Oral Medicine

Salivary gland diseases II

Lecture 18

Dr. Mohanad Jameel

Necrotizing Sialometaplasia (NS)

Description and Etiology

Necrotizing sialometaplasia (NS) is a benign, self-limiting, reactive inflammatory disorder of salivary tissue. NS can resemble a malignancy and its misdiagnosis has resulted in unnecessary radical surgery.

The etiology is unknown, although it likely represents a local ischemic event, infectious process, or perhaps an immune response to an unknown allergen.

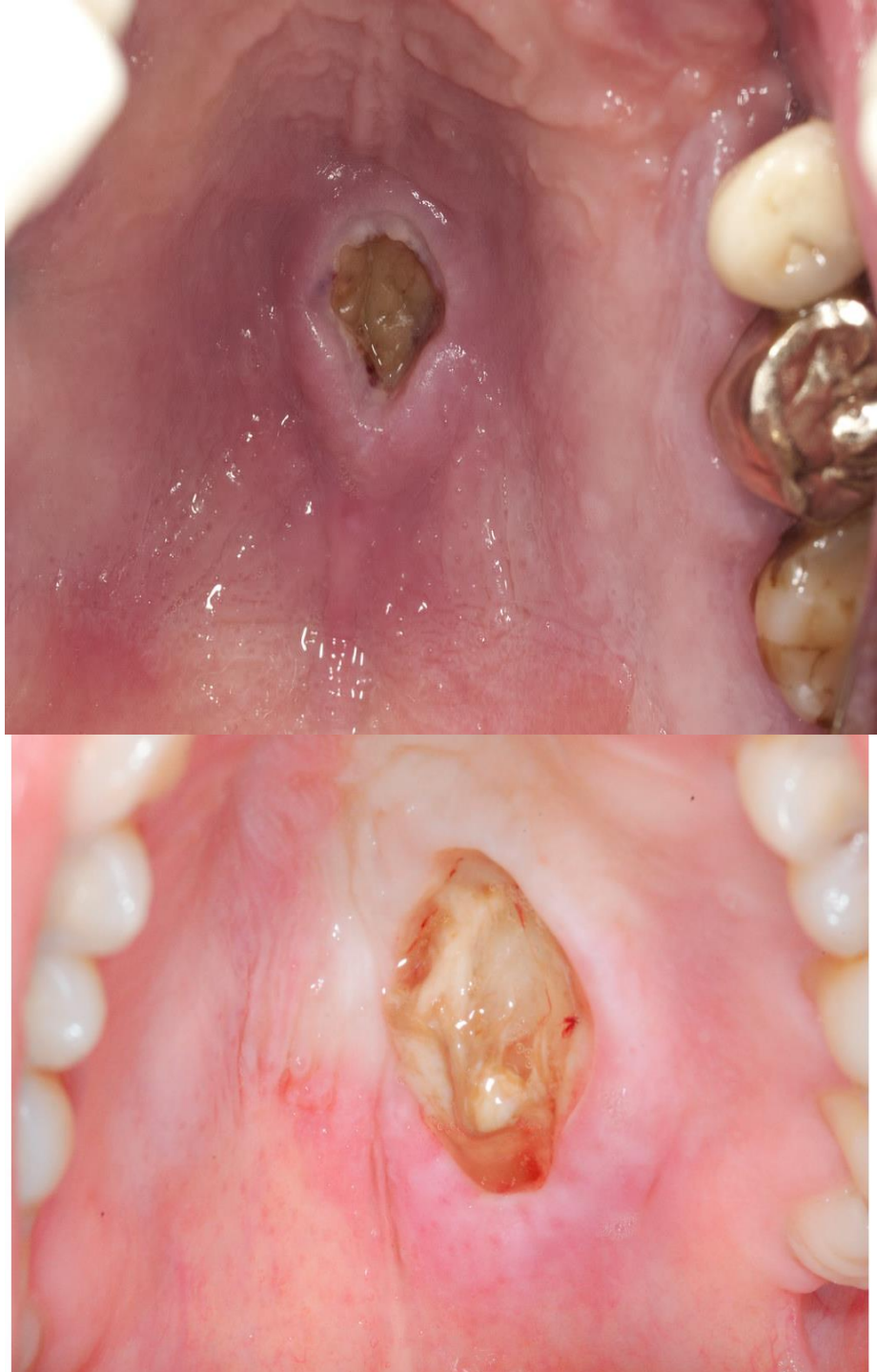
Development of NS has been associated with smoking, local injury, blunt force trauma, denture wear, and surgical procedures.

It has been reported in pregnant patients and those with diabetes mellitus, sickle-cell disease, cocaine abuse, bulimia, and chronic vomiting.

The incidence of NS appears to be higher in male patients and especially in those older than 40 years

Clinical Presentation

- NS has a spectrum of clinical presentations. Most commonly it presents as a painful, rapidly progressing swelling of the hard palate with central ulceration and peripheral erythema.
- The associated pain is often described as sharp in character and may precede mucosal changes. Numbness or anesthesia in the associated area may be an early finding.
- The lesions are of rapid onset and range in size from 1 to 3 cm.
- Lesions occur predominantly on the palate; however, lesions can occur anywhere salivary gland tissue resides.
- Although the lesions are usually unilateral, bilateral cases have been reported.
- Lesion affecting the hard palate clinically resemble salivary gland malignancies particularly mucoepidermoid carcinoma and adenoid cystic carcinoma.



- Rapid onset of NS may be a distinguishing feature.
- Lesions often occur shortly after an inciting event to the area such as oral surgical procedures, restorative dentistry, or administration of local anesthesia.
- It is also not uncommon for lesions to develop in an individual with no history of trauma or oral habit

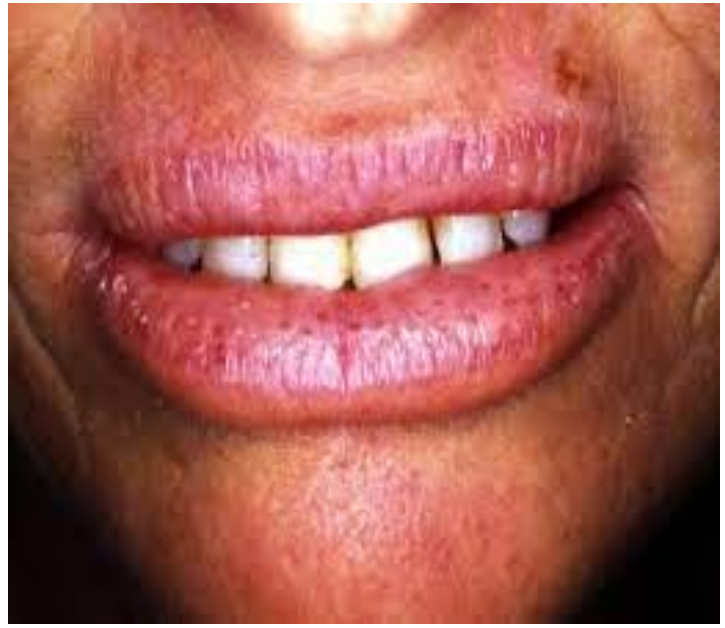
Diagnosis

Histopathologic diagnosis with complete clinical & medical history.

