderma, etc.

Large joint arthritis is common, but mild, self-limiting and non-deforming.

Neurological manifestations are uncommon, but when present, may present with dementia, impairement of speech, movement and balance; all of which are associated with poor prognosis.

**Diagnosis**

Diagnosis is made on the basis of clinical examination alone.

The pathergy test is a simple test in which the forearm is pricked with a small, sterile needle. Occurrence of a small red bump or pustule at the site of needle insertion constitutes a positive test which could be of helpful for the diagnosis of BD.

**Treatment**

The treatment of BD is to prevent irreversible damage that occurs primarily early in the course of disease. The goal is to prevent exacerbations of mucocutaneous and joint involvement. Topical steroids and non–immunosuppressive medications (such as colchicine, thalidomide, dapsone and others) may be effective.

The multisystem involvement mandates collaboration between different specialties.

(Hong Hua)

**d. Erythema multiforme**

Erythema multiforme (EM) is an acute inflammatory mucocutaneous disease caused by HSV infection and the use of certain medications such as nonsteroidal anti-inflammatory drugs (NSAIDs), sulfonamides, penicillin, anticonvulsants, et al.

**Clinical manifestations**

EM is generally classified as mild and severe forms. There is little clinical resemblance between typical EM and SJS. Clinically, EM extends from a mild rash with typical target lesions of the hands and feet to a severe illness with widespread involvement of the skin and mucous membranes as in the Stevens-Johnson syndrome

The oral mucosa is the most common mucosa site affected, including labial and buccal mucosa and vermillion border of the lip. Lesions manifest with rapidly rupturing vesicles and bullae, erosions with pseudomembrane formation and inflammatory erythema. EM may occur once or many times.

The skin lesion also called target lesion or iris lesion is a typical lesion of EM on skin, consisting of a central bulla or pale clearing area surrounded by edema and bands of erythema.

**Diagnosis**

Careful enquiry into drug-intake is recommended. The diagnosis of EM is mainly based on typical clinical manifestations.

**Treatment**

Topical analgesics and corticosteroids.are reconmmended in managing EM and SJS.such as patients received corticosteroids (prednisone or prednisolone 1 mg/kg/day) for one week with progressive decrease.

(Hong Hua)

**e. Pemphigus vulgaris**

Pemphigus is a rare group of blistering autoimmune diseases that affect the skin and mucous membranes, and is mediated by circulating autoantibodies directed against keratinocyte cell surface molecules desmoglein 1 and/or desmoglein 3.which cause cell separate from each other.

Male-to-female ratio is approximately equal. Mean age of onset is approximately 50-60 years.

**Clinical manifestations**

There are several types of pemphigus including pemphigus vulgaris, pemphigus foliaceus and paraneoplastic pemphigus et al. Pemphigus vulgaris (PV) is the most common form of the disorder

Mucosal lesions of PV may precede cutaneous lesions by months. Almost all patients have mucosal lesions and they may be the sole manifestation of the disease. Intact bullae are rare in the mouth. More commonly, irregularly shaped erosions secondary to the rupture of blisters may be seen in the clinic. Erosions can be scattered and often extensive, which is painful and limit the patient's daily activities. The erosions extend peripherally with shedding of the epithelium.

The primary lesion of PV in skin is a flaccid blister with clear fuild, which usually arises on normal-appearing skin but may be found on erythematous skin. The contents soon become turbid, or the blisters rupture producing painful erosions, Nikolsky sign is positive.

Other mucosal surfaces may be involved in PV, including the conjunctiva, esophagus, labia, vagina, cervix, penis, urethra, and anus.

**Diagnosis**

The diagnosis of PV is based on the clinical characteristics and histological as well as imunohistological findings

Nikolsky sign is positive. Smear taken from the base of a blister or an oral erosion showed acantholytic cells –Tzanck cells.

Histopathology demonstrates an intradermal blister. Suprabasal epidermal cells separate from the basal cells to form clefts and blisters.

Direct immunofluorescence assay (DIF) usually shows IgG or Complement components such as C3 deposited on the surface of the keratinocytes in and around lesions.

In the patient's serum, IIF demonstrates the presence of circulating IgG autoantibodies that bind to epidermis/epithelium. The titer of circulating antibody correlates with disease course.

**Treatment**

The aim of treatment in PV is to stop, or greatly reduce, the number of blisters that form.

Corticosteroids can provide rapid remission and ongoing control of symptoms of PV. However this may present an increased risk of some side effects such as opportunistic infections. A high dose is usually needed at first. The initial dose is usually equivalent to 0.5 ～ 1.5 mg of prednisolone per kilograms daily. The dose of steroid is reduced once new blisters have stopped forming. Systemic corticosteroids are usually combined with other immunosuppressive agents to allow for rapid reduction of the corticosteroid dose. Adjuvant immunosuppressive agents include azathioprine, mycophenolate mofetil, cyclophosphamide and methotrexate as well as cyclosporine et al.

Topical steroids could be used on the skin or oral blisters or erosive lesions. Mouthwashes containing antiseptic or local anaesthetic may also be helpful for these patients.

Antifungal medication is needed if candida infection was found in the the mouth.

**Prognosis**

PV is a potentially life-threatening autoimmune mucocutaneous disease with a mortality rate of approximately 5~15%. Prognosis is worse in patients with extensive disease and in older patients.

(Hong Hua)

# 10-5. Infectious diseases of oral mucosa

**Viral infections**

Viral infection is one of the common diseases of oral mucosa. The lesion is mostly restricted within oral mucosa and is also occurred on surrounding skin or other mucosa such as labial and facial skin with or without intra-oral lesions. The overall clinical features are acute onset, a history of direct contact or decrease resistant or with local and systemic diseases, generalized prodromal symptoms that precede the local lesions. The lesions are mostly consist of vesicles and ruptured shallow ulcers. Laboratory tests are rarely required for diagnosis, but nonspecific blood test of white blood cells without increase of neutrophilic leukocyte is helpful. The most common viral infections are herpesvirus infections such as herpes simplex, herpes zoster. Nevertheless hand-foot-mouth disease and herpetic pharyntitis frequently occur in epidemics that have their highest incidence seasons and ages.

**a. Herpes simplex**

**Etiology**

Herpes simplex is an acute infection of oral mucosa and surrounding skin, caused by herpes simplex viruses (HSV). HSV is a nuclear replicating, icosahedral, enveloped DNA virus and HSV genome must enter the cell for the initiation of infection. HSV is a highly adapted human pathogen with rapid lytic replication cycle, and yet with the ability to invade sensory neurons. Both herpes simplex virus 1(HSV-1) and herpes simplex virus 2 (HSV-2) can cause herpes simplex. HSV1 and 2 can be distinguished serologically or by restriction endonuclease analysis of the nuclear DNA. HSV-1 is implicated in a majority of cases of oral and pharyngeal infection, meningoencephalitis, and dermatitis above the waist; however HSV-2 is often detected in the genital and the skin infection below the waist.

Infection with HSV1 is almost universal. This is known nearly 100% of adults have antibodies in their serum. Many HSV infections are sub-clinical. Most individuals become infected in the first few years of life. Humans are the only natural reservoir of HSV infection, and spread occurs by direct intimate contact with lesions, for example, through kissing (HSV1) or sexual intercourse (HSV2); or by secretions (saliva and genital secretions) from an asymptomatic carrier.

Latency, a characteristic of all herpes viruses, occurs when the virus is transported from mucosal or cutaneous nerve endings by neurons to ganglia where

the HSV viral genome remains present in a nonreplicating state. During the latent phase, herpes DNA is detectable, but viral proteins are not produced. Reactivation of the latent virus occurs when HSV switches to a replicative state; this can occur as a result of number of factors including peripheral tissue injury from trauma or sunburn, fever, stress or immunosuppression.

**Clinical manifestation**

It is the most common viral infection in the oral cavity and referred to as “fever blisters “in traditional Chinese Medicine.The most common clinical futures are painful blisters and sores. Infection with the herpes virus is categorized into several disorders based on the site of infection. Oral herpes (also called *cold sores*) is the most common form of infection, which infects the face and mouth; Infection of the genitals is the second most common form of herpes. Others such as herpetic whitlow, herpes gladiatorum, ocular herpes (keratitis), cerebral herpes infection encephalitis, Mollaret’s meningitis, neonatal herpes are the least common disorders. In this chapter, we introduce oral herpes only. Oral herpes can be seen at all the ages, may reappear periodically and is normally self limiting. For chronically ill people and newborn babies, the viral infection can be serious, but rarely fatal.

**Primary herpetic gingivostomatitis**

Primary herpetic infections develop in people who have not been previously exposed to the virus and do not have antibody to HSV, resulting from direct contact with an individual who has active HSV primary or recurrent lesions. Primary HSV may also be spread by asymptomatic shedders with HSV present in salivary secretions. Most often, exposure to HSV in children results in a subclinical infection (without clinical signs and symptoms), or only producing antibody. Only a small proportion (approximately 1 percent) of primary herpes infection leads to primary herpetic gingivostomatitis, which is often seen in infants and children under 5 years old, mostly after 6 months. The incidence of primary herpetic gingivostomatitis reaches a peak between 2 and 3 years of age. Primary herpetic infections do occur in adults, but are often misdiagnosed by dentists.

Patients with primary oral herpes have a negative past history of recurrent herpes labialis and a positive history of direct intimate contact with a patient with primary or recurrent herpes. The incubation period is most commonly 4 to 7 days but may range from 2 to 12 days. The patients normally have a history of generalized prodromal symptoms such as fever, headache, malaise, nausea, and vomiting. The submandibular and cervical lymph nodes are characteristically enlarged and tender.

