**Oral pathology Sheet#9**

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**This sheet is mainly based on our new lecture not on past sheets**

**Cont. of salivary gland diseases**

**Sialosis/Sialadinitis :**

**clinical presentation:**

- when the patient comes with a bilateral swelling of the parotid gland which is usually painless.

**histopathalogically:**

-always remember that taking biopsy from parotid is generally a contraindication , except if the clinician suspects a malignancy.

-but if biopsy was taken, the main findings are;

1. hypertrophy in the acini and edema of the connective tissue.

2. no inflammation or tumor like findings

so inflammation isn’t the cause and its not bacterial or viral infections, it’s just a cell enlargement.

**definition:**

-Non-inflammatory , non-neoplastic , bilateral parotid gland enlargement.

**Aetiology :**

-unknown etiology but might be due to a problem with the innervations

of the gland ( sympathetic and parasympathetic systems)

- no reduction in the saliva flow (not affecting the function)

- in these patients we should exclude other causes like Mumps ( mumps has signs and symptoms like pain) , and masseter muscle hypertrophy

-How to differentiate between Sialosis and Masseter muscle hypertrophy?

Masseter muscle hypertrophy appears more anterior over the ramus while the swelling in sialosis appears more posterior, and when the patient clenches , the masseter will be more prominent and the things will be clear.

-in spite of the unknown etiology; sialosis appears to be associated with certain systemic diseases such as alcoholism or liver cirrhosis, diabetes mellitus, hypothyroidism (edema), acromegaly (over growth in soft tissues), pregnancy , bulimia nervosa,

Antipsychotic drugs (like clozapine) , malnutrition and chronic renal failure .

**Dry mouth :**

More common than sialosis , challenging for the doctors because it’s hard to treat, patient complaining of dryness , burning sensation ,impaired mastication and swallowing (so they prefer to eat soft food ,because hard food may cause trauma to them),metallic taste , oral structures stick to each other , impaired speaking, may awake during night -feeling of suffocation.

**Clinically :**

1. General view: shrinkage of the mucosa and the tongue, so may they look lobulated and the tongue may look fissured even it’s not in reality.
2. No pooling of saliva in the floor of the mouth
3. Frothy saliva ( looks like soap bubbles) and sticky ,and this can happen if the patient was very stressed and afraid of the dentist.
4. Many tests: mirror can stick to the buccal mucosa , gauze/cotton roles also can stick to the vestibule – this may cause trauma if gaze is not wetted before removal. And so you must be carful of every thing you put in the patients mouth.

**One of the causes of Dryness of the mouth in our region is Sojegren’s Syndrome**

**Sojegren’s Syndrome:**

**pathogenesis:**

-Damage of the salivary glands , destructed acini because of inflammation via cell-mediated immunity-lymphocytes , T-cells attack the salivary glandes and destruct the acini -and these inflammatory cells occupies the dead acini ,so if we take a biopsy the gland look as a mass of these cells instead of acini and ducts. So this change is irreversible, so there’s no curative treatment

- so Sojegren’s Syndrome is an immune mediated chronic inflammatory disease, non-organ specific autoimmune disease (cell mediated disease), so it has symptoms all over the body but more concentrated in exocrine glands (salivary and lacrimal glands)

-so mainly it’s a lymphocytic infiltration & replacement of glandular parenchyma

-xerostomia (dry mouth) and xerophthalmia (dry eyes) are the major signs and symptoms, and the disease is named after the ophthalmologist who described the disease

**Clinically :**

-it affects 1% of the population

-for the diagnosis it’s important to exclude the other known causes of xerostomia ( the most common cause of xerostomia is Drugs; antihypertensives , antihistamines , TCA-tricyclic antidepressants…etc )

-middle age : most of them are postmenopausal females , 90% of overall cases are females.

**Two types** according to the severity of the disease :

1-primary: localized in the oral cavity and eyes (xerostomia & Xerophthalmia)

2- secondary: if associated of with connective tissue disease (xerostomia & xerophthalmia + CT disease)

CT diseases that may associate with secondary SS :

-rheumatoid arthritis (15% of rheumatoid arthritis patients has sojegren’s syndrome)

-systemic lupus erythematosus (30% of them has sojegren’s syndrome)

-systemic sclerosis

-primary biliary cirrhosis and dermatomyostits .