Treatment

- NS is considered a self-limiting condition typically resolving within 3–12 weeks.
- During this time, supportive and symptomatic treatment is usually adequate. Appropriate analgesics combined with use of an antiseptic mouthwash such as 0.12% chlorhexidine gluconate have been recommended.
- Surgical intervention is typically not required in cases of NS; however, there are reports of resolution following debridement for particularly large lesions and those secondarily infected with bacterial species and *Candida*.

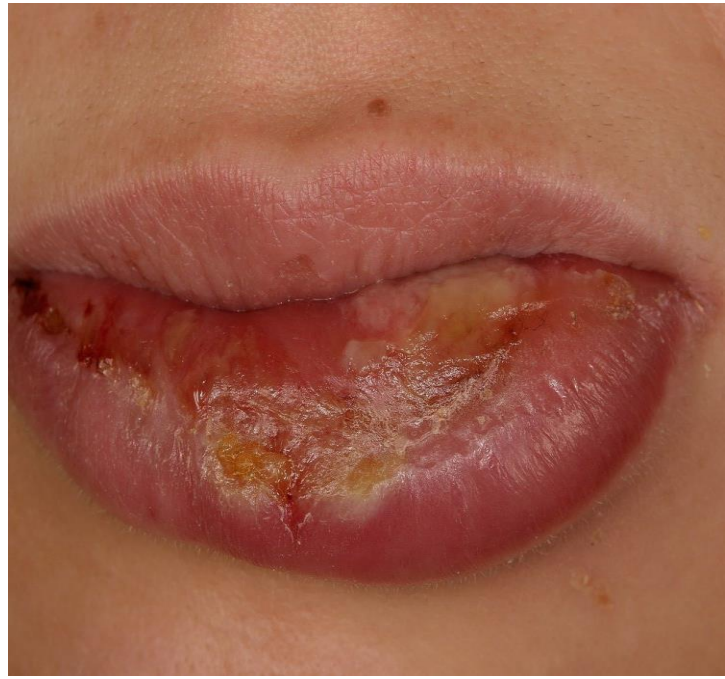
Cheilitis Glandularis



Description and Etiology

Is a chronic inflammatory disorder affecting the minor salivary glands and their ducts in which thick saliva is secreted from dilated ductal openings.

It is characterized by superficial ulceration, painless crusting, swelling, and induration of the lip; a mucinous exudate is apparent at the ductal openings.



- Although the etiology of CG is still undetermined, it has been suggested that it is an autosomal dominant hereditary disease.
- External factors (mainly UV rays) have been implicated as the condition occurs more frequently in fair-skinned adults and albino patients appear particularly prone to this condition.
- Additional proposed predisposing factors include poor oral hygiene, chronic exposure to sunlight and wind, smoking & an immunocompromised state.

Occur in middle-aged and elderly men with only a few cases reported in women and children.

Clinical Presentation

CG presents with a secretion of thick saliva secreted from dilated ostia of swollen labial minor salivary glands. This saliva often adheres to the vermilion causing discomfort to the patient.
Edema and focal ulceration may also be present.
CG primarily affects the lower lip, but there are reports of upper lip and even palatal involvement.

Treatment

Elimination of potential predisposing factors and the use of lip balms, emollients, and sunscreens for those with excessive exposure to the sun and wind are advised.

Conservative treatment of CG may involve using topical, intralesional or systemic steroids, systemic anticholinergics, systemic antihistamines, and/or antibiotics.

Refractory cases require surgical intervention such as cryosurgery, vermillionectomy, and/or labial mucosal stripping.

Several reports documented the development of squamous cell carcinoma in areas affected by CG, leading some to call CG a premalignant lesion.

External Beam Radiation–Induced Pathology

Description and Etiology

External beam radiation therapy is standard treatment for head and neck cancers, and the salivary glands are often within the field of radiation.

Although therapeutic dosages for cancer are typically in excess of 65 Gy, permanent salivary gland damage and symptoms of oral dryness can develop after only 24–26 Gy.

The etiopathogenesis of radiation-induced salivary gland destruction is multifactorial, including programmed cell death (apoptosis) in conjunction with production of reactive oxygen species and other cytotoxic products.

In addition, radiation cause damage to blood vessels (end arteries obliteration) where narrowing and occlusion of blood vessels by scar that impaired blood flow lead to ischemia that lead to the destruction of glandular acinar and ductal cells that healed by fibrosis that lead to disturbance of the function of the gland.

Clinical Presentation

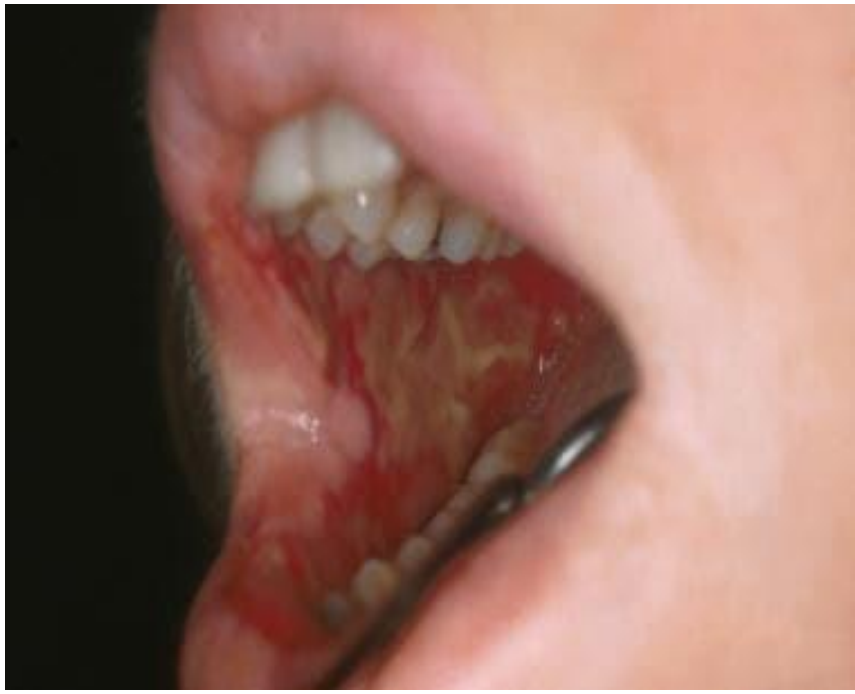
Acute effects on salivary function can be recognized within a week of initiating radiotherapy, with symptoms of oral dryness and thick, viscous saliva developing by the end of the second week.