Approximately 1 or 2 days after the prodromal symptoms occur, small vesicles appear on the oral mucosa; these are thin-walled vesicles surrounded by an inflammatory base. The vesicles exist with a character of clustering. The vesicles quickly rupture, leaving shallow round discrete ulcers. In some cases, the discrete ulcers may fuse to form larger ulcers, become covered with a greyish slough when secondary infection exists. The lesions occur on all portions of the mucosa including gingival, which is especially evident on the surrounding upper palate or gingival margin of deciduous molars. An important appearance of the disease is generalized acute marginal gingivitis. The entire gingival is edematous. In some cases of children, labial and facial skin vesicle and edema where the infected saliva flowing by, are also seen, in addition to intra-oral lesions. On occasion, primary HSV may cause lesions of the labial and facial skin without intraoral lesions. Primary HSV in otherwise healthy children is a self-limiting disease. The fever ordinarily disappears within 3 or 4 days, and the lesions begin healing in a week to 10 days.

**Secondary herpetic stomatitis**

Following primary infection, the virus enters sensory nerve endings and travels up the axon and establishes a latent infection in the trigeminal ganglion. The HSV genome persists in an episomal form (plasmid) in the nucleus of the neurone. No viral genes are expressed. This state of latency may persist for many years. In a percentage of people, the HSV will reactivate and a cycle of viral replication occurs in the neurone and virus particles travel down the axon to reinfect the skin or mucous membrane in the area supplied by the nerve. Recurrent infections are usually shorter and less severe than the primary infection. About 30%-50% of patients with primary HSV infection have tendency of secondary infection, which is more localized with little generalized symptoms. Then clinical manifestation is divided into two types, labial herpetis and introral recurrent herpes simplex, the latter is less common and rare.

**Labial herpes**

Labial herpes also called recurrent herpes labialis (RHL) or cold sores, fever blisters, which is the most common type of HSV infection. These recurrent infections represent reactivation and not reinfection of HSV, which persists in a latent state in the trigeminal (semilunar) ganglion. Reactivation may be provoked by a number of stimuli: including sunlight, stress, febrile illnesses, oral trauma, menstruation or immunosuppression. The most common site of labial herpetis is on

the muco-cutaneous junctions of the mouth or nose, such as vermilion of the lip and vermilion border as well as the surrounding skin, the area supplied by the sensory nerve ending.

An outbreak of labial herpes is usually preceded by prodromal signs or symptoms such as burning, tingling, soreness or swelling at the site where the lesions will develop. Within hours, small vesicles develop in clusters along the vermilion border of the lips. The vesicles quickly rupture, resulting in erosions that can coalesce to form larger irregular lesions with a crusted surface. The diameter of each vesicle is normally less than 1mm for the HSV-1 infection, with a character of clustering. If it is caused by HSV-2, the diameter of each vesicle may be larger. For patients with frequent recurrent infections, the vesicles occur usually in the same place of the mouth. The lesions may grow in size and cause irritation and pain. Most lesions disappear within 7-10 days without treatment, and they generally heal without scarring and pigmentation. (Fig. 10-5-1).

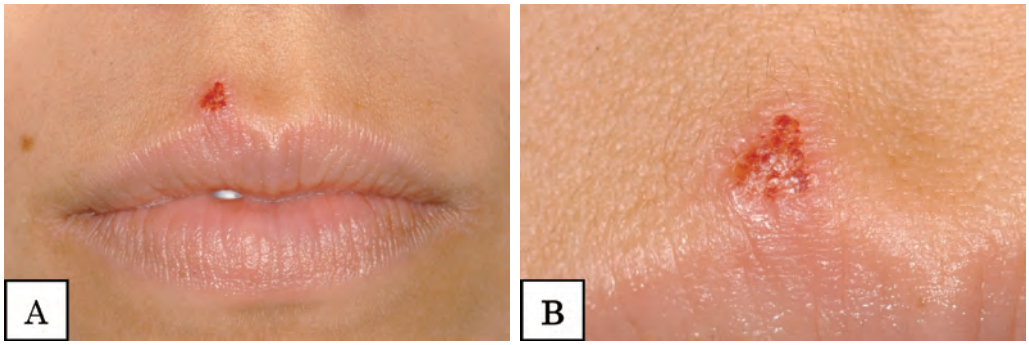


Fig. 10-5-1 Herpes labialis
(A) A cluster of vesicles near the vermilion border, (B) enlarged.

**Recurrent introral HSV infection (RIH)**

Recurrent introral HSV infection (RIH) occurs less frequently than does recurrent herpes labialis. Lesions of RIH begin as clusters of tiny vesicles that rupture rapidly, leaving small discrete erosions or superficial ulcerations of the keratinized oral tissues. These erosions or ulcers are superficial and coalesce to form larger, irregular lesions. RIH develops primarily on oral tissues that are firmly bound down to the underlying bone (that is, the hard palate, attached gingiva and edentulous alveolar ridges). This is in direct contrast to recurrent aphthous ulcerations, which develop on mucosal tissues (such as the buccal mucosa and tongue) that are not bound down to underlying bone. Lesions of RIH may be triggered by dental therapy; local, thermal or chemical injury; or trauma from mastication.

The chronic form of herpes is a variation of recurrent herpes simplex infection rather than a primary infection. AIDS patients, transplant patients taking immunosuppressed drug therapy, patients on high doses of corticosteroids, and patients with leukemia, lymphoma, or other disorders that alter the T-lymphocyte response are those most susceptible to aggressive HSV lesions.

**Diagnosis**

Clinical manifestations: herpetic infections represent a reactivation of the herpes simplex virus, which is highly infectious to patients, their families, dentists and staff members. The diagnosis is usually achieved clinically and is based on the history and characteristic clinical appearance and the location of the lesions. Such as, patients, especially children between age of 6 months to 5 yrs, are easily diagnosed as having primary herpetic gingivostomatitis who present with typical clinical picture of generalized symptoms followed by an eruption of oral vesicles.

Laboratory diagnosis is sometimes needed to confirm infection, especially in compromised patients. This include:

1. Cytological demonstration: characteristic multinuclear giant cells in scraping from lesions, such as Giemsa stain of scraping.
2. HSV isolation by tissue culture. Vesicular fluid and cells from an ulcer base should be placed in viral transport media. The specimen is inoculated into cell cultures and after 24 to 48 hrs the cell lines show characteristic cytopathic effects. This is the most positive method of identification, but it must be remembered that isolation of HSV from oral lesions does not necessarily mean that HSV cause the lesions. Studies have indicated that between 2% to 4% of the population are asymptomatic carriers of HSV. Polymerase chain reaction (PCR) tests are very sensitive tests. While PCR testing is likely to replace the viral culture in the future, PCR are not as readily available as culture at many sites and there are no commercially available kits at this time.
3. Direct demonstration of viral antigen in vesicular fluid or scraping by electron microscopy of immunofluorescence.
4. Antibody titers: blood test for HSV antibody is rarely used in routine clinical situation. In special circumstances such as immunocompromised patients an acute serum specimen should be obtained within 3 or 4 days of the onset of the symptoms. Antibody to HSV will begin to appear in a week and reach a peak in 3 weeks. If antibody titers are similar in both acute and convalescent sera, then the infection were recurrent lesions. IgG for HSV appears soon after infection and stays in the blood for life. IgM is actually the first antibody that appears after

infection, but it may disappear thereafter. The accurate herpes blood test is to detect IgG antibodies. Unlike IgM, IgG antibodies can be accurately broken down to either HSV-1 or HSV-2. There are many blood tests commercially available, they can accurately distinguish between antibodies for type-1 and type-2 herpes by ELISA, immunoblot or Western blot.

**Treatment**

Management should be directed toward shortening the course of the disease, preventing post-bacterial infection.

Routine supportive measures and symptom, secondary infection management: these include medicine for fever and fluids to maintain proper hydration and electrolyte balance if the patient has difficulty eating and drinking. Infants who are not drinking should be referred to a pediatrician. Vitamin C and B is also recommended. Topical medicine can be used for bacteria infection prevention or temporary relief from the discomfort. Anesthetic for the oral mucosa such as 0.5% Dycolnie hydrocholoride or Procaine is useful before eating and drinking. Topical antibiotic medications can be used in short period of time when needed. Mild cases can be managed with above supportive care only.

Antiviral treatment: acyclovir, valacyclovir, famciclovir have been specifically developed for the treatment of HSV infection, which can interfere with viral DNA synthesis. Antiviral treatment should be administered for severe cases in the early prodromal phase of the disease for the best results.

Traditional Chinese antiviral herbs or topical herb complex power for accelerating healing are recommended to be used when necessary. (Fig. 10-5-2, -3).