**The most common disease associated with SS ?**

**Rheumatoid arthritis** , because it’s far more common in the population than SLE

-And to exclude other causes and to **confirm** the diagnosis of **Sojeren’s Syndrome** you should ask the patient precisely about those signs and symptoms the mouth , eyes and other exocrine glandes ::

Sings and symptoms in the **Mouth:**

- Clinically we can see lobulation and shrinkage of the surfaces.

-Discomfort

-Difficulties in eating, swallowing & speech

-Disturbed taste sensation

-Suspected to infections -because of diminished saliva- like: Candidosis, acute ascending bacterial sialadenitis, root caries

-Dry, red & shiny mucosa

-Red, atrophic, lobulated (cobble-stone) tongue ; redness and burning sensation may be a result of the infection by candida, so the we tend to give them antifungals as prevention.

**Eyes:**

- Keratoconjunctivitis sicca (inflammation of the conjunctiva and cornea)

- Corneal keratotic lesions ( keratin in the cornea and this may lead to blindness)

- Failure of tear secretion ( burning sensation , and feel as if there’s sand in their eyes) , to **confirm** that there’s **diminished tear secretion/dryness of the eye** , **Schirmer test** is used ;special filter paper ( by ophtamlologist) put in the inner canthus of the eye

**Other** signs and symptoms related to other exocrine glandes are :

-Severe tiredness laziness , sleep for long durations up to 20 hours daily, Arthralgia

-xeroderma ( dry skin ) ,dryness of upper respiratory tract and genetal areas ;so also these areas are susceptible for infections

-Sinusitis, tracheitis, dysphagia, atrophic gastritis, pancreatitis, purpura

-Anaemia, leucopenia, thrombocytopenia

-bilateral enlargement of the salivary glands ( so there’re many causes of SG enlargement ; sialosis , mumps also Sojegren’s Syndrome)

**Histologically :**

Also here the biopsy is not indicated , but if biopsy is taked we see:

-normal lymphocytes

-rests of epithelial cells of the acini and myoepithelial cells ; called Epimyoepithelial islands

- the T-lymphocytes appear firstly around the Intralobular ducts then start to spread to other parts but they doesn’t cross the interlobular fibrous septa , so this lymphoid tissue doesn’t cross between different lobules and it doesn’t cross the capsule ; so if we noticed lymphoid tissue crosses the capsule we expect presence of **lymphoma**

**Diagnosis:**

-remember that dryness of the mouth may be psychological and it’s not real , so you can see normal presence of saliva of the patients mouth , so to **confirm** that there’s **dryness of the mouth** : we do sialometry to measure the salivary flow, a very simple test , done using a graded tube ; you ask the patient to sit quietly, without talking or chewing , and spit any saliva that accumulates in the floor of your mouth into that tube for 5 mins then we divide the result by 5 to measure the salivary flow rate per one minute , and this is called non-stimulatory /resting sialometry

-If the mixed unstimulatory salivary flow rate was less than 0.1 ml/min then there’s a xerostomia , and for **Schirmer test** if the wetting was less than 5 mm/5min there’s a xerophtalmia.

1 -**sialometry** and **Schirmer’s tests** confirms that there’s **dryness** in the mouth or in the eye , but this’s **not enough** for confirmation that the cause is **SS** in the salivary glands, because if the cause was the drugs also we’ll get the **same results** by these tests,

2- so we need **a biopsy** to confirm that , so we take it from the minor salivary glands in the lower lip –easy to take- and examine them under the microscope , if we can see foci of lymphocytes, each focus consists of more than 50 cell, and there’s more than one focus per **4 mm2** of the gland >> this is a confirmation that the cause is **SS** (The features that are seen in the minor SG are the same in major SG, and is easier to take the biopsy from minor SG since a biopsy from the parotid is contraindecated)

**3-**other test that may help is **Sialography-** doneby injection of radio-opaque material in the ductal system:

in these patients their will be sialectasis( dilatation of the ducts, susceptible for infections ) so the ducts system appears in the sialograph as a “snowstorm”/”cherry blossom” and not clear as the normal ductal system

1. **Salivary scintiscanning** [99T m ] pertechnetate : if given`to person, it will be concentrated in the salivary gland and execrated with saliva , so salivary glands of SS patients will not uptake the maker and will not apper positive .