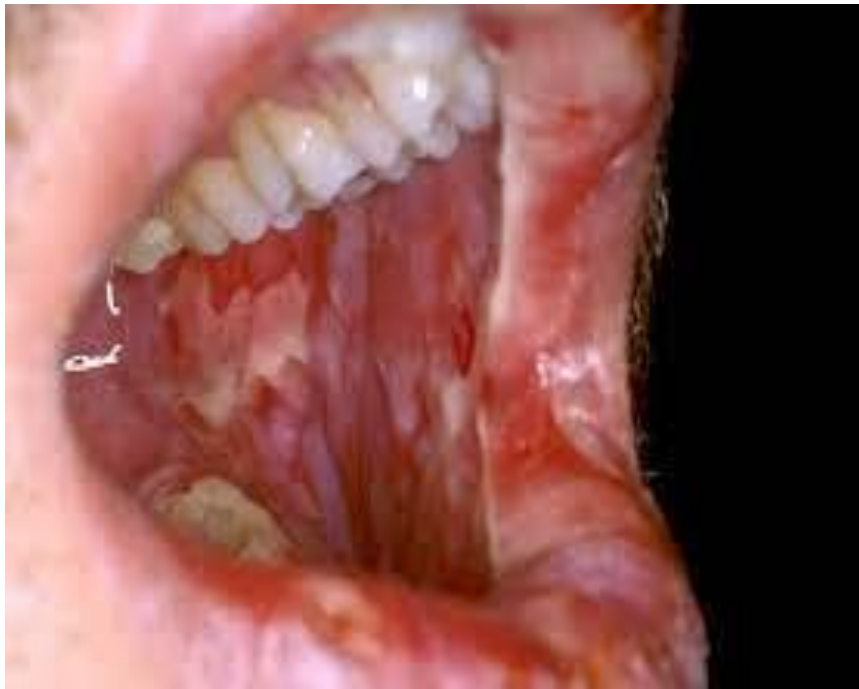
Oral mucositis is a very common consequence of treatment and can become severe enough to alter the radiation therapy regimen.

Mucositis appears as a sloughing of the oral mucosa with erythema and ulceration.
The pain associated with mucositis is described as a burning.

Mucositis generally persists throughout radiotherapy, peaks at the end of the irradiation, and continues for one to three weeks after cessation of treatment.

By the end of a typical six-seven weeks course of radiotherapy, salivary gland function is nearly absent.





Hypofunction remains at a steady rate postradiation, with only small increases to two years post-radiotherapy (post-RT).

This can be permanent if the major salivary glands receive more than 24–26 GY.
Permanent xerostomia and oral complications of salivary hypofunction impair a patient's quality of life.

Signs and symptoms of radiation-associated xerostomia include a burning sensation of the tongue, fissuring of the tongue and lips, new and recurrent dental caries, difficulty in wearing oral prostheses, and increased thirst.

Additional sequelae of radiation-induced salivary dysfunction include candidiasis, microbial infections, plaque retention, gingivitis, difficulty in speaking and tasting, dysphagia, and mucosal pain.

Internal Radiation-Induced Pathology

Description and Etiology

Radioactive iodine (RAI) is the standard treatment in cases of papillary and follicular thyroid carcinomas following thyroidectomy or in cases of suspected or known metastases.

A significant portion of the RAI taken up by thyroid tissue is concentrated and secreted through the salivary gland tissue resulting in radiation exposure of the salivary parenchyma and possible damage.

Standard doses of RAI often cause obstructive duct symptoms, while hyposalivation from parenchymal damage is usually observed with larger or repeated doses of RAI.

Acute risks associated with RAI include ageusia, salivary gland swelling, and pain, while long-term side effects include recurrent sialadenitis with xerostomia, stomatitis, and dental caries.

In some circumstances, RAI treatment may lead to glandular fibrosis and permanent salivary gland hypofunction.

Clinical Presentation

The glandular effect of RAI can be mild to severe. Patients may be asymptomatic or may complain of parotid gland swelling (usually bilaterally), pain, xerostomia, and decreased salivary gland function almost immediately after treatment.

RAI-induced salivary gland injury is irreversible; however, residual functioning salivary gland tissue is often present and responsive to therapy.

Following administration of 131 I, patients should undergo an aggressive salivary stimulation routine that includes sugar-free lozenges, sour candies, and gums to stimulate salivary flow. This will aid in clearing the 131 I from the salivary glands and potentially decrease salivary gland damage.

Stimulation of salivary flow by these means, however, should not be initiated within the first 24 hours after 131 I therapy as this has been shown to potentially increase the salivary gland side effects of the RAI.

Pilocarpine and cevimeline used before and after RAI treatment may decrease transit time through the salivary glands, thereby diminishing exposure.

Allergic Sialadenitis

Enlargement of the salivary glands has been associated with exposures to various pharmaceutical agents and allergens.

It is unclear whether all of the reported cases are true allergic reaction or whether some represent secondary infections resulting from medication that reduced salivary output.

Compounds associated with allergic sialadenitis

- Ethambutol.
- Heavy metals.
- Iodine compounds
- Isoproterenol.
- Phenobarbital.
- Phenothiazine.
- Sulfisoxazole.