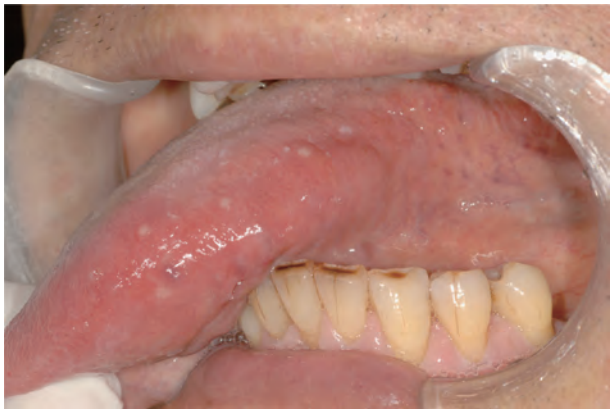

Fig. 10-5-2 Herpetic stomatitis.
Multiple small aphthae on the tongue

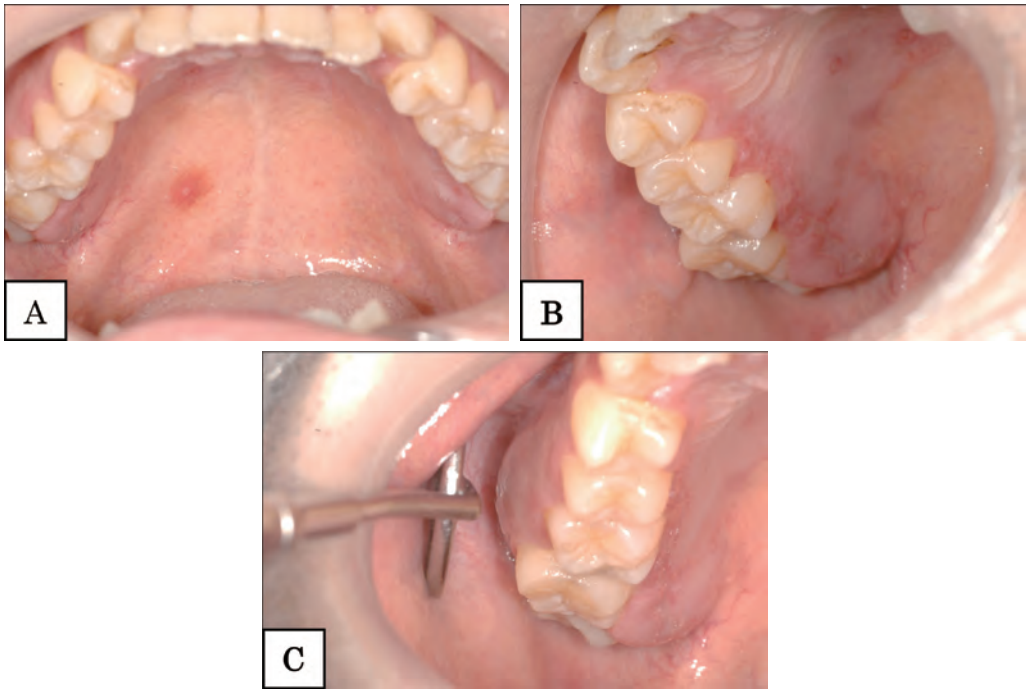


Fig. 10-5-3 Herpetic stomatitis.
Multiple small aphthae on the gingiva (A)(B)(C).

(Yan-ying Xu, Yoshiki Sugiyama)

**b. Herpes zoster**

Herpes zoster (or simply zoster), commonly known as shingles, is a viral disease characterized by a painful skin rash with blisters in a limited area on one side of the body, often in a stripe. Herpes zoster is less common than herpes simplex, as unlike herpes simplex, repeated attacks of herpes zoster are rare, and it is extremely rare for patients to suffer more than three recurrences. Herpes zoster is more likely to occur in people whose immune system is impaired due to aging, immunosuppressive therapy, psychological stress, or other factors.

**Etiology**

Herpes zoster virus(VZV) is a herpes virus which can causes both a primary and a recurrent infection and remain latent in nerve tissue. VZV is responsible for two major clinical infections: chickenpox (varicella) and shingles(herpes zoster). Chickenpox is a generalized primary VZV infection that occurs the first time an

individual contacts of the virus, which we are not going to discuss below.

Most people are infected with VZV as children, and suffer from an episode of chickenpox. The immune system eventually eliminates the virus from most locations, but it remains dormant (or latent) in the ganglia adjacent to the spinal cord (called the dorsal root ganglion, usually trigeminal ganglia) in the base of the skull. Herpes zoster occurs only in people who have had chickenpox, and although it can occur at any age, the majority of sufferers are more than 50 years old. The disease results from the virus reactivating in a single sensory ganglion. Zoster is triggered by trauma, drugs, neoplastic disease or immunosuppression. Thoracic nerves supplying the chest wall are most often affected. The trigeminal nerve is affected in about 15%of cases, with involvement of the ophthalmic, maxillary and mandibular divisions. In the skin, the virus causes local inflammation and blisters. The short and long-term pain caused by herpes zoster comes from the widespread growth of the virus in the infected nerves, which causes inflammation. Until the rash has developed crusts, a person is extremely contagious.

**Clinical manifestation**

Herpes zoster is more often onset in the season of spring and autumn. Oral and facial lesion result from herpes zoster of the second and third divisions of the trigeminal nerve. The earliest symptoms of herpes zoster, which include headache, fever, and malaise, are nonspecific. These symptoms are commonly followed by sensations of burning pain, itching, hyperesthesia, or paresthesia. The pain may be extreme in the affected area and easily confused with toothache. In most cases, after several days the initial phase is followed by the appearance of the characteristic skin rash, which normally resulting in a stripe or belt-like pattern along with the distribution of the trigeminal nerve, that is limited to one side of the face and does not cross the midline. Later, the rash becomes vesicular, forming small blisters filled with a serous exudate. Usually the crusts fall off and the skin heals: but sometimes after severe blistering, scarring and discolored skin remained. Some sufferers experience residual nerve pain for months or years, a condition called postherpetic neuralgia, as a result of scarring of the nerve. (Fig. 10-5-4).

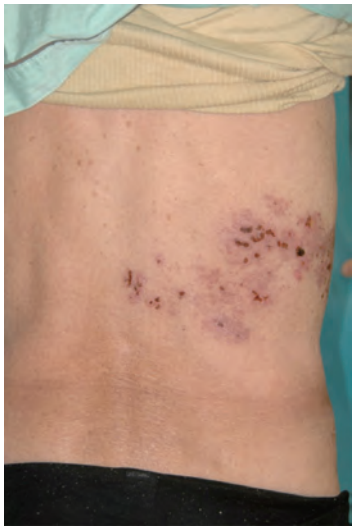

Fig. 10-5-4 Herpes zoster
The belt-like appearance of vesicles on the right side of the back

Involvement of the ophthalmic nerve may lead to eye lesions and sometime blindness. Ramsay Hunt syndrome type II is a rare manifestation of zoster, with vesicular rash on the tympanic membrane and the external auditory canal, together with unilateral facial palsy.

**Diagnosis**

The diagnosis of herpes zoster is based on a history of pain and the unilateral nature and lesion distribution sharply demarcated by the distribution of the trigeminal nerve with a stripe or belt-like pattern both on oral mucosa and skin, when the clinical appearance is typical and vesicles are present, oral herpes is easily differentiated from others.

Laboratory test, such as cytology or fluorescent antibody stained smear, VZV-specific IgM antibody blood test, sample of lesions detection with real-time PCR or with viral culture, can be used only in cases where diagnosis is uncertain. (Fig. 10-5-, -6).

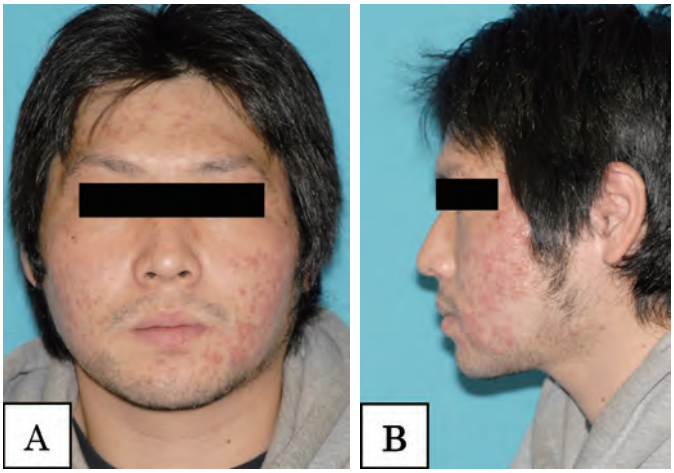


Fig. 10-5-5 Herpes zoster.
Lesions on the face appear in the second and third divisions of the trigeminal nerve (A) (B).

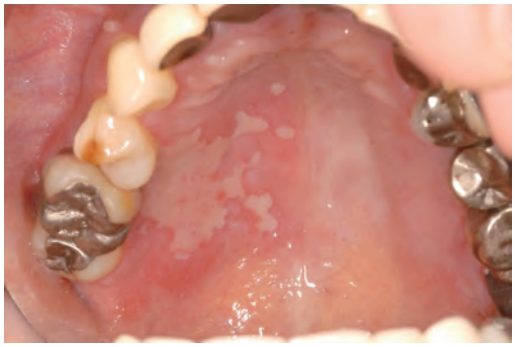

Fig. 10-5-6 Herpes zoster.
Vesicles on the right side of the palatal mucosa.

**Treatment**

Management should be directed toward shortening the course of the disease, limiting the severity and duration of pain and reducing complications (post herpetic neuralgia in patients over 50yrs). Mild cases in young healthy individuals may be treated symptomatically, the same as the cases of herpes simplex.

Antiviral treatment is recommended for all immunocompetent individuals with herpes zoster over 50 years old, preferably given within 72 hours of the appearance of the rash. Antiviral drugs inhibit VZV replication and reduce the severity and duration of herpes zoster with minimal side effects, but do not reliably prevent post herpetic neuralgia. Aciclovir has been the standard treatment, but the new drugs valaciclovir and famciclovir demonstrate similar or superior efficacy and good safety and tolerability.

