Oral Pathology

Salivary gland lesions and tumors

Salivary glands are tubulo-acinar exocrine organs responsible for the production and secretion of saliva. They comprise the three-paired major glands, the parotid, submandibular, and sublingual. There are also several hundred minor glands, which are widely distributed throughout the oral and oropharyngeal submucosa and, in some cases, the underlying muscle. Similar seromucous glands are present in the upper respiratory and sinonasal tracts, The functional unit of salivary glands is the secretory acinus and related ducts and myoepithelial cells. Acini may be serous, mucous, or mixed.

Normal function & health of the mouth depend on normal secretion of the saliva by the major & minor salivary glands.

Failure of salivary secretion causes a dry mouth which promotes oral infections.

Both the major & minor glands are composed of parenchymal elements which are supported by C.T. The parenchyma derived from the oral epithelium consists of terminal secretary units leading into ducts that open into the oral cavity.

The C.T. forms a capsule around the gland & extends into it. The blood & lymph vessels & nerves that supply the gland are contained within the C.T.

The most important function of S.G. is the production of saliva which contains various organic & inorganic substances & help in the mastication, deglutition & digestion of food.

Sialadenitis

Inflammation of the salivary glands **(sialadenitis)** can arise from various infectious and non infectious causes. The most common viral infection is mumps, although a number of other viruses also can involve the salivary glands, including Coxsackie A, ECHO, choriomeningitis, parainfluenza, and cytomegalovirus (CMV) (in neonates). Most bacterial infections arise as a result of ductal obstruction or decreased salivary flow, allowing

retrograde spread of bacteria throughout the ductal system. Blockage of the duct can be caused by sialolithiasis, congenital strictures, or compression by an adjacent tumor. Decreased flow can result from dehydration, debilitation, or medications that inhibit secretions.

CLINICAL AND RADIOGRAPHIC FEATURES

Acute bacterial sialadenitis is most common in the parotid gland and is bilateral in 10% to 25% of cases. The affected gland is swollen and painful, and the overlying skin may be warm and erythematous. An associated low-grade fever and trismus may be present. A purulent discharge often is observed from the duct orifice when the gland is massaged the main organisms involved being Streptococcus pyogenes and staphylococcus aureus, less commonly Haemophilus species. Recurrent or persistent ductal obstruction (most commonly caused by sialoliths) can lead to a chronic sialadenitis. Periodic swelling and pain occur within the affected gland, usually developing at mealtime when salivary flow is stimulated. In the submandibular gland, persistent enlargement may develop **(Küttner tumor),** which is difficult to distinguish from a true neoplasm. Sialography often demonstrates sialectasia (ductal dilatation) proximal to the area of obstruction In chronic parotitis, Stensen's duct may show a characteristic sialographic pattern known as "sausaging," which reflects a combination of dilatation plus ductal strictures from scar formation. Chronic sialadenitis also can occur in the minor glands, possibly as a result of blockage of ductal flow or local trauma.

HISTOPATHOLOGIC FEATURES

In patients with acute sialadenitis, accumulation of neutrophils is observed within the ductal system and acini. Chronic sialadenitis is characterized by scattered or patchy infiltration of the salivary parenchyma by lymphocytes and plasma cells. Atrophy of the acini is common, as is ductal dilatation. If associated fibrosis is present, then the term **chronic sclerosing sialadenitis** is used

TREATMENT AND PROGNOSIS

The treatment of acute sialadenitis includes appropriate antibiotic therapy and rehydration of the patient to stimulate salivary flow. Surgical drainage may be needed if there is abscess formation. Although this regimen is usually sufficient, a 20% to 50% mortality rate has been reported in debilitated patients because of the spread of the infection and sepsis. The management of chronic sialadenitis depends on the severity of the condition and ranges from conservative therapy to surgical intervention.

MUMPS (EPIDEMIC PAROTITIS)

Mumps :

Is a glandular viral disease usually affecting the parotid gland.
The sub mandibualr & sub lingual gland may also be affected.
Mumps is due to paramyxo virus (mumps virus), children are mainly affected, the incubation period of about 21 days, the infection start with high fever followed by a painful swelling behind the ear, the papilla of parotid (stensen's) duct may be swollen & secretion of the parotid are less so the mouth may be dry.
The pain subsides but the swelling persist for 5 days &then decrease. Permanent nerve deafness & meningitis are possible complication. In adult complications of mumps may develop orchitis.
After an attack immunity is long lasting, with wide use of immunization childhood mumps is becoming infrequent & mumps in adult may take a typical form.

TREATMENT AND PROGNOSIS

The treatment of mumps is palliative in nature. Frequently, non aspirin analgesics and antipyretics are administered. In an attempt to minimize orchitis, bed rest is recommended for males until the fever breaks.
Avoidance of sour foods and drinks helps to decrease the salivary gland discomfort. As with measles and rubella, the best results come from prior vaccination, thereby preventing the infection.