Viral Diseases

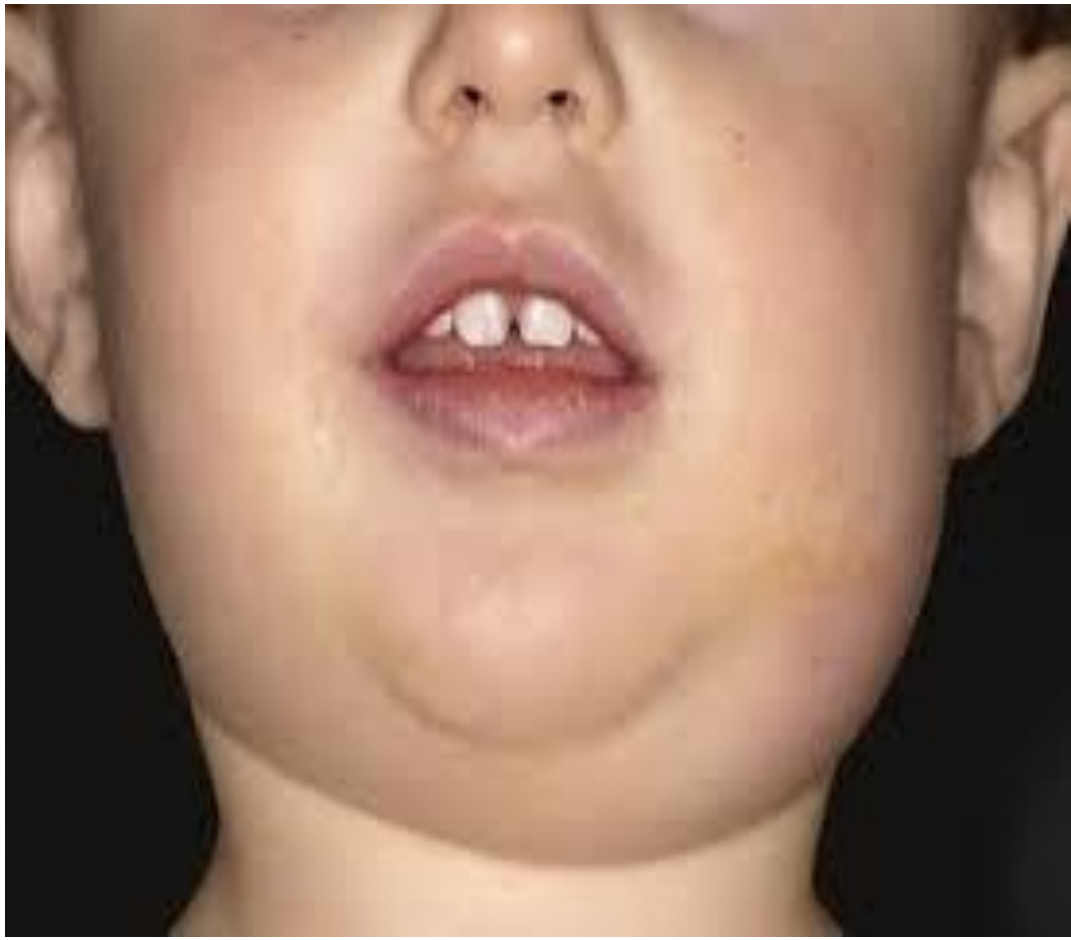
MUMPS (PARAMYXOVIRUS OR EPIDEMIC PAROTITIS) :

Acute viral infection caused by a ribonucleic acid (RNA) paramyxovirus and is transmitted by direct contact with salivary droplets.

Clinical Presentation

- Mumps typically occurs in children between the ages of 4 and 6 years.
- The incubation period is two to three weeks.
- Mumps usually presents with one to two days of malaise, anorexia, and low grade pyrexia with headache followed by non-purulent gland enlargement.
- Glandular swelling increases over the next few days, lasting about one week.
- 25% of cases may involve unilateral salivary gland swelling, or swelling may develop in the contralateral gland after a time delay.
- 95% of symptomatic cases involve the parotid gland only, while about 10% of cases involve the bilateral submandibular and sublingual glands concomitant with the parotid swelling. A minority of cases may involve the submandibular glands alone.

Salivary gland enlargement is sudden and painful to palpation with edema affecting the overlying skin and the duct orifice.
If partial duct obstruction occurs, the patient may experience pain while eating.



Complications of mumps:-
Mild meningitis and encephalitis, deafness, myocarditis, thyroiditis, pancreatitis, hepatitis, and oophoritis .
Males can experience epididymitis and orchitis, resulting in testicular atrophy and infertility if the disease occurs in adolescence or later.

Treatment
The treatment of mumps is symptomatic and may involve the use of analgesics and antipyretics.

Bacterial Sialadenitis

Bacterial infections of the salivary glands are most commonly seen in the patients with reduced salivary gland function.
An acute and sudden onset of a swollen and painful salivary gland is termed an acute bacterial sialadenitis, whereas repeated infections are termed chronic bacterial sialadenitis .

Bacterial sialadenitis occurs more frequently in the parotid glands.

It is theorized that the submandibular glands may be protected by the high level of mucin in the saliva, which has potent antimicrobial activity.
It is thought that the antimicrobial activity of mucin, found in the saliva of the submandibular and sublingual glands, may competitively inhibit bacterial attachment to the epithelium of the salivary ducts.

The serous parotid gland saliva also contains less lysosomes, IgA antibodies, and sialic acid.
Anatomy may also play a protective role; tongue movements tend to clear the floor of the mouth and protect Wharton's duct.
In contrast, the orifice of Stensen's duct is located adjacent to the molars, where heavy bacterial colonization occurs.