*“ is a noninvasive test. The patient is positioned under a gamma scintillationcamera that detects radiation. The patient then is injected with a low-level radioactive marker, usually technetium-99m or technetiumpertechnetate.*

*Immediately after the injection, imaging begins. For accurate results, the patient must stay still during imaging. After several images, thepatient is given lemon drop candies to suck on, which stimulate the salivary glands. Another set of images is made for comparisonpurposes. The entire process takes about ten minutes for the injection and 30-45 minutes for the scan.*

***Normal results***

*Normally functioning salivary glands take up the radiopharmaceutical then secrete it when stimulated by the lemon drops.*

***Abnormal results***

*Abnormally functioning salivary glands fail to exhibit a normal uptake and secretion pattern”*

\*\*It’s known that SS is an autoimmune disease but it’s not known what is the antigen that elicits the immune response and also it’s not proven yet if it’s cell mediated or antibody mediated because there’s production of auto-antibodies in addition to cell mediated response, so **AB scanning**  can help in the diagnosis

**5-AB scanning :** A significant percent of patients have a positive Rheumatoid factor, antinuclear antibodies,SS-A**, SS-B (especially , because it’s the most specific to SS )**

-if a SS patient of comes with dry mouth and dry eye ,and we asked for AB scanning and the RF was + , it’s not necessarily that the patient has a secondary SS (that is associated with RA), we can say that it’s secondery SS only if it’s associated with RA symptoms , so those antibodies other than SS-B are not that specific and can’t tell if the disease is primary or secondarty.( diagnosis of secondary sojegren’s syndrome is done clinically not by immunological tests)

**6** - **Serology**: elevated ESR and hypergammaglobulinaemia because of high Conc. Of autoantibodies.

**Aetiology :**

-Unkonwn ; it’s Autoimmune disease but with Unkown Antigen

-some viruses are accused : CMV, EBV, HHV-6, Retrovirus

**• Complications:**

-part of the patients up to 5% especially in the primary SS , there’s a risk for B-cell malignant lymphoma

Higher by 44 times than general population.

**Salivary gland tumers**

* Uncommon
* Incidence around 1-6 cases per 100000 annualy.( in Jordan: if we suppose that the population counts for 10 millions , Incidence= 100-600 cases)
* Mainly females ,more common in females than males.
* 5th decade of life , or above.
* **80%** of these tumors develop in the major glands ( parotid, submandibular and sublingual ) .

90% in the parotid gland(72% of the overall tumors in major and minor SGs), 10% in the submandibular gland, less than 0.5% in sublingual gland, so it’s rare to have tumors in the sublingual glands.

* **20%** in the minor salivary glands. The most common site of is the palate (55%) and the second most common site is the upper lip, while it is rare to have salivary gland tumor in the lower lip .

***\*note:*** the most common site of mucoceles is in the lower lip because of higher chance for trauma in the lower lip than the upper.(lip biting habit)

So the vast majority of tumors develop in the parotid glands.

**In term of malignancy:**

- Around 15% of parotid glands tumors are malignant.

-Double this ratio for submandibular (30%).

-The vast majority of sublingual gland tumors are malignant (85%).

-Rare to have a tumor in the sublingual gland, but when you have a tumor, 85% it is malignant.

I-n the minor salivary gland, 50% chance for malignancy.

**Classification:**

1. **Benign tumors ( adenomas ),** how to recognize them clinically?

1)Slow growing , over years

2)Soft or rubbery on palpation, not hard ( induration is a sign of malignancy)

3)Do Not cause ulceration to the mucosa in the oral cavity or in the skin

4)Do Not cause neural manifestations ( numbness, paresthesia or paralysis ),

but in some cases when the tumor has a very big size,it may cause pressure on a nerve.