Other causes of viral sialadenitis

1- Cytomegalic inclusion disease (salivary gland inclusion disease)

Infection with cytomegalovirus, a member of herpesvirus group, is common in human and endemic worldwide. Most primary infections are asymptomatic, but the virus can cause severe disseminated disease in neonates and in immunocompromised hosts such as transplant patients and HIV infected persons

2-Postirradiation sialadenitis

Radiation sialadenitis is a common complication of radiotherapy and there is a direct correlation between the dose of radiation and the severity of the damage

3-sarcoidosis

Sarcoidosis may affect the parotid and minor salivar gland, parotid involvement presents as a persistent, often painless, enlargement and ma be associated with involvement of the lacrimal glands in Heerfordt syndrome

Salivary calculi (sialoliths)

Sialoliths are calcified structures that develop within the salivary ductal system. Researchers believe that they arise from deposition of calcium salts around a nidus of debris within the duct lumen. This debris may include inspissated mucus, bacteria, ductal epithelial cells, or foreign bodies. The cause of sialoliths is unclear, but their formation can be promoted by chronic sialadenitis and partial obstruction. Their development is not related to any systemic derangement in calcium and phosphorus metabolism.

CLINICAL AND RADIOGRAPHIC FEATURES

Sialoliths most often develop within the ductal system of the submandibular gland; the formation of stones within the parotid gland system is distinctly less frequent. The long, tortuous, upward path of the submandibular (Wharton's) duct and the thicker, mucoid secretions of this gland may be responsible for its greater tendency to form salivary calculi. Sialoliths also can form within the minor salivary glands, most often within the glands of the upper lip or buccal mucosa. Salivary stones

can occur at almost any age, but they are most common in young and middle-aged adults. Major gland sialoliths most frequently cause episodic pain or swelling of the affected gland, especially at mealtime. The severity of the symptoms varies, depending on the degree of obstruction and the amount of resultant backpressure produced within the gland.
Sialoliths typically appear as radiopaque masses on radiographic examination. However, not all stones are visible on standard radiographs (perhaps because of the degree of calcification of some lesions). They may be discovered anywhere along the length of the duct or within the gland itself Minor gland sialoliths often are asymptomatic but may produce local swelling or tenderness of the affected gland. A small radiopacity often can be demonstrated with a soft tissue radiograph.

Sjogren's syndrome:

This is a condition characterized by a triad of keratoconjuctivitis sicca (dry eye), xerostomia (dry mouth) & rheumatoid arthritis.
Sjogren's syndrome is divided into:

1. Primary Sjogren's syndrome: also called sicca syndrome which consist of xerostomia & xerophthalmia.
2. secondary sjogren's syndrome: there is an associated rheumatoid arthritis or other connective tissue disease cyst (lupus erythromatosis, scleroderma)

The etiology is though to be auto immune.

Clinical features:

1. Occur predominantly in middle-aged women.
2. Dryness of the mouth & eyes as a result of the hypo function of the salivary & lacrimal glands.

The oral mucosa is obviously dry, red, shiny & wrinkled & sticks to the fingers or mirror during examination.
The tongue appears red, atrophy of the papillae & the dorsum becomes lobulated.
With diminished saliva secretion the oral flora changes & candidal infection are common.

Histopathology:

A labial biopsy is characterized by atrophy of the acini & replacement by lymphocytes mainly T-lymphocytes.

Diagnostic aspect:

Normal salivary flow is between 1&2 ml/min:

1. Diminished mixed salivary flow rate
   May be reduced to 0.5 ml/min or less.
2. Labial salivary gland biopsy showing periductal lymphocytic infiltrate.
3. Antibody screen especially rheumatoid factor.
4. Sialectasis on sialography (iodine-containing contrast medium)

Poor elimination of the contrast medium is noted with retention of the material for over a mouth, because of the reduced salivary flow.

Snow storm appearance of blobs of contrast.

Treatment:

The treatment of patient with Sjogren's syndrome is mostly supportive.

1. Periodic use of artificial tears for the dry eye.
2. Artificial saliva for xerostomia & because of increase risk of dental caries.
3. Daily fluoride application may be indicated in edentulous patients; also antifungal therapy is often needed to treat secondary candidiasis.

Malignant lymphoma can develop in Sjogren's syndrome.

Salivary Gland Tumors

Tumors of the salivary glands constitute an important area in the field of oral and maxillofacial pathology. Although such tumors are uncommon, they are by no means rare. The annual incidence of salivary gland tumors around the world ranges from about 1.0 to 6.5 cases per 100,000 people. Although soft tissue neoplasms (e.g., hemangioma), lymphoma, and metastatic tumors can occur within the salivary glands

Pleomorphic adenoma (benign mixed tumor)

Is a benign tumor which is the commonest of all salivary gland tumors, it account for about 75% of parotid gland tumors. The origin of this tumor is thought to arise from the myoepithelial cell or duct epithelium.