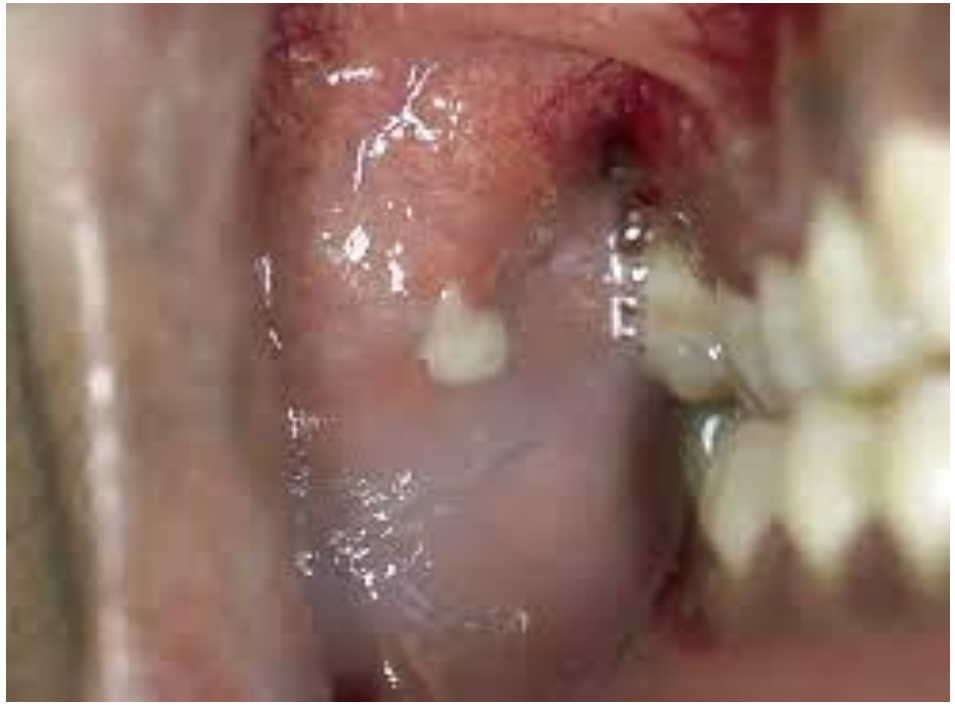
Risk factors

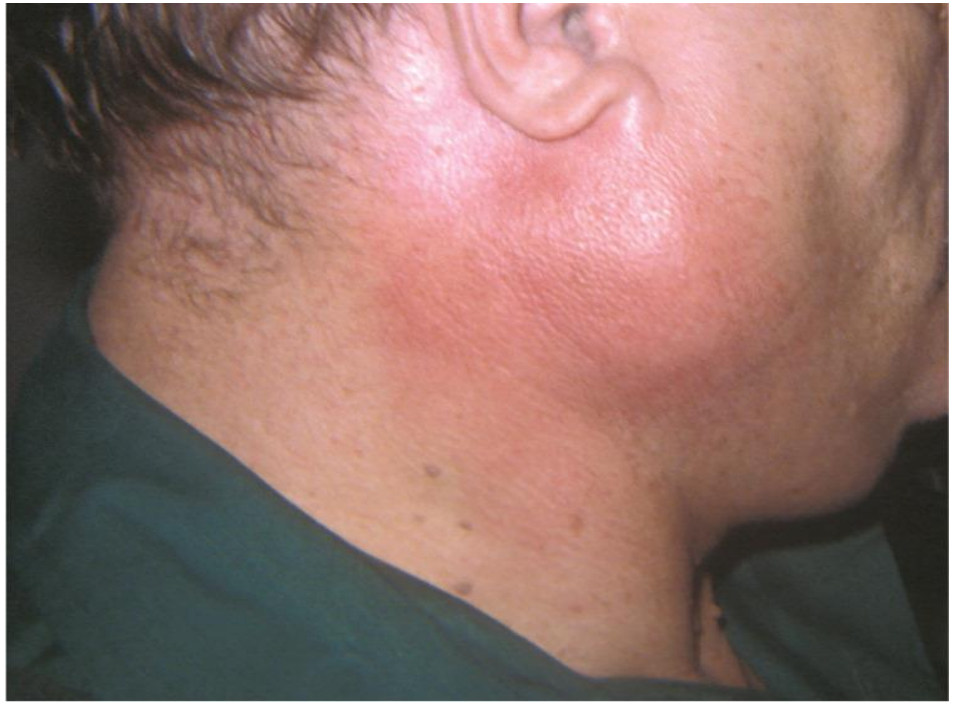
Include dehydration, the use of xerogenic drugs, salivary gland diseases, nerve damage, ductal obstruction, irradiation, and chronic diseases such as diabetes mellitus and SS.

Retrograde bacterial parotitis following surgery under general anesthesia is a well-recognized complication. It is due to the markedly decreased salivary flow during anesthesia, often as the result of anticholinergic drugs and relative dehydration.

Clinical Presentation

- Patients usually present with a sudden onset of unilateral or bilateral salivary gland enlargement. Approximately 20% of the cases present as bilateral infections.
- Complaints of fevers, chills, malaise, trismus, and dysphagia may accompany these findings. Observation of dry oral mucosa may indicate systemic dehydration.
- The involved gland is enlarged, warm, painful, indurated, and tender to palpation.
- If stensen’s duct is involved, it may appear erythematous and edematous.
- There may also be erythema of the overlying skin.
- Clinical examination of the involved glands involves bimanual palpation along the path of the excretory duct.
- In approximately 75% of cases, purulent discharge may be expressed from the orifice.





Diagnosis

Bacterial parotitis is largely a clinical diagnosis. If purulent discharge can be expressed from the duct orifice, samples should be cultured for aerobes, anaerobes, fungi, and mycobacteria.

Differentiating between viral and bacterial infectious parotitis can be challenging.
In general, viral infections are bilateral, affect younger patients, have prodromal symptoms, do not involve purulent drainage, and patients appear to have less toxicity.

Although systemic symptoms follow the development of asymptomatic gland in suppurative parotitis, the order is usually reversed in viral parotitis.

Sialoendoscopy, US, CT, MRI sialography, or percutaneous aspiration may be helpful to rule out chronic salivary gland infections, cysts, obstructions, or neoplasms

Treatment

Treatment goals of bacterial sialadenitis include resolution of signs and symptoms of infection, elimination of the causative bacteria, rehydration, and elimination of obstruction where present. This may involve the use of antibiotics, analgesics, heat application, fluids, glandular massage, oral hygiene products, and sialogogues.

Anti-inflammatory agents including steroids may help to rapidly reduce pain and swelling. Patients should also be instructed to massage the gland several times a day.

Where possible, medications implicated in salivary gland hypofunction should be discontinued. With these measures, significant improvement should be observed within 24 –48 hours.

Appropriate antibiotic regimens should include coverage for *S. aureus* as well as oral polymicrobial aerobic and anaerobic infections.

It is estimated that up to 75% of infections are caused by β-lactamase–producing bacteria, and therefore, treatment with anti-staphylococcal penicillin, a combination β-lactamase inhibitor, or a first-generation cephalosporin is appropriate.

Macrolides such as azithromycin with metronidazole can be an alternative for those with a penicillin allergy.

Antibiotics should not be started routinely unless bacterial infection is clinically obvious.

Under all circumstances, purulent discharge from the salivary gland should be cultured to confirm the diagnosis and determine antibiotic sensitivity. Antibiotic therapy may need to be modified later based on culture results.