Most common type is pleomorphic adenoma (and the most common salivary gland tumor generally), the second most common benign SGs tumor is warthin tumor and there’s many others but generally they are rare( basal cell adenoma, oncocytoma ,canalicular adenoma and ductal papillomas)

1. **Malignant tumors** (adenocarcinomas) :
2. Fast growing
3. Hard (they may not appear hard at the beginning , thus causes confusion)
4. They “may “ cause ulceration to the overlying mucosa or skin, and when there’s ulcer ; malignancy is more likely.
5. Invasion to surrounding tissues
6. The patient may develop neural manifestations because of invasion to the nerves like facial paralysis if the tumor was in the parotid , and loss of sensation in the area of the greater palatine nerve if the tumor was in the palat.
7. The Most common : 1- Mucoepidermoid Ca 2- Adenoid cystic Ca

**Pleomorphic adenoma (PA)**

- The term pleomorphic does not imply cellular pleomorphism , but because there is a variation in the histology and the components of the tumor ( epi. component + CT component ) from area to another . for the same reason it is also called mixed tumor which doesn’t mean it develops from connective tissue and epithelium; the origin is only from the epithelial/myoepithelial cells

- it is the commonest tumor, 60% of all salivary gland tumors, so it is important to know its details .

- 84% of PA cases develop in the parotid gland which represents 70% of all parotid gland tumors and 80% of which develop in the superficial lobe (the vast majority ).

-8% of PA develop in the submandibular gland and it represents 50% of submandibular gland tumors .

- 7% of PA cases originate in minor glands, representing about 45% of all tumors of the minor salivary glands , mostly in the palate without any ulceration , destruction or paresthesia. Also it is common in the upper lip.

**clinically :**

1) well-defined , capsulated ( benign)

2) painless

3) rubbery swelling on palpation

4) in parotid appears as a swelling overlying the angle of the mandible

5) sometimes it is multinodular or lobulated ( multiple swellings ) **not** just single mass smooth swelling(this feature is more related to mumps) and this is related to the capsule , the capsule of the tumor is deficient in some areas which leads to growth outside the capsule giving another nodule. This lobulation is also a feature of recurrent PA.

**histologically :**

1- extensive variations

2- Fibrous capsule , as we said there is a deficiency in some areas of the capsule so the tumor grows this deficient area leading to another nodule formation ( the cause of the nodulated growth) . the second significance (the clinical significance) of the deficiency that it may lead to recurrence; the sergeon may remove the main mass and mistakenly leaving the other small parts; thus recurrence occurs.

\*so , nodulation may be due to : 1- deficient area in the capsule 2-recurrence

3- epithelial component :

1. Epithelial duct cells ( makes duct-like structures )
2. Myoepithelial cells : spindle/stellate-shaped → a lot of forms (sheets, clumps & strands ) .
3. Some myoepithelial cells resemble plasma cells , called Plasmacytoid cells
4. Some myoepithelial cells undergo squamous metaplasia , production of **keratin** inside pleomorphic adenoma .

4- stroma/connective tissue component ( very important in diagnosis and this’s which makes PA diagnosis easy) could be :

1. Fibrous and may undergo hyalinization
2. Myxoid ( mucoid material ) , soft clinically . upon surgery it ruptures , increasing the recurrence rate ,so it’s the hardest to be removed surgically.
3. Chondroid , resemble cartilage.
4. Bone: Even bone could be present .

**Warthin tumor :**

* Second most common benign SG tumor
* Origin , it most likely arises from epithelium entrapped within lymph nodes in salivary gland during development that’s why it is sometimes called Adenolymphoma although it is wrong/misleading nomenclature because actually this is not a lymphoma and it’s benign, it’s benefit that it reflects the histological form of the tumor (the main component/the background is a normal lymphoid tissue)
* It is considered as Hamartoma , so it is a very benign.

**Clinically :**

1. 7% of salivary gland tumors.
2. occurs almost exclusively in the parotid gland , 9% of parotid tumors.
3. Slightly More common in females, and in the past it was though that it’s more common in males.
4. Bilateral in some cases
5. Sometimes multiple in the same gland ( more than one focus ) .
6. Usually it appears in the tail of the parotid gland , near the angle of the mandible , you may diagnose it as cervical lymphadenopathy .
7. Smokers have an 8 folds greater risk than non-smokers

**Good luck**