Clinically:

The most common site is the parotid gland, typically present as a painless size slowly reaching to several cm, there is no fixation to the deeper tissue or to the overlying skin, the skin rarely ulcerated.

Pleomorphic adenoma is also the most common intraoral salivary gland tumor, its usual location is the palate, when it presents as a smooth surface swelling resemble a fibroma, the upper lip is the next common site.

The lesion can occur at any age but is most common in young adults between the age of 30&50 years. There is a slight female predilection.

Histopathological features:

A pleomorphic adenoma is a circumscribed encapsulated tumor characterized by its pleomorphic or mixed appearance. The capsule may be incomplete or show infiltration by tumor cells.

The lesion shows a great variation in appearance, some area show:

1. Cuboidal cells arranged in tubes or duct like structure which may contain an easinophilic coagulum.
2. The tumor epithelial cells may be arranged in sheets or strands about these tubular structures. Some time the cells may assume a stellate, polyhydrate or spindle form.
3. Squamous epithelial cells are relatively common & there may be keratin pearls form.
4. Loose myxoid material can be seen.
5. The hyaline, mucoid, cartilage or even bone is a common finding.

Treatment:

Is by wide excision, in the parotid gland, the tumor & the involved lobe should be removed, recurrent rate in this position is high because of difficult surgical complete removal of tumors from the parotid, where the facial nerve is present.

The recurrence rate is low in skilled hands.

In the submandibular gland, tumor is removed with the whole gland because of malignancy.

Lesion of the minor salivary gland of the palate should be excised with the overlying mucosa, while those in the lip, soft palate & buccal mucosa treated successfully by encapsulation.

The tumors are radio resistant. Recurrence may occur due to incomplete resection or incomplete encapsulation.

Benign pleomorphic adenoma may undergo malignant changes either to a carcinoma, adenocarcinoma or cylindroma.

Warthins tumor: (Adenolymphoma, papillary cystadenoma lymphomatosum).

Is a benign neoplasm of the parotid gland. It accounts 9% of all parotid tumors. The pathogenesis of these tumors is uncertain, it is thought that they arise from heterotopic salivary gland tissue found within parotid lymph nodes.

It has also been suggested that these tumors may develop from a proliferation of SG ductal epithelium that is associated with secondary formation of lymphoid tissue, besides these several studies demonstrated a strong association between the development of this tumor and smoking.

Clinically:

This tumor present as slowly growing, painless, nodular mass of the parotid gland. It is most frequently occur in the tail of parotid near the angle of the mandible.

This tumor has a tendency to occur bilaterally but most of these bilateral tumors do not occur simultaneously but are occurring at different times, most common in man usually middle aged.

Histopathological features:

The tumor is composed of a mixture of ductal epithelium & lymphoid stroma. The epithelium is oncocytic in nature, forming uniform rows of

cells surrounding cystic spaces. The cells have abundant, finely granules, eosinophilic cytoplasm & are arranged in two layers.
The inner terminal layer consists of tall columnar cells with centrally placed pyknotic nuclei. Beneath this, is a second layer of cuboidal or polygonal cells with more vesicular nuclei. The lining epithelium demonstrates multiple papillary projections into the cystic spaces. The epithelium is supported by a lymphoid stroma.

Treatment:

Surgical removal, these tumors are well encapsulated & seldom reoccur after removal.

BASAL CELL ADENOMA

The basal cell adenoma is a benign salivary tumor that derives its name from the basaloid appearance of the tumor cells. It is an uncommon neoplasm that represents only 1% to 2% of all salivary tumors. Because of its uniform histopathologic appearance, it often has been classified as one of the monomorphic adenomas

ADENOMA)

The **oncocytoma** is a benign salivary gland tumor Surrounded by a thin capsule and consisted of large epithelial cells known as **oncocytes**.
The prefix *onco-* is derived from the Greek word *onkoustai*, which means *to swell*. The swollen granular cytoplasm of oncocytes is due to excessive accumulation of mitochondria.