Additional potential complications include facial nerve palsy, sepsis, mandibular osteomyelitis, internal jugular vein thrombophlebitis, and respiratory obstruction.

Systemic Condition with Salivary Gland Involvement

1- METABOLIC CONDITIONS

- Diabetes
- Anorexia Nervosa/Bulimia
- Chronic Alcoholism
- Dehydration

2- MEDICATION-INDUCED SALIVARY DYSFUNCTION

There are over 400 medications that are listed as having dry mouth as an adverse event.
Some drugs may not actually cause impaired salivary output but may produce alteration in saliva composition that lead to the perception of oral dryness.

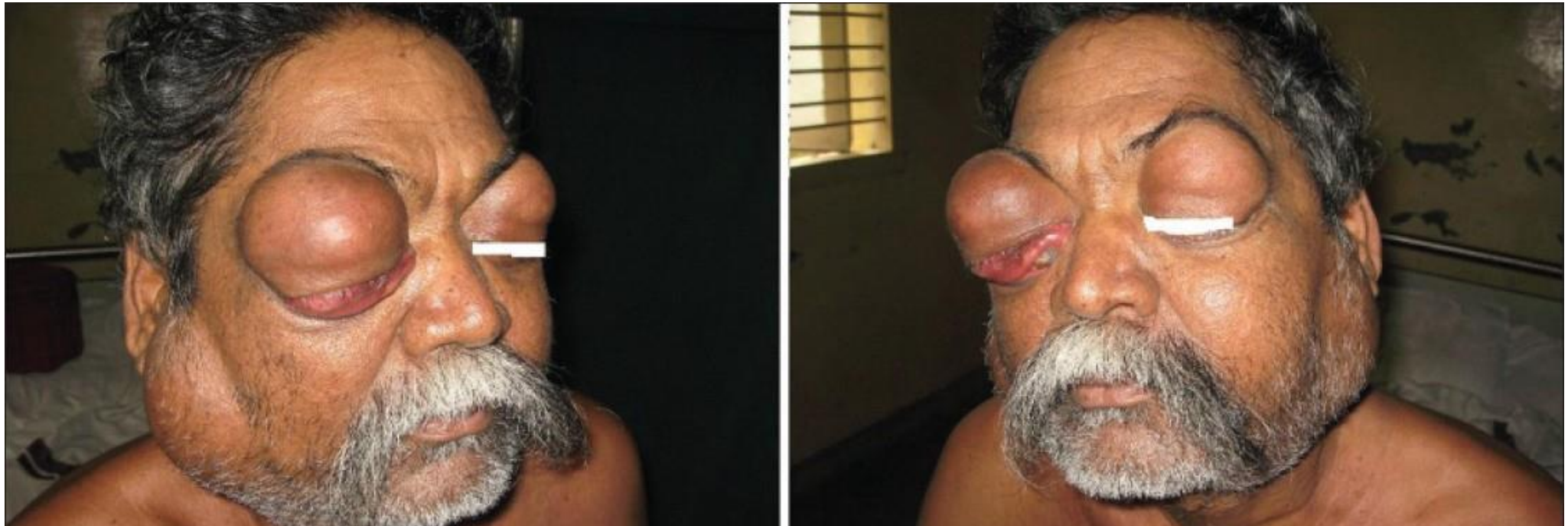
Common medication categories associated with salivary hypofunction:

- Anticholinergics
- Antihistamines
- Antihypertensive
- Anti-Parkinson's disease
- Antiseizure
- Sedative and tranquilizers,
- Skeletal muscle relaxants,
- Tricyclic antidepressants
- Cytotoxic agents

3- IMMUNE CONDITIONS

A- Mikulicz's disease

- Previously known as benign lymphoepithelial lesion.
- It is characterized by symmetrical lacrimal, parotid, and submandibular gland enlargement with associated lymphocytic infiltrations.
- Histopathologically: prominent infiltration of IgG4-positive plasmacytes in to involved exocrine glands.
- Diagnosis is based on finding of salivary gland biopsy and the absence of the alterations in peripheral blood and autoimmune serologies that seen in sjogren 's syndrome.



B- Sjogren’s syndrome (Primary and Secondary)

Is a chronic autoimmune disease characterized by symptoms of oral and ocular dryness, exocrine dysfunction and lymphocytic infiltration, and destruction of the exocrine.

The clinical presentation of both xerostomia & xerophthalmia is also sometimes called sicca syndrome.

Two forms of disease are recognized :

1. Primary SS (sicca syndrome alone no other autoimmune disorder present).
2. Secondary SS (the patient manifest sicca syndrome in addition to another associated autoimmune disease. the most common associated disorders are rheumatoid arthritis and systemic lupus erythematosus).

4- GRANULOMATOUS CONDITIONS

A-Tuberculosis (TB)

Is a chronic bacterial infection, caused by Mycobacterium tuberculosis, leading to the formation of granulomas in the infected organ.
Diagnosis depends on the identification of the bacterium.
Treatment of the salivary involvement involves standard multidrug anti-TB chemotherapy.

B- Sarcoidosis

Is a chronic condition in which T lymphocytes, mononuclear phagocytes, and granulomas cause destruction of involved tissue.
Parotid gland involvement occurs in approximately 6% of patients with sarcoidosis.
Unilateral salivary gland enlargement has been reported.
Examination of a minor salivary gland biopsy specimen can confirm the diagnosis of sarcoidosis with classic noncaseating granuloma.

MANAGEMENT OF XEROSTOMIA

1- Preventing Therapy :

- The use of topical fluorides in a patient with salivary gland hypofunction is absolutely critical to control dental caries.
- Avoiding cariogenic foods and beverages and brushing immediately after meals. Chronic use of alcohol and caffeine can increase oral dryness and should be minimized.

2- Symptomatic Treatment :

- Patients should be encouraged to sip water throughout the day; this will help moisten the oral cavity, hydrate the mucosa, and clear debris from the mouth.
- There are a number of oral rinses, mouthwashes, and gels available for dry mouth patients.
- The frequent use of products containing aloevera or vitamin E should be encouraged.
- Saliva replacements (‘artificial salivas’) can be use.

3-Saivary Stimulation :

Local or topical stimulation:
Chewing sugar-free gums.
Acupuncture, with application of needles in the perioral and other regions, has been proposed as a therapy for salivary gland hypofunction and xerostomia.

Systemic stimulation:
Parasympathomimetic drugs (Pilocarpine and Cevimeline).

