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Numerous Diagnostic Methods for Salivary Gland Tumors - A Review

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Abstract---Salivary gland neoplasms are usually slow growing and non-tender. A slow-growing swelling of the salivary gland is suggestive of a neoplasm, whereas a sudden, painful swelling is suggestive of an infective pathology although it can sometimes indicate a malignant tumor with secondary infection. Salivary gland pathologies may be neoplastic, non-neoplastic, inflammatory, or non-inflammatory. Early surgical intervention after a good clinical, radiological, and

histopathological diagnosis is need of an hour to minimize the postoperative complications.

Keywords---salivary gland tumors, diagnosis, clinical, radiographical, histopathological.

Introduction

The salivary gland are exocrine glands comprising ducto-acinar units that produce and secrete saliva. Saliva has many protective functions like protection, buffering, tooth integrity, tissue repair, Anti-microbial activity, digestion and taste., They are divided into major and minor salivary glands, but histologically it classified based on cells serous salivary gland, mucous salivary gland, mixed salivary glands.

Revised classification of salivary gland tumors (2017)

<i>Malignant Tumors</i>	<i>Benign Tumors</i>
Mucoepidermoid carcinoma	Pleomorphic adenoma
Adenoid cystic carcinoma	Myoepithelioma
Polymorphous adenocarcinoma	Basal Cell Adenoma
Epithelial-myoepithelial carcinoma	Warthin's tumor
Clear cell carcinoma	Oncocytoma
Basal cell adenocarcinoma	Lymphadenoma
Sebaceous adenocarcinoma	Cystadenoma
Intraductal carcinoma	Sialadenoma papilliferum
Cystadenocarcinoma	Ductal papillomas
Adenocarcinoma, NOS	Sebaceous adenoma
Myoepithelial carcinoma	Canalicular adenoma and other ductal adenomas
Carcinoma ex pleomorphic adenoma	<i>Other Epithelial Lesions</i>
Carcinosarcoma	Sclerosing polycystic adenosis
Poorly differentiated carcinoma	Nodular oncocytic hyperplasia
1) Neuroendocrine and non-neuroendocrine	Lymphoepithelial lesions
2) Undifferentiated carcinoma	Intercalated duct hyperplasia
3) Large cell neuroendocrine carcinoma	<i>Soft Tissue Lesions</i>
4) Small cell neuroendocrine carcinoma	Hemangioma
Lymphoepithelial carcinoma	Lipoma/ sialolipoma
Squamous cell carcinoma	Nodular fasciitis
Oncocytic carcinoma	<i>Hematolymphoid Tumor</i>

<i>Borderline Tumors</i>	Extranodal marginal zone lymphoma of MALT
Sialoblastoma	

Diagnostic Methods(1,2)

Clinical:-

- Onset
- Duration
- Progress &
- Rapidity of growth
- Extent of growth
- Symptoms associated with growth
- Coincidental condition
- Secretions

Radiographic Imaging:-

- Routine radiographs
- Ultrasound
- Doppler ultrasound & color flow imaging
- Sialography
- Radionucleotide scanning
- CT Scan
- MRI Scan
- Arteriography
- Positron emission tomography

HistoPathology:-

- FNAC
- Biopsy
- IHC
- Frozen section

Clinical diagnosis:

(a) Onset :

Nature of onset of growth is often significant, if onset is painless gradually but continuous a tumor is suggested, if it is sudden and painful suggested of inflammatory pathology.

(b) Duration:

An old lesion with history of slow steady growth is usually benign or low grade malignant tumor. If an old lesions has an history of remission and exacerbation associated with pain it is most often inflammatory.

(c) Progress and rapidity of growth:

A malignant tumor grows rapidly, where benign tumors grow slowly and steadily.

(d) Extent of growth:

Benign tumor might attain a huge size and produce only a cosmetic defect but a malignant tumor will produce functional defect and it invades

adjacent structures, ultrasound, CT scan, MRI Scan are of immense help in knowing the extent of growth.

- (e) Symptoms associated with growth:
Pain suggests inflammation or secondary infection. Paresthesia, tingling and numbness, weakness of muscles supplied by nerve may be suggestive of infiltration of nerve by tumor cells, Salivary glands tumors most commonly present as asymptomatic mass
- (f) Coincidental conditions:
Sometimes salivary gland tumors may be associated with other conditions. Breast cancer is associated with high risk of parotid tumors.
- (g) Secretions:
Secretions if purulent may suggest an infective pathology

Diagnostic / Radiographic imaging (1,2,4)

- (a) Routine radiographs: It is useful only for diagnosing sialoliths and parenchymal calcifications. Radiopaque salivary calculi in the gland or duct can be picked up on plain films such as occlusal X-ray for submandibular gland and duct and a posteroanterior (PA) skull with blown-out cheeks for parotid calculi.
- (b) Ultrasonography: Ultrasonography (USG) is a noninvasive modality that utilizes non-ionizing radiation, gives good soft tissue discrimination, has excellent sensitivity for mass lesions, and can be repeated as frequently as required. USG with color Doppler is useful to rule out vascular lesions and also aids in assessing vascularity of lesions
- (c) Sialography: It assesses obstructive pathology by instillation of radiopaque contrast medium to locate obstruction in the ductal system. The technique is more or less obsolete now with the advent of MRI imaging. It is a technique which involves injection of a radiopaque dye into the ductal system of the major salivary glands and taking plain X-rays to see the pattern of the dye into the ductal systems. Most commonly the contrast dyes used are iodine based. Sialography is indicated to diagnose obstructive pathologies and duct anomalies, degenerative changes in the gland, chronic inflammatory conditions, and intra- and extraglandular tumors. It is contraindicated in acute infections of the gland and in case of allergies to the dye.
- (d) Radionuclide scanning: It is used to distinguish between obstructive and nonobstructive sialadenitis. It involves both dynamic and static scanning. Radionuclide scanning is useful when a sialogram is contraindicated to distinguish between acute obstructive and nonobstructive sialadenitis
- (e) CT scan: It is used to evaluate masses in parotid glands and surrounding structures as it gives excellent soft tissue details. Plain computed tomography (CT) scans have a major role to play for diagnosis of obstructive pathologies like a calculus. When used with a contrast dye. Bony changes in the course of facial nerve like erosions, sclerotic margins, and widening of stylomastoid foramen suggest involvement of nerve.
- (f) MRI scan: It allows assessment of salivary masses and early diagnosis