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The **canalicular adenoma** is an uncommon tumor that occurs almost exclusively in the minor salivary glands. Because of its uniform microscopic pattern, the canalicular adenoma also has been called a *monomorphic adenoma*

Malignant tumors of salivary gland

Malignant tumors of salivary gland are relatively uncommon, accounting for about 1 per cent or less of all malignancies and about 5 percent of malignant tumors in the head and neck region.
Although carcinomas of salivary gland arise most frequently in major glands especially parotid

Mucoepidermoid carcinoma

MUCOEPIDERMOID CARCINOMA

The **mucoepidermoid carcinoma** is one of the most common salivary gland malignancies. Because of its highly variable biologic potential, it was originally called **mucoepidermoid tumor.** The term recognized one subset that acted in a malignant fashion and a second group that appeared to behave in a benign fashion with favorable prognosis. However, researchers later recognized that even low-grade tumors occasionally could 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. Rarely is it seen in the first decade of life, The mucoepidermoid carcinoma is most common in the parotid gland and usually appears as an asymptomatic swelling. Most patients are aware of the lesion for 1 year or less, although some report a mass of many years' duration. Pain or facial nerve palsy may develop, usually in association with high-grade tumors

Minor gland tumors

also typically appear as asymptomatic swellings, which are sometimes fluctuant and have a blue or red color that can be mistaken clinically for a mucocele. Although the lower lip, floor of mouth, tongue, and retromolar pad areas are uncommon locations for salivary gland neoplasia

Histopathological features :

From its name the mucoepidermoid CA is composed of a mixture of mucous –producing cells and epidermoid or squamous cells .

If the mucous – secreating cells are mainly predominant then the tumor tend to be cystic, if mainly epidermoid the tumor is solid and then more aggressive.

There is no well-defined capsule, and is invasive and occasionally metastasise.

Traditionally, mucoepidermoid carcinomas have been categorized into one of three histopathologic grades based on the following:
1. Amount of cyst formation
2. Degree of cytologic atypia
3. Relative numbers of mucous, epidermoid, and
intermediate cells

Low-grade tumors show prominent cyst formation, minimal cellular atypia, and a relatively high proportion
of mucous cells.

High-grade tumors consist of solid islands of squamous and intermediate cells, which can demonstrate considerable pleomorphism and mitotic activity. Mucus-producing cells may be infrequent, and the tumor sometimes can be difficult to distinguish from squamous cell carcinoma

Intermediate-grade tumors show features that fall between those of the low-grade and high-grade neoplasms. Cyst formation occurs but is less prominent than that observed in low-grade tumors. All three major
cell types are present, but the intermediate cells usually predominate. Cellular atypia may or may not be observed.

Treatment: is by wide excision but the tumor may recur

ADENOID CYSTIC CARCINOMA

The adenoid cystic carcinoma is one of the more common and best-recognized salivary malignancies. Because of its distinctive histopathologic features, it was originally called a **cylindroma,** and this term still is used sometimes as a synonym for this neoplasm. However, use of the term *cylindroma* should be avoided because it does not convey the malignant nature of the tumor, and also because this same term is used for a skin adnexal tumor that has a markedly different clinical presentation and prognosis.

ADENOID CYSTIC CARCINOMA usually grows slowly but usually shows distinct infiltrative spread. The tumor cells are of two types, duct lining cells and cells of myoepithelial type. It

occurs most frequently in the minor salivary gland of the palate, the parotid, submandibular and accessory gland in the tongue is also involved.

The lesion is most common in middle –aged adult equal sex distribution. It present as slowly growing mass, there is early local pain, facial paralysis may develop with parotid tumors; palataltumors can be smooth- surfaced or ulceration and may show radiographic evidence of bone destruction.

Histopathology:

1. Composed of small, deeply staining uniform cells resemble basal cells, which are commonly arranged in anastamosing cords or duct like pattern with mucoid material in the center. This produce a typical cribriform (honey comb or Swiss cheese appearance). pattern
2. In the tubular pattern, the tumor cells are similar but occur as multiple small ducts or tubules within a hyalinized stroma.
3. The solid form consist of larger islands or sheets of tumor cells which show little tendency toward duct or cyst formation.

Spread of the tumor cells along the perineural sheaths is a common feature of the disease.

Treatment:

Surgical removal with radiation. Metastasis occurs late in the course of the disease.

Carcinoma in pleomorphic adenoma (Malignant pleomorphic adenoma)

Pleomorphic adenoma can undergo malignant change; this is seen in a slowly growing lesion which rapidly starts to increase

in size, or sudden development of pain or facial palsy. The diagnosis require evidences evidence of a pre-existing pleomorphic adenoma

Histologically:

There may be only a few foci of malignant change or the lesion may be entirely malignant. The malignant transformation is either into:

1. Epidermoid carcinoma.
2. Adenocarcinoma.
3. Some time into both types.

The treatment is by surgery, although the lesion shows a high tendency to reoccur as well as a high incidence of regional lymph node involvement & some time distant metastasis

CT CARCINOMA)

The **polymorphous low-grade adenocarcinoma** is a more recently recognized type of salivary malignancy that was first described in 1983. Before its identification as a distinct entity, examples of this tumor were categorized as pleomorphic adenoma, an unspecified form of adenocarcinoma, or sometimes as adenoid cystic carcinoma. Once recognized as a specific entity, however, it was realized that this tumor possesses distinct clinicopathologic features and is one of the more common minor salivary gland malignancies