4- Therapy of underlying systemic disorders:-
Anti-inflammatory therapies to treat the autoimmune exocrinopathy of sjogren’s syndrome.

SIALORRHEA

Sialorrhea is defined as an excessive secretion of saliva or hypersalivation.
The cause is an increase in saliva production or a decrease in salivary clearance.

Causes

- Medications (pilocarpine, cevimeline, lithium, and nitrazepam),
- Hyperhydration,
- Infant teething,
- The secretory phase of menstruation,
- Idiopathic paroxysmal hypersalivation,
- Heavy metal poisoning (iron, lead, arsenic, mercury, thallium),
- Organophosphorous (acetylcholinesterase) poisoning,
- Nausea, gastroesophageal reflux disease, obstructive esophagitis,
- Neurologic changes such as in a cerebral vascular accident (CVA),
- Neuromuscular diseases, neurologic diseases, and central neurologic infections.
- Minor hypersalivation may result from local irritations, such as aphthous ulcers or an ill-fitting oral prosthesis.

- Most cases of hypersalivation are a secretion clearance issue.
- If it is not a clearance issue, a salivary flow rate should be obtained.
- Blood samples should also be obtained and evaluated for heavy metals
- There are three types of treatments for hypersalivation: Physical therapy, medications, and surgery.

SALIVARY GLAND TUMORS

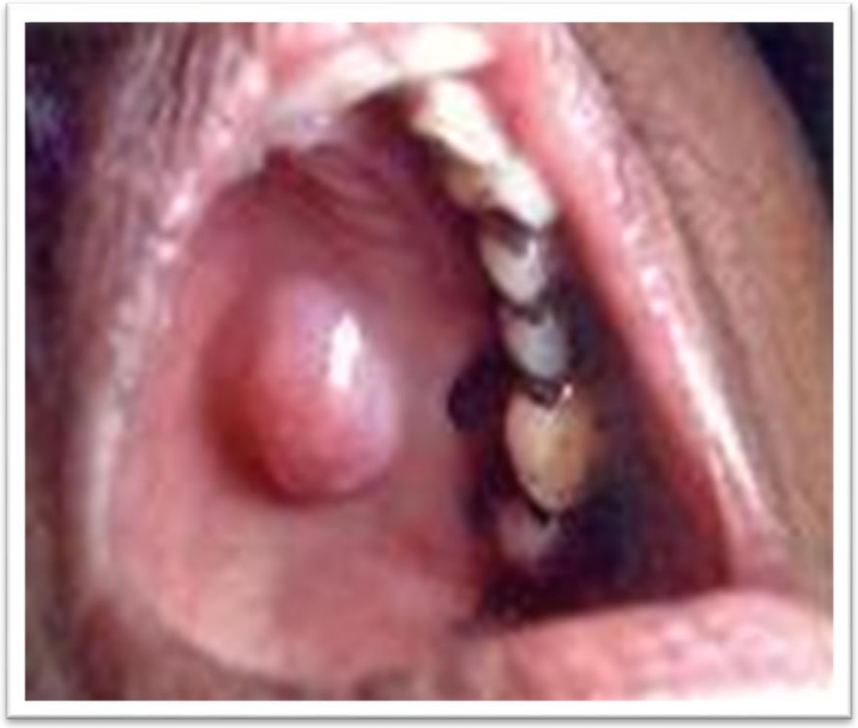
The majority of salivary gland tumors (about 80%) arise in the parotid glands. The submandibular glands account for 10 to 15% of tumors, and the remaining tumors develop in the sublingual or minor salivary glands.
Approximately 80% of parotid gland tumors and approximately half of submandibular gland and minor salivary gland tumors are benign. In contrast, more than 60% of tumors in the sublingual gland are malignant.

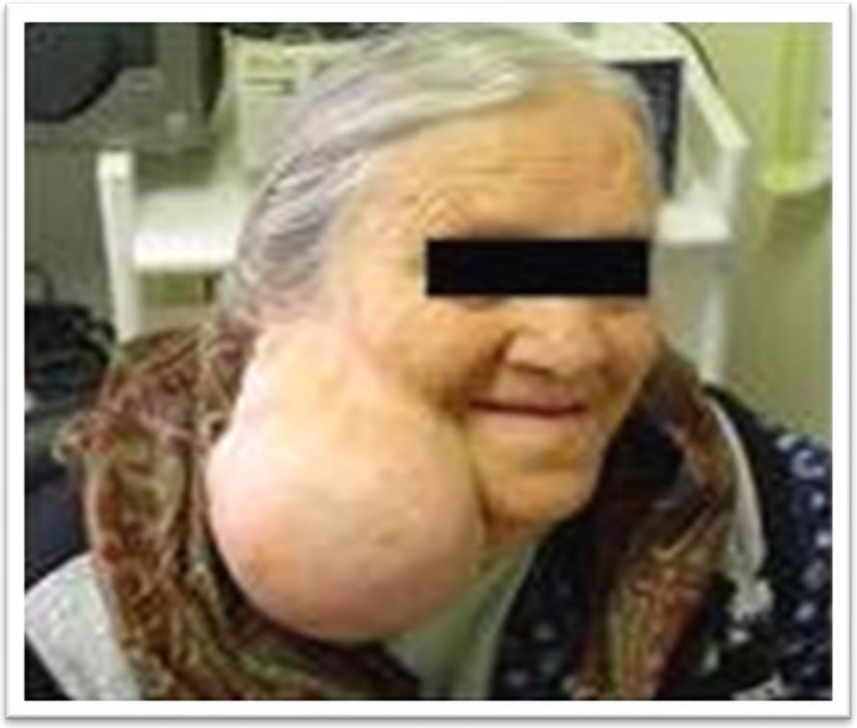
Benign Tumors

1. PLEOMORPHIC ADENOMA .

It’s the commonest salivary gland tumor, the majority arise in the parotid glands.
Histologically, the lesion demonstrates both epithelial and mesenchymal elements.
Pleomorphic adenoma are derived from mixture of ductal and myoepithelial elements. In addition, there is a remarkable microscopic diversity can exist from one tumor to the other as well as in different areas of the same tumor, so it called pleomorphic due to it's the unusual histopathologic features. Moreover, the presence of the different elements accounts for the name pleomorphic tumor or mixed tumor.