The use of systemic corticosteroids to prevent post-herpetic neuralgia in patients over 50 is controversial. One trial studying immunocompetent patients older than 50 years of age with localized herpes zoster, suggested that administration of prednisone with aciclovir improved healing time and quality of life.

(Yan-ying Xu, Yoshiki Sugiyama)

**c. Herpangina**

This is a systemic viral infection caused by group A Coxsackievirus. It's less common in dental practice.

**Etiology**

Usually, herpangina is produced by one particular strain of Coxsackievirus A, but it can also be caused by Coxsackievirus B. Typically spreads via the fecal-oral route or via the respiratory droplets

**Clinical manifestation**

It is most common in children but may affect any age group. The disease is characterized by fever, headache, sore throat, dysphagia, anorexia. These symptoms are accompanied by the appearance of oral and pharyngeal lesions. The incubation time is 2 to 10 days. The lesion in the oral cavitiy is small, papulovesicular about 1-2mm in diameter, with a grayish-white surface surrounded by red areolae involving the posterior pharynx, tonsils, and soft palate. The disease is usually mild and will heal without treatment in 1 week.

**Diagnosis**

Herpangina is mainly diagnosis by clinical picture and history. It occurs in epidemics, the lesion occurs on the pharynx and posterior part of the oral mucosa without a generalized acute gingivitis and the lesion tend to be smaller than those of herpes simplex. (Fig. 10-5-7)

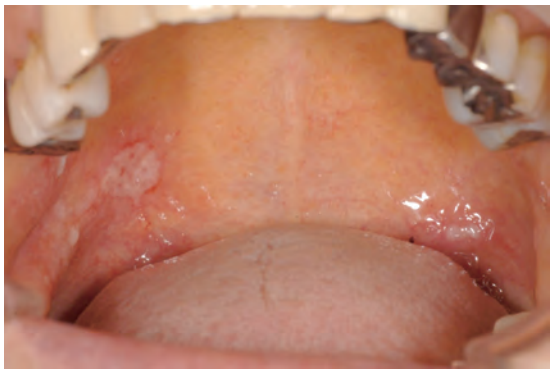

Fig. 10-5-7 Herpangina.
Vesicles rupture and leave multiple small aphthae in the posterior part of the oral cavity

**Treatment**

Treatment is supportive only, as the disease is self-limiting and usually runs its course in less than a week, including proper hydration and topical symptomatic treatment.

(Yan-ying Xu, Yoshiki Sugiyama)

**d. Hand-foot-mouth disease**

Hand, foot and mouth disease (HFMD) is an epidemical viral infection caused by intestinal viruses of the Picornaviridae family. The disease is characterized by low-grade fever, oral vesicles and ulcers, macules and vesicles particularly on the extensor surfaces of the hands and feet. Since the first outbreak in New Zealand in 1957, more and more cases were reported worldwide. HFMD usually affects infants and children and is extremely uncommon in adults.

**Etiology**

The most common strains causing HFMD are Coxsackie A(5,7,9,10) virus and Enterovirus 71, (EV71), less common strains is Coxsackie B(2,5) virus. All serotype of coxsackievirus have a world wide distribution. They are highly

infectious within families and closed communities such as kindergarten or nursery schools and greatest epidemic spread occurs in the summer and autumn. Viral transmission is by the faecal-oral route and from nasal and pharyngeal secretions.

**Clinical manifestation**

The common incubation period of HFMD is from 3 to 5 days and resolution occurs within a week. Because of the more frequent oral involvement dentists are more likely to see patients than with herpangina. The onset of the oral and skin lesions eruptions is accompanied or followed by low-grade fever, headache, malaise and sore throat. The oral lesions are more extensive and lesions on buccal mucosa around duct orifice, palate and tongue are common. The oral lesions are generally bright-red macules which later form oval or grey vesicles. A rash may become evident on the plantar surface of the feet and the palmar surface of the hands and sometimes the buttocks. These skin lesions are macules with pale centers which develop into thin-walled bullae or small ulcers with surrounding erythema. (Fig. 10-5-8)

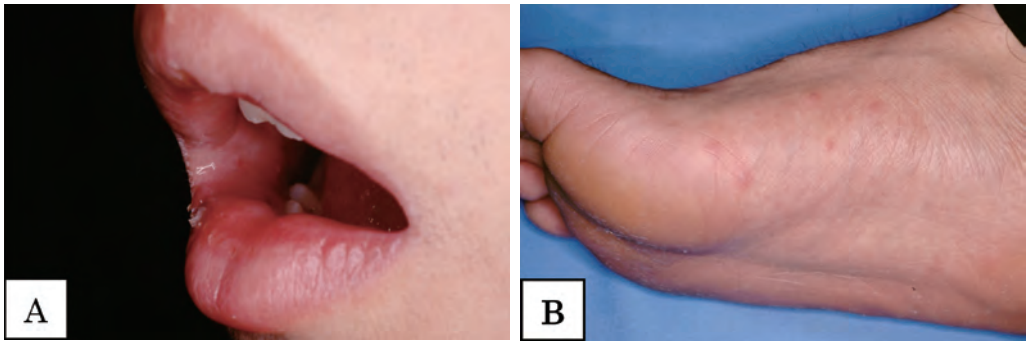


Fig. 10-5-8 Hand, foot, and mouth disease.
Multiple small aphthae in the mouth (A) and rash on the feet (B).

**Diagnosis**

HFMD is mainly diagnosis by clinical picture and history. HFMD is not to be confused with foot-and-mouth disease (also called hoof-and-mouth disease), which is a disease affecting sheep, cattle, and swine, and which is unrelated to HFMD.

**Treatment**

There is no specific treatment for HFMD. Routine supportive measures and symptomatic management are the main measures. The children with HFMD are advised to be away from public community to avoid the spread of the disease.

(Yan-ying Xu, Yoshiki Sugiyama)

**e. Fungal infection**

Fungi are eukaryotic microorganisms. By far the most important fungus of relevance in dentistry is a yeast which belongs to the genus *Candida*. It is an oral commensals of about one-half of the general population. The disease caused by *candida* in oral cavity is called oral candidosis or oral candidiasis.

**Oral candidosis**

Oral candidiasis is an infection of yeast fungi of the genus *Candida* on the mucous membranes of the mouth. It is frequently caused by *Candida albicans*, or less commonly by *Candida glabrata* or *Candida tropicalis*.

**Etiology**

The infection is usually endogenous in origin. Several species in the genus *Candida* are found in man, including *C. albicans*, *C. glabrata*, *C. krusei* and *C. tropicalis*, *C.dubliniensi*, *C. guillermondii*, *C. Paraposilosis*. Oral candidosis is an opportunistic infection. The yeastlike fungus that causes oral candidosis occurs in both yeast and mycelial forms in the oral cavity. Growth of the organism occurs by budding of the yeast cells to form germ tubes and individual hyphal elements, which undergo limited peripheral branching to form a pseudomycelium. These phenomena can be demonstrated in smears and tissue sections from the oral cavitiy. *Candida* species are normal inhabitants of the oral flora of many individuals, but are present in the mouth of the healthy carrier in low concentration. Because *Candida* species are normal oral inhabitants, like other microoganisms involved in endogenous infections, *Candida* are of low virulence, are not usually considered contagious, and are involved in mucosal infection only when there is a definite local or systemic predisposition to their enhanced reproduction and invasion. There are a variety of predisposing factors for oral candidosis.

1) Marked changes in the oral microbial flora following administration of broad-spectrum antibiotics, excessive use of antibacterial mouth-rinse or aerosolized inhalant treatment.
2) Chronic local irritants such as denture trauma, orthodontic appliance, heavy smoking.
3) Xerostomia secondary to radiation of head and neck, to medicine, to salivary gland disease.
4) Immunologic deficiency (such as AIDS patients)or hospitalization and lower the host resistant. Diabetics with poorly controlled diabetes. Women undergoing hormonal changes, like pregnancy or those on birth control pills.

**Clinical manifestation**

The clinical features of oral candidosis are divided into several types.

**Pseudomembranous candidosis:** acute or chronic, the former is the most common type of pseudomembranous candidosis, also called thrush. It is the superficial infection of the upper layers of the mucosal epithelium and results in the formation of patchy white plagues on the mucosal surface that are composed of desquamated epithelial cells, inflammatory cells, fibrin, yeasts and *candida* mycelial element. The surrounding mucosa may or may not be reddened, but removal of the plaques by gently scraping usually reveals an area of erythema or even shallow ulceration, depending the duration of lesion and virulence of the pathogen.

**Acute erythematous candidosis:** also called acute atrophic candidosis, antibiotic sore-mouth. The clinical features are red patch of atrophic or erythematous, generalized depapillation of the tongue and angular cheilitis. Mucosa may be painful. Antibiotic sore-mouth should be suspected in a patients who develops symptoms of oral burning, bad taste, or sore throat.

**Chronic erythematous candidosis:** also called chronic atrophic candidosis, denture sore-mouth or denture stomatitis. Denture sore mouth is a diffuse inflammation of the denture bearing area with or without cracking and inflammation of the oral commissures (angular cheilitis). Pain and burning sensation are the common symptoms.

**Chronic hyperplastic candidosis:** also called candida leukoplakia. The clinical features are a variety of clinically recognized conditions in which mycelial invasion of the deeper layers of the mucosa. A firm, white, leathery plagues are found on the cheeks, lips and tongue. Epithelial dysplasia occurs four to five times more frequently in candida leukoplakia than in leukoplakia in general.

**Chronic mucocutanous candidosis:** persistent infection with candida usually occurs as a result of a defect in cell mediated immunity.