of perineural spread due to excellent soft tissue contrast. In the case of neo-plasms, it helps in demonstrating involvement of the facial nerve

- (g) Arteriography: It assesses the vascularity and source of vascular supply of the tumors.
- (h) Positron emission tomography (PET): Uptake of radiotracer fluorodeoxyglucose used with PET scans by salivary glands makes this diagnostic technique useful for salivary gland tumors. Although this is an expensive technique, measurement of metabolic activity makes it more reliable than CT and MRI scans. It can be used to diagnose recurrences, tumor hypoxia, and proliferation rates

Histopathology:

The gold standard of diagnosis for neoplasms will always be histopathology (HPE).

(a)Fine Needle Aspiration Cytology (FNAC) (2,7)

Fine needle aspiration cytology is a technique whereby cells are obtained from a lesion using a thin bore needle and smears are made for cytopathological diagnosis. The technique is based on the fact that tumor cells are less cohesive and are easily aspirated.

Advantage:-

- Painless procedure
- Rapid diagnosis
- Economical
- Sample from multiple site in same sitting

Disadvantage:

Difficult to differentiate in situ v/s invasive carcinoma

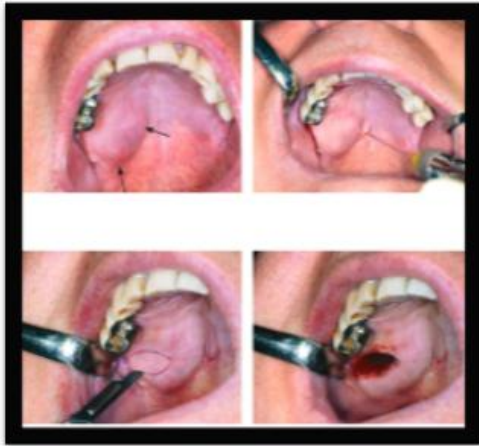
(b)Biopsy: (1,2,6)

Biopsy is a Greek word- (By-op- see)= Bio- Life Opsee- To look(vision), Study of tissues removed from living being to confirm the diagnosis through histopathological study to Determine the prognosis and the treatment required.

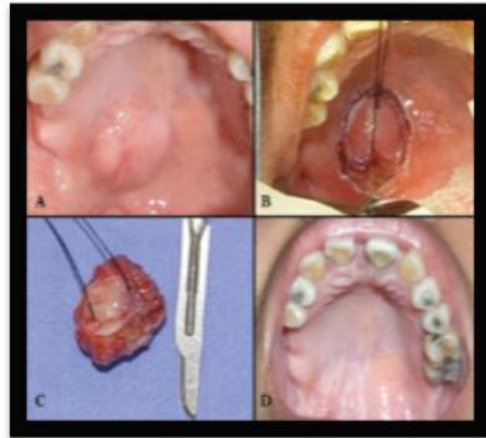
Procedures

- Fixation
- Tissue processing
- Embedding the tissue in paraffin
- Microtomy
- Staining the tissue in H&E

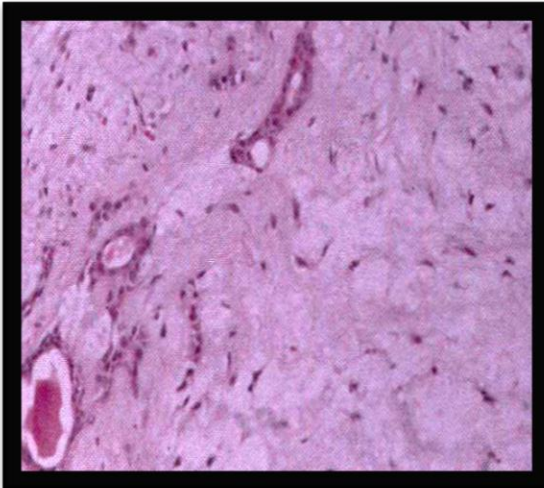
INCISIONAL BIOPSY



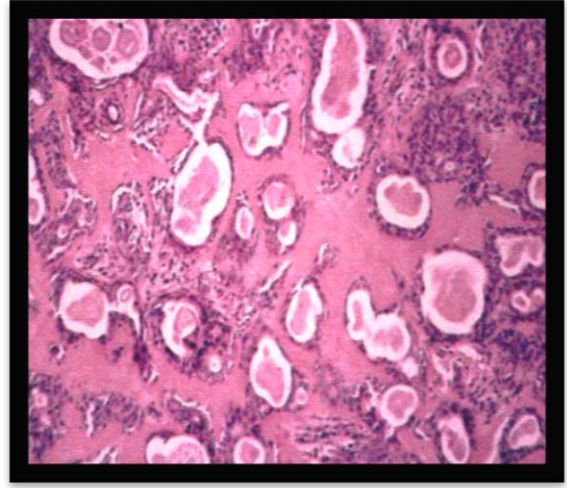
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Pleomorphic Adenoma