They present as slow growing, painless, rubbery nodule often in the lower lobe of the parotid.
Intraorally the commonest sites affected are the palate and upper lip.
In the palate they give the appearance of fixation to underlying bone although there is no actual invasion.
One characteristic of a pleomorphic adenoma is the presence of microscopic projections of tumor outside of the capsule.
Surgical removal with adequate margins is the principal treatment.





MONOMORPHIC ADENOMA

A monomorphic adenoma is a tumor that is composed predominantly of one cell type.

2. Warthin Tumor

Is a benign neoplasm that occur almost exclusively in the parotid gland, although it much less common than the pleomorphic adenoma but it represent the second most common benign parotid tumor accounting for 5-15% of all parotid neoplasms.

It presents as a painless, slowly growing mass, the swelling is frequently soft or cystic in consistency and there may be some fluctuation.

One unique feature is the tendency of warthin tumor to occur bilaterally, most of these bilateral tumors do not occur simultaneously but occurring at different times.

3. ONCOCYTOMA

A benign salivary gland tumor composed of large epithelial cells known as oncocytes.

Less common benign tumors that make up less than 1% of all salivary gland neoplasms.

This tumor occurs almost exclusively in the parotid glands.

Bilateral presentation of this tumor can occur, and it is the second most common salivary gland tumor that occurs bilaterally (after Warthin’s tumor).

These tumors appear noncystic and firm.

The treatment for parotid oncocytomas is superficial parotidectomy with preservation of the facial nerve.

Malignant Tumors

1. Mucoepidermoid Carcinoma

Is one of the most common salivary malignancies, mostly arise in parotid gland although the relatively incidence in the minor salivary glands especially in the palate.

Frequently the tumor present in similar manner to that of pleomorphic adenoma as asymptomatic swelling.
Pain or facial nerve palsy may develop, usually in association with high grade tumors.

Treatment

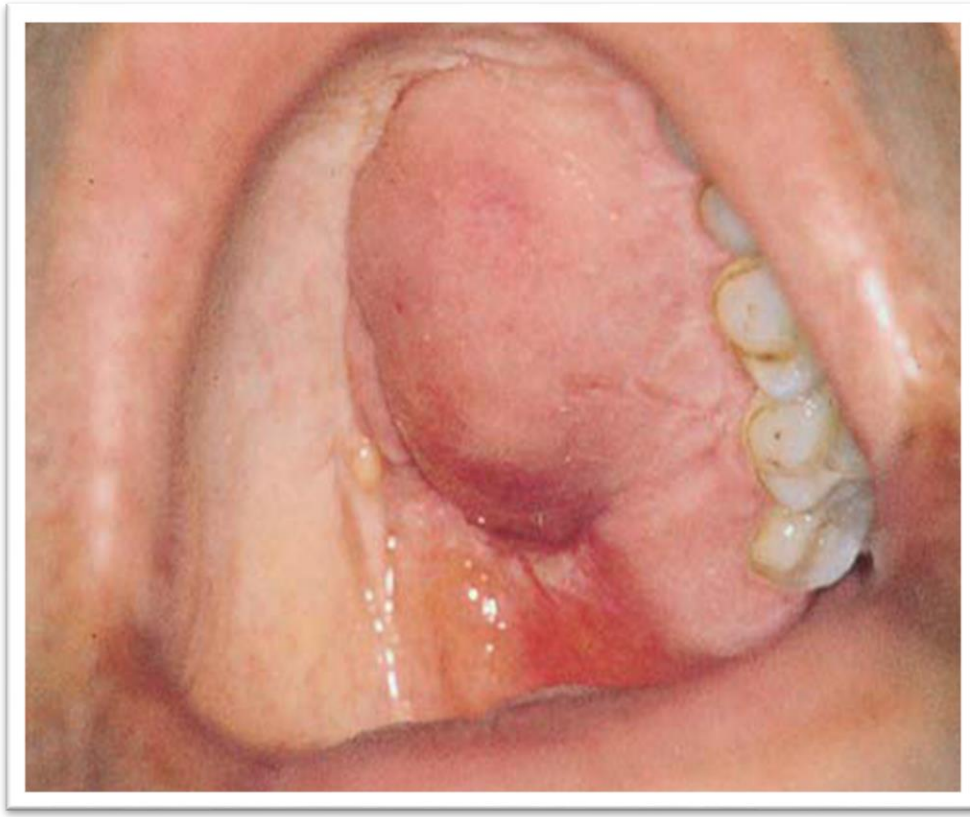
Treatment of mucoepidermoid carcinoma is predicated by location, histopathological grade and clinical stage of the tumor, early stage tumors of parotid often can treated by subtotal parotidectomy with preservation of facial nerve.

Advanced tumors may required total removal of the parotid gland with sacrifice of the facial nerve.

2. ADENOID CYSTIC CARCINOMA

Is one of the more common and best recognized salivary malignancy because of it's distinctive histopathological features.

It occur most commonly in minor salivary glands of the palate.



It usually appear as a slowly growing mass, pain is a common and important finding, occasionally occurring early in the course of the disease before there is notable swelling.

Patients often complain of a constant, low grade, dull ache which may gradually increase in intensity.

Facial nerve paralysis may develop with parotid tumors.
Palatal tumors can be smooth surface or ulcerated.

Tumors arising in the palate may show radiographic evidence of bone destruction.

Surgical excision is the treatment of choice.

3. ACINIC CELL CARCINOMA

Represents about 1% of all salivary gland tumors.

Between 90 and 95% of these tumors are found in the parotid gland; almost all of the remaining tumors are located in the submandibular gland.

It is the second most common malignant salivary gland tumor in children, second only to mucoepidermoid carcinoma.

The superficial lobe and the inferior pole of the parotid gland are common sites of occurrence.

Bilateral involvement of the parotid gland has been reported in approximately 3% of cases.

Treatment consists of superficial parotidectomy, with facial nerve preservation if possible. When these tumors are found in the submandibular gland, total gland removal is the treatment of choice.

Malignant mixed tumors

CARCINOMA EX PLEOMORPHIC ADENOMA

Malignant change within a preexisting pleomorphic adenoma, it is relatively uncommon which represents 2 to 5% of all salivary gland tumors and appear to occur only if the tumor has been allowed to grow over a long period.

The malignant cells in this tumor are epithelial in origin.

Clinical features which may signify malignant change include rapid change in size of a previously slow-growing lesion, pain , fixation to skin or underlying structures and facial palsy.

Surgical removal with postoperative radiation therapy is the recommended treatment.

Early removal of benign parotid gland tumors is recommended to avoid the development of this lesion.