**Diagnosis**

The diagnosis of oral candidosis should be based on the clinical features and laboratory findings (smear, culture for candida and histopathology for heperplastic candidosis), as *candida* is a opportunity pathogen.

1) Clinical manifestation and symptoms of oral candidosis, such as burning and dry sensation of the oral mucosa, loss of taste; typical white adherent patch on the oral mucosa; red patch of atrophic or erythematous, generalized depapillation of the tongue and angular cheilitis or leathery plagues.
2) History of medicine taken or other predisposing factor exist.

3) Demonstration of yeast and hyphae form of *Candida* in 10% KOH smear or Gram-stained smear, followed by culture of specimen on Sabouraud agar. Saliva culture, concentrated rinse culture or cotton swab are common used in the clinic.
4) Histopathological examination of a biopsy of lesion of chronic hyperplastic candidosis demonstrate tissue invasion by candidal hyphae.
5) Serology is helpful in the diagnosis of disseminated candidosis.

**Treatment**

As oral candidosis is almost always endogenous in origin, correction of predisposing factors and treatment of the underlying disease is very important, such as anbiotics usage, loosing denture, underlying keratotic lesion or immune deficiency.

Anti-fungal agents: Superficial infections can be treated topically with polyene(nystatin or amphotericin) or an imidazole(miconazole, clotrimazole).

The new triazole agent fluconazole is effective for both superficial and systemic candidosis. Patients who are immunocompromised, either with HIV/AIDS or as a result of chemotherapy, may require systemic treatment with oral or intravenous administered anti-fungals.

The majority of acute oral candidosis respond rapidly to topical nystatin, that is seven to ten days use of nystatin rinse or allowing dissolve slowly under the tonge, three to four times daily.

The response of chronic oral candidosis to either topical antifungal agents, nystatin or fluconazole may be less dramatic, usually because of the persistence of predisposing factors. Treatment of 2 to 4 week or more with triazole agent is needed for patients with chronic hyperplastic candidosis. It must be remembered that treatment of denture sore mouth and angular chelitis must include elimination of *Candida* from the denture surface either by making a new denture or by adding nystatin suspension or cream before it it inserted in the mouth and soak the denture overnight by the suspension.

(Yan-ying Xu)

**f. Oral candidiasis**

Oral candidiasis is a fungal infection of the oral cavity caused by the yeast *Candida albicans* (*C. albicans*), a commensal micro-organism found to inhabit

different sites of the body, including the oral cavity in healthy individuals[1, 2]. There are various clinical presentations of oral candidiasis[3]. The dorsum of the tongue and the palate are commonly affected (Fig. 10-5-9, -10). Erythematous, pseudomembranous, and hyperplastic candidiasis are most commonly recognized[1, 2]. Erythematous candidiasis is a clinical form of oral candidiasis characterized by localized erythema of the oral mucosa. This lesion has been demonstrated to be associated with HIV infection and chronic use of broad-spectrum antibiotics and corticosteroids. Pseudomembranous candidiasis, clinically presenting as confluent whitish-yellow creamy plaques on the surfaces of the oral mucosa and tongue (Fig. 10-5-11), is most common in immunocompromised individuals, particularly those of extreme age, those with poorly controlled diabetes mellitus, HIV infections, and AIDS, and those who have been receiving long-term broad-spectrum antibiotics and psychotropic medications[1-3].

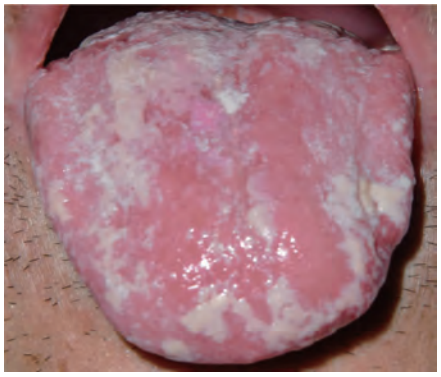

Fig. 10-5-9
Pseudomembranous candidiasis on the dorsum of the tongue.

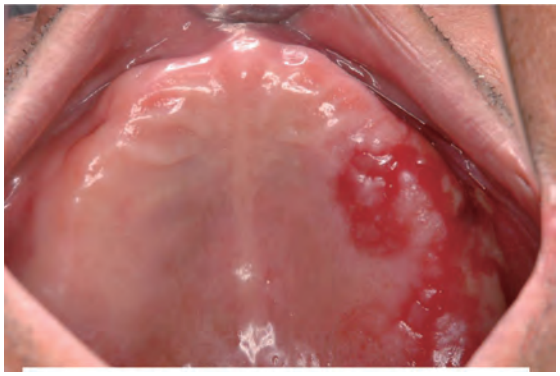

Fig. 10-5-10
Erythematous candidiasis on the palatal gingiva

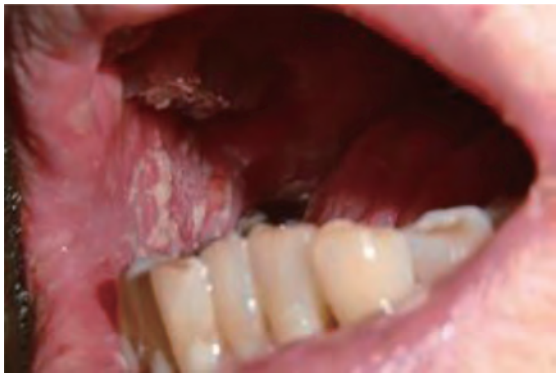

Fig. 10-5-11
Pseudomembranous candidiasis on the right buccal mucosa.

Hyperplastic candidiasis presents as well-demarcated, slightly elevated, adherent white lesions on the oral mucosa, ranging from small translucent lesions to large, dense opaque plaques. The most frequent site is the post-commissural buccal mucosa[1-3]. It is important to recognize that this lesion has a higher degree of dysplasia and malignant transformation than leukoplakia without candidal infection. Generally, the diagnosis of oral candidiasis should be based on medical history and thorough examination. Direct examination of a swab or smear and culture of a whole saliva or mouth rinse sample have been described. In particular, biopsy has been suggested to be useful for the diagnosis of hyperplastic candidiasis. For the management of oral candidiasis, it is essential to recognize the underlying causes and eliminate them as much as possible[1-3]. Any deficiencies (e.g., of iron, folate, or vitamins $B_{12}$ and C); presence of diabetes mellitus; and any drug histories (e.g., antimicrobials, corticosteroids) should be investigated. In denture-associated erythematous candidiasis, in particular, dentures should be adjusted or replaced[4, 5]. Particular attention should be paid to oral and denture hygiene. If elimination of the underlying causes is not effective, administration of antifungal agents (e.g., nystatin, miconazole, amphotericin lozenges) may be necessary[6, 7].

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(Kei Tomihara, Makoto Noguchi)

**g. Coccigenic stomatitis**

Coccigenic stomatitis is one of the acute bacterial infection of oral mucosa, mainly caused by cocci. The clinical feature of the disease is the formation of pesudomembrane. Coccigenic stomatitis also called membranous stomatitis, cocus stomatitis, pseudomembranous stomatitis.

**Etiology**

In health the nose, throat and the mouth are colonized by a wide spectrum of bacterial species which lead a commensal existence. In health these endogenous organisms are unable to gain access to the tissue and cause disease because there is an effective array of defence mechanisms. Membranous stomatitis occurs only when the host defence mechanisms were broken. The most common pathogens are *Streptococcus pneumoniae*, *Streptococus pyogenes* and *Staphlococcus aureu*s.

**Clinical manifestation**

**Staphylococcal stomatitis:** It is most common in children. The lesions are usually located on gingiva. The typical signs are gingival erythema, swollen gingvae covered with grey white thin peudomembrane composed of fibrin exudation, without marginal ulcer or erosion.

**Streptococcal stomatitis:** It is also most common in children. The disease is characterized by upper respiratory tract infection, fever, sore throat, headache. The sign and symptoms are accompanied by the diffused acute gingival stomatitis, covered with grey white peudomembrane. The peudomembrane can be scraped,usually reveals an area of shallow ulceration, the peudomembrane will soon re-formed. The patient feel painful and with halitosis.

**Pneumococcal stomtitis:** It's seldom seen in clinic and relatively common in children and aged people. The most affect site of oral mucosa are hard palate, buccal mucosa and the ventral surface of the tongue. Sometimes, the disease is accompanied with pneumonia.

**Diagnosis**

The diagnosis of membranous stomatitis is basically on the clinical features such as peudmembrane formation and smear from the peudmembrane with positive cocci.

**Treatment**

Antibiotic should be used to control the infection. Supportive and symptomatic treatments are also needed.

(Yan-ying Xu)

**h. Acute necrotizing ulcerative gingivitis**

It is also known as acute ulcerative gingivitis, gangrenous stomatitis, "Plaut-Vincent angina", "Vincent's stomatitis", "Vincent's angina", "Vincent's infection", or "trench mouth." Acute necrotizing ulcerative gingivitis (ANUG) is an endogenous oral infection that is characterized by necrosis of the gingiva. Occasionally, ulcers of the oral mucosa also occur in patients with hematologic disease or severe nutritional deficiencies.

**Etiology**

The disease is a specific, anaerobic, polymicrobial infection due mainly to the combined activity of fusobacteria (*F. nucleatum*) and oral spirochaetes (*Treponema spp*.) ; the so-called *fusospirochaetal complex*.

The disease is commonly associated with poor oral hygiene, severe malnutrition, heavy smoking, emotional stress, acquired immunosuppression and infection with HIV. Systemic disorders associated with ANUG are diseases affecting neutrophils. The mortality rate without appropriate therapy exceeds 70%.

**Clinical manifestation**

It is characterized by acutely inflamed, red shiny and bleeding gingivae with irregularly-shaped ulcers, which initially appear on the tips of the interdental paplillae. The lesions are extremely painful and are covered by a pseudomembrane which can be wiped from the surface. The pseudomembrane consists of leucocytes, erthrocytes, fibrin, necrotic tissue debris and microoganisms. The patient's breath is malodorous.

**Diagnosis**

The diagnosis is based mainly on clinical sign (bleeding, interdental paplillae necrotic ulceration and pseudomembrane ) and symptoms(painful, halitosis and fever). Confirmatory evidence is abtained by microscopy of a Gram-stained smear prepared from the surface of the ulcerated lesion.

**Treatment**

Oral hygiene advice and mouthwashes should be given to the patient regarding vigorous mouth rinsing ( with hydrogen peroxide 1.5 % in water and chlorhexidine 1.2% three times a day).and gentle brushing with a soft brush.

Initial local debridement is essential, but complete debridement may not be possible on the first visit because of soreness. After the disease is resolved, the patient should return for a complete periodontal evaluation.

Anti-anaerobic bacteria treatment: Antibiotics are usually not necessary for routine cases of ANUG confined to the marginal and interdental gingivae. These cases can be successfully treated with local débridement, irrigation, curettage, and home care instruction. Antibiotics should be prescribed for patients with extensive gingival involvement, lymphadenopathy, or other systemic signs, and in cases in which mucosa other than the gingivae is involved. metronidazole is the drug choice.

(Yan-ying Xu)

**i. Tuberculosis**

Tuberculosis is a common and often deadly infectious disease caused by mycobacteria, in humans mainly *Mycobacterium tuberculosis*. Tuberculosis usually attacks the lungs but can also affect the central nervous system, the lymphatic system, the circulatory system, the genitourinary system, the gastrointestinal system, bones, joints, and even the skin. Oral lesions of tuberculosis are usually secondary to primary infection elsewhere, commonly the lung. The major oral lesions are ulceration more commonly found in the posterior part of the mouth.

**Etiology**

Tuberculosis is spread through the air, when people who have the disease. One–third of the world's current population has been infected with M. tuberculosis, and new infections occur at a rate of one per second. However, most of these cases will not develop the full-blown disease; asymptomatic, latent infection is most common. About one in ten of these latent infections will eventually progress to active disease. Other mycobacteria such as *Mycobacterium bovis*, *Mycobacterium africanu*m, *Mycobacterium canetti*, and *Mycobacterium microti* also cause tuberculosis, but these species are less common in humans.

**Clinical manifestation**

There is a wide spectrum of tuberculous lesions of the oral mucosa, including indolent ulcers, diffuse inflammatory lesions, granulomas and fissures; pain may be mild or absent. The tongue is the most commonly affected but lesions have been noted on the buccal mucosa, gingivae, floor of the mouth, lips, and the hard and soft palates. Primary tuberculosis of the oral mucosa is more common in children and adolescents than in adults.

**Diagnosis**

Tuberculosis is diagnosed definitively by identifying the causative organism (*Mycobacterium tuberculosis*) in a clinical sample. The diagnosis of tuberculosis oral infection is based on clinical feature (indolent ulcer persisting for a long time without healing). Smear and culture for M. tuberculosis, biopsy for tuberculous nodus are helpful to confirm the diagnosis.

**Treatment**

The two antibiotics most commonly used are rifampicin and isoniazid. However, instead of the short course of antibiotics typically used to cure other bacterial infections, TB requires much longer periods of treatment (around 6 to 12 months). Topical injection of streptomycin is available to treat the oral lesions.

(Yan-ying Xu)

**j. Measles**

Measles is an extremely infectious childhood viral disease. It is caused by a measles virus (paramyxovirus) infection, and a systemic rash develops (Fig. 10-5-12A). Measles has a 7-14 day incubation period. Koplik's spots appear 1-2 days before the onset of the systemic rash and they assist in diagnosis. Koplik's spots consist of a few or a cluster of white or yellow-white pinpoint papules on an inflamed, red background on the buccal mucosa (Fig. 10-5-12B). A measles vaccination is recommended at age one for prevention.

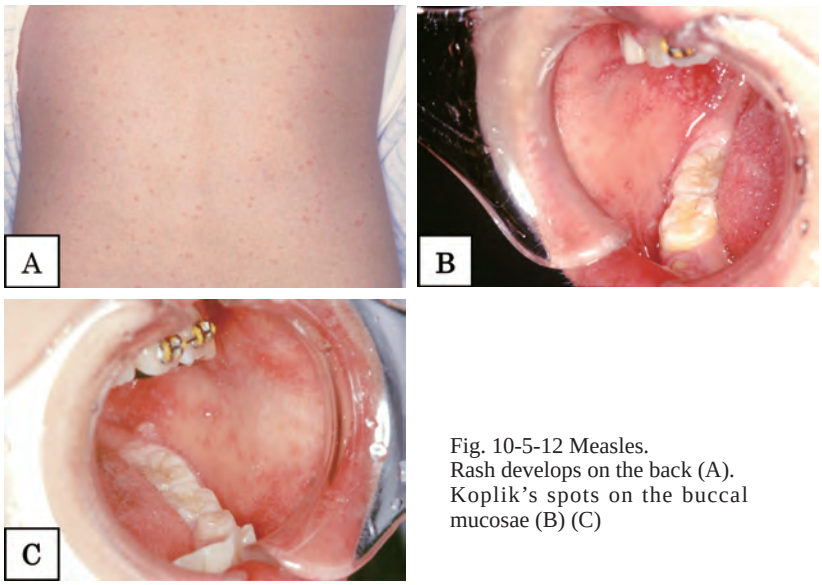


Fig. 10-5-12 Measles.
Rash develops on the back (A).
Koplik's spots on the buccal mucosae (B) (C)

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(Yoshiki Sugiyama)

**k. Syphilis**

**Etiology**

Syphilis is a sexually transmitted disease caused by the spirochetal bacterium *Treponema pallidum* subspecies *pallidum*. The route of transmission of syphilis is almost always through sexual contact, although there are examples of congenital syphilis via transmission from mother to child in utero.

**Clinical manifestation**

The signs and symptoms of syphilis are numerous; before the advent of serological testing, precise diagnosis was very difficult. In fact, the disease was dubbed the "Great Imitator" because it was often confused with other diseases, particularly in its tertiary stage.

**Primary syphilis:** Chancre is the characteristic sign of primary syphilis and normally appears in the genitalia, but extragenital lesions, mostly in the oral cavity, occur in some of 10% of cases. The common sites affected are the lips and tongue, gingivae and tonsillar area. The lesions heal spontaneously about 5 weeks after appearing.

**Secondary syphilis:** It is the most oral manifestation of syphilis. The so-called"mucous patch" is the typical lesion of secondary syphilis, which is a slightly raised, greyishwhite glistening pathches on the oral mucosa of tonsils, soft palate, tongue and cheek; gingivae are rarely involved. Pain may be mild or absent or not comparable to the extent of the patches. The lesions may heal in 2-6 weeks. However, typical lesions may not always be present because of unsuitable antibiotics usage by the patients themselves. Sirochaetes are easily found in the mucous patch.

**Tertiary syphilis:** The gumma is the typical sign of this stage. The most common site of gumma is the hard plalate, but the soft palate, lips and tongue may be involved. Another manifestation of tertiary syphilis is the atrophic glossitis of both

atrophy of filiform and fungiform papillae which resluts in a smooth, sometimes wrinkled, lingual surface; subsequent leucoplakia may develop.

**Latent syphilis:** Latent syphilis is defined as having serologic proof of infection without signs or symptoms of disease. Latent syphilis is further described as either early or late. Early latent syphilis is defined as having syphilis for two years or less from the time of initial infection without signs or symptoms of disease. Late latent syphilis is infection for greater than two years but without clinical evidence of disease. The distinction is important for both therapy and risk for transmission.

**Diagnosis**

Microscopy of fluid from the primary or secondary lesion using darkfield illumination can diagnose treponemal disease with high accuracy. It is useful for the early diagnosis of chancre.

Rapid Plasma Reagin (RPR) and Venereal Disease Research Laboratory (VDRL) tests are fast but not specific, as many other conditions can cause a positive result. It's useful for the diagnosis of secondary syphlis. False positives on the rapid tests can be seen in viral infections (Epstein-Barr, hepatitis, varicella, measles), lymphoma, tuberculosis, malaria, Chagas Disease, endocarditis, connective tissue disease, pregnancy, intravenous drug abuse, or contamination. As a result, these two screening tests should always be followed up by a more specific treponemal test. Tests based on monoclonal antibodies and immunofluorescence, including Treponema pallidum hemagglutination assay (TPHA) and Fluorescent Treponemal Antibody Absorption (FTA-ABS) are more specific.

**Treatment**

The main principals of antibiotic treatment are early treatment, sufficient time of treatment, regular checking of the titer of RPR. The most common and effective use of antibiotic for syphilis remains penicillin in the form of penicillin G. Non-pregnant individuals who have severe allergic reactions to penicillin may be effectively treated with oral tetracycline or doxycycline. Follow-up includes clinical evaluation at 1 to 2 weeks followed by clinical and serologic evaluation at 3, 6, 9, 12, and 24 months after treatment.

Individuals sexually exposed to a person with primary, secondary, or early latent syphilis within 90 days preceding the diagnosis should be assumed to be infected and treated for syphilis, even if they are currently seronegative. Patient education is important as well.

(Yan-ying Xu)

**l. Gonorrhea**

**Etiology**

Gonorrhea is caused by the bacterium Neisseria gonorrhoeae and is a common sexually transmitted infection.

**Clinical manifestation**

Between 30% and 60% of people with gonorrhea are asymptomatic or have subclinical disease. The combination of urethritis and cervicitis on examination strongly supports a gonorrhea diagnosis. The infection is transmitted from one person to another through vaginal, oral, or anal sexual relations, though transmission occurs rarely with safe sex practices of condom usage with lubrication. Non-genital sites in which it thrives are in the rectum, the throat (oropharynx), and the eyes (conjunctiva).

The oropharynx lesions are seen in about 20% of patients with gonorrhea. Primary oral gonorrhea is related to have oral-sex with infected partners; secondary oral gonorrhea may be a result of blood spread of the disease, The oropharynx lesions are non-specific inflammation with purulent secretion, with mild sore throat.

**Diagnosis**

History and clinical feature, confirmed by culture and biopsy.

**Treatment**

Antibiotics are available to be used to treat gonorrhea, e.g. Amoxicillin, Ampicillin. follow-up are usually advised to phone for results five to seven days after diagnosis to confirm that the antibiotic they received was likely to be effective, as drug resistant strains are known to exist. Patients are advised to abstain from sex during treatment.

(Yan-ying Xu)

**m. Condyloma acuminatum**

**Etiology**

Condyloma acuminatum(or Genital warts, Condyloma) is a highly contagious sexually transmitted infection caused by some sub-types of human papillomavirus (HPV). It is spread through direct skin-to-skin contact during oral, genital, or anal

sex with an infected partner. Warts are the most easily recognized sign of genital HPV infection. They can be caused by strains 6, 11, 30, 42, 43, 44, 45, 51, 52 and 54 of genital HPV; types 6 and 11 are responsible for 90% of genital warts cases. Less than 1% of those infected develop clinically obvious warts, but those infected can still transmit the virus.

**Clinical manifestation**

Genital warts often occur in clusters and can be very tiny or can spread into large masses in the genital or penis area. When present, they usually are seen on the tip of the penis. Rarely, genital warts also can develop in the mouth or throat of a person who has had oral sex with an infected person. The tongue is most common site involved oral mucosa.

**Diagnosis**

The diagnosis of Condyloma acuminatum is based on the history and tissue histopathology finding by biopsy as well as HPV strains results.

**Treatment**

There is no cure for HPV at present, but there are methods to treat visible warts, which could reduce infectivity. Surgical excision is best for large localized warts. Liquid nitrogen cryosurgery is safe for pregnancy. It kills warts 71-79% of the time, but recurrence is 38% to 73% 6 months after treatment. Trichloroacetic acid (TCA) has effectiveness similar to cryosurgery.

(Yan-ying Xu)

**n. HIV infection and acquired immune deficiency syndrome**

Acquired immune deficiency syndrome or acquired immunodeficiency syndrome (AIDS) is the name given to a group of disorders characterized by a profound cell-mediated immunodeficiency caused by the human immunodeficiency virus (HIV).

**Etiology**

HIV is a retrovirus that primarily infects vital organs of the human immune system such as $CD4^+$ T cells, macrophages and dendritic cells. It directly and indirectly destroys $CD4^+$ T cells. The disease is transmitted by sexual intercourse,

exposure to blood-borne pathogens and perinatal transmission. The main groups of individuals affected are promiscuous individuals (both homosexuals and heterosexuals, intravenous drug abusers, haemophiliacs receiving contaminated blood; offspring of infected mothers. There are no documented cases of HIV infection from casual or social contact.

**Clinical manifestation**

AIDS is characterized by opportunistic infections and malignancies, the estimated incubation period varies from 5 months to 10 years. About 50 to 70% percent of HIV-infected individuals progress to full-blown AIDS. By far, the most common features of AIDS are Kaposi's sarcoma and *Pneumocystis carinii* pneumonia. Oral manifestation of HIV infection are fungal infections (oral candidosis), viral infections(hairy leukoplakis, palillomas,herpes infection), bacterial infections (gingivitis and periodontitis).

Oral candidosis: oral candidosis is a very common feature seen very commonly with HIV infection. It is often seen in the early stage of the disease. It is a relatively reliable prognostic indicator of the disease progression to AIDS. Pseudomembranous and erythematous oral candidosis are the common clinical types of the infection.

Hairy leukoplakia: the typical clinical feature is asymptomatic, grayish-white or white, corrugated lesion on the lateral margin of the tongue, which is thought to be related to Epstein-Barr virus(EBV) infection. It is considered as a poor prognostic indicator of the disease.

Herpetic stomatitis: This includes herpes simplex, herpes zoster and papilloma virus infection. The herpetic infection is often extensive, severe and prolonged.

Necrotizing ulcerative gingivitis and periodontitis: The anterior gingiva is most commonly affected and sometimes not responsive to routine treatment,

**Diagnosis**

A significant proportion of individuals who are infected with HIV produce antibodies within 1-2 weeks. The diagnosis of HIV infection is based on the: demonstration of antibody serologically by immunoassay, followed by a confirmatory Western blot assay.

**Treatment**

There is currently no vaccine or cure for HIV or AIDS. The only known methods of prevention are based on avoiding exposure to the virus or, failing that, an antiretroviral treatment directly after a highly significant exposure, called post-

exposure prophylaxis. PEP has a very demanding four week schedule of dosage. Current treatment for HIV infection consists of highly active antiretroviral therapy, or HAART. Standard goals of HAART include improvement in the patient's quality of life, reduction in complications, and reduction of HIV viremia below the limit of detection, The drugs which are widely used comprise the antiviral azidothymidine(AZT) and didanosine, some 100 potential drugs are currently being tested.

(Yan-ying Xu)

# *10-6. Other diseases*

**a. Focal fibrous hyperplasia**

Focal fibrous hyperplasia also known as irritational fibroma, oral fibroma, or fibrous nodule, is a common benign lesion of the oral mucosa and is caused primarily by physical injury such as lip- and cheek biting or denture irritation. The buccal mucosa, lips, and tongue are commonly affected. Clinically, this condition presents as a dome-shaped, nodular, or polyp-like painless mass with a smooth mucosal surface of normal color. Histopathologically, it is characterized by a mass of dense, fibrous connective tissue composed of collagen, fibroblasts, and chronic inflammatory infiltrations. The overlying surface epithelium may exhibit hyperkeratosis. The differential diagnosis of submucous fibrosis includes lipoma, mucocele, amyloid deposit, and extramedullary plasmacytoma[2-4]. The treatment of submucous fibrosis consists of surgical excision of the lesion[1].

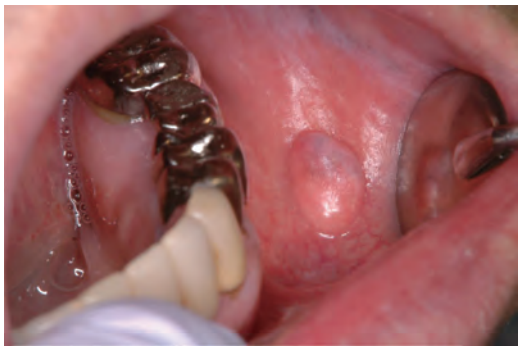

Fig. 10-6-1
Exophytic submucosal mass on the left buccal mucosa

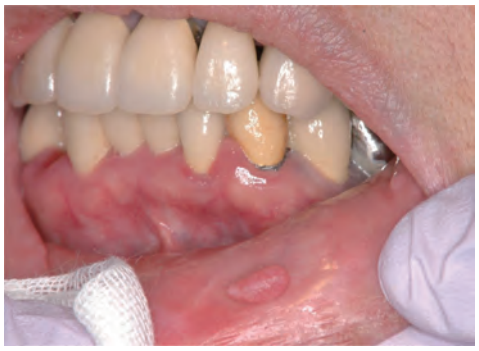

Fig. 10-6-2
Exophytic submucosal mass on the lower lip

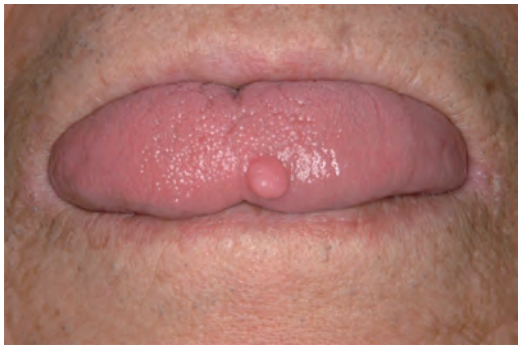

Fig. 10-6-3
Exophytic submucosal mass on the tip of the tongue

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**b. Oral pigmentation**

Pigmentation of oral mucosa is defined as a change in the color of the oral mucosa, which can result from various clinical entities such as physiologic changes (e.g., racial pigmentation), manifestation of systemic illnesses (e.g., Peutz–Jeghers syndrome, Addison's disease, Albright syndrome, von Recklinghausen's disease), and malignant neoplasms (Kaposi's sarcoma, malignant melanoma)[1-3]. Oral pigmentation may be a feature of lesions of exogenous or endogenous origin. Oral pigmentation of endogenous origin is associated with melanin, hemoglobin, hemosiderin, and carotene deposition. Pigmentation caused by increased melanin deposition may appear brown, blue, grey, or black, depending on the amount and the location of melanin in the tissue. Several medications, including antimalarial drugs, tetracycline, or chemotherapeutic agents, and smoker's melanosis may also cause oral pigmentation[4, 5].

In contrast, oral pigmentation of exogenous origin is associated with foreign bodies such as heavy metals or amalgam[6]. The most common cause for heavy metal pigmentation is occupational exposure to heavy metal vapors. Amalgam tattoo is also one of the most common causes of oral pigmentation. Differential diagnosis of the pigmented lesion is made on the basis of clinical findings, including systemic signs and symptoms, intraoral and extraoral findings, and laboratory data[1-3]. Medication or smoking habits should also be assessed. Regular borders, small size, uniform color, and flatness may suggest benign lesions. In contrast, irregular borders, color variation, and surface ulceration may suggest malignancy[7].

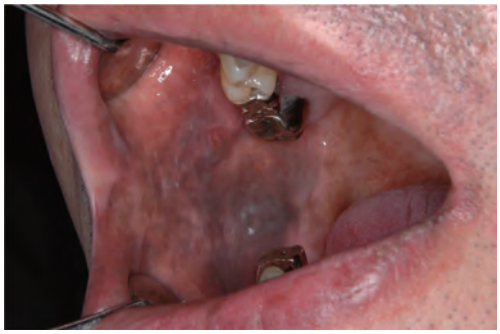

Fig. 10-6-4
Pigmented lesion on the buccal mucosa

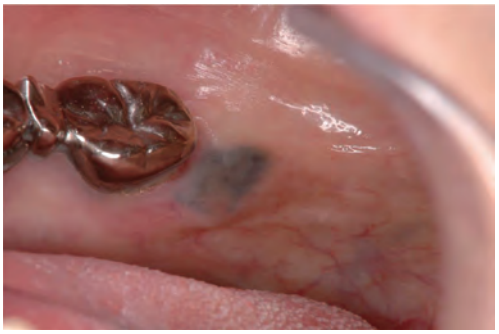

Fig. 10-6-5
Pigmented lesion on the attached gingiva

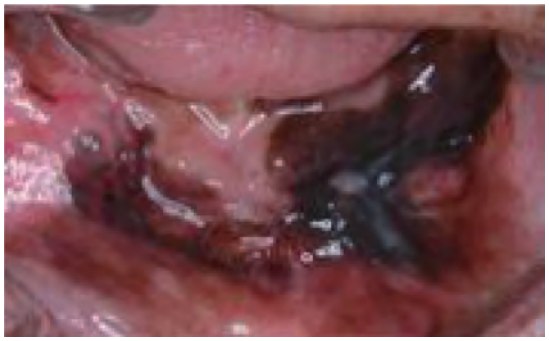

Fig. 10-6-6
Malignant melanoma of the mandibular gingiva. The lesion appears brownish-black with irregular borders.

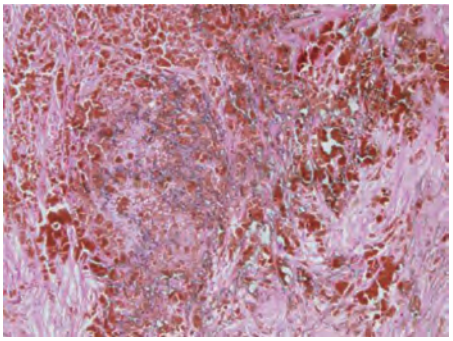

Fig. 10-6-7
Histopathology of oral mucosal melanoma.

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(Kei Tomihara, Makoto Noguchi)

**c. Stomatitis**

Stomatitis presents as single or multiple, variably sized, painful ulcers of the oral mucosa (Figs 10-6-8, -9)[1]. Various causes such as bacterial infection (e.g., actinomycosis, syphilis, candidiasis); viral infection (e.g., HSV, VSV, herpangina, HIV, EBV, cytomegalovirus, influenza); systemic disorders (e.g., Behçet's disease, cyclic neutropenia, Sweet's syndrome); drugs (e.g., antibiotics, chemotherapeutic agents); physical injury; and radiation have been suggested[2-6]. Mouth rinses, topical corticosteroids, silver nitrate sticks, and $CO_2$ laser treatment have been prescribed for local treatment; administration of vitamin $B_{12}$, antimicrobial drugs, an antiviral drug, corticosteroids, and immunosuppressive drugs have been prescribed for systemic treatment[7].

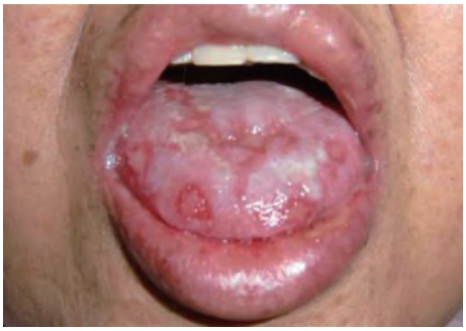

Fig. 10-6-8
A presentation of chemotherapy-related oral mucositis.

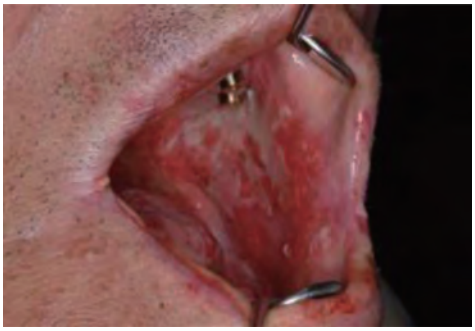

Fig.10-6-9
A presentation of oral mucositis in a patient receiving radiation therapy.

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(Kei Tomihara, Makoto Noguchi)

**d. Epulis**

**Overview**

Epulis refers to inflammatory or reactive proliferation arising in the gingiva, and is not classed as a true tumor. It is considered to represent a chronic proliferative mass formed by periodontal tissue, typically the periodontal membrane, and both systemic and local factors have been identified as contributing to its origin. As epulis generally occurs more commonly in women, systemically, hormones are believed to be involved, while irritation from periodontal disease, prostheses, dentures and other sources may contribute locally.

**Characteristics**

Epulis occurs in individuals in their 20s and above, peaking among those in their 40s. It develops later in women than in men, and is twice as common in women. When it occurs in pregnant women, this type of mass is known as “pregnancy epulis.” It is somewhat more common in the upper jaw than the lower, and in both cases is more frequent in the incisor region (Fig. 10-6-10, 10-6-11), followed by the molars, and is comparatively infrequent in the premolars. In terms of buccolingual position, it tends to occur more often on the buccal side than the lingual side, but large masses may extend across both sides. In the majority of cases, it occurs at sites where teeth are present, particularly the interdental papillae, but it may also arise at locations with no teeth. This lesion is usually pedunculated, and the surface mucosa is often of normal color, but in some cases it may be red, and erosion or ulcer formation due to irritation may occur. It varies in hardness from elastic-soft to bony-hard. Its growth is slow, and it does not cause pain or other subjective symptoms. Chronic bone resorption may be evident at the site of the mass. In epulis with the formation of hard tissue, radioopacity may be apparent in accordance with the degree of calcification.

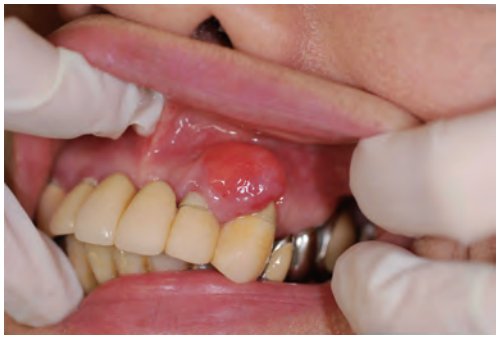

Fig. 10-6-10 Epulis (maxillary gingiva)

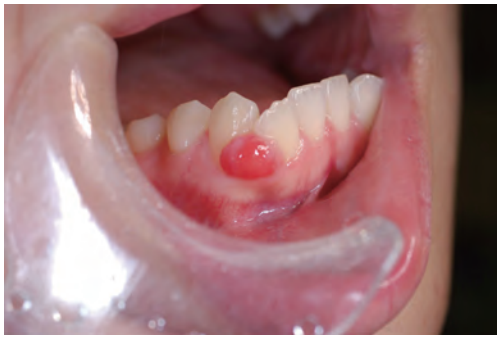

Fig. 10-6-11 Epulis (lowe r gingiva)

**Diagnosis**

Pathologically, epulis is classified as follows.

1) Epulis granulomatosa
   Composed of weak connective tissue with abundant capillary vessels, and associated with inflammatory cell infiltration.
2) Epulis fibrosa
   Pronounced fibrous tissue proliferation, with few capillary vessels and little inflammatory cell infiltration.
3) Epulis hemangiomatosa
   Capillary vessel growth and dilation are pronounced in an old epulis granulomatosa, with numerous dilated capillary vessels contained within fibrous components.
4) Epulis osteoplastica (epulis cementoplastica)
   Hard tissue formation is evident within fibrous tissue.
5) Epulis gigantocellularis
   Numerous giant cells resembling osteoclasts are contained within granulomatous tissue, with hemorrhage and hemoglobin deposition, and the proliferation of giant cells in close association with capillary vessels.

**Treatment**

Epulis may be resected, but resection of the surface layer may only result in recurrence. Sufficient curettage of the periodontal membrane and alveolar bone is necessary, and extraction is sometimes required. Pregnancy epulis may resolve spontaneously after delivery.

(Yutaka Imai, Yutaka Doi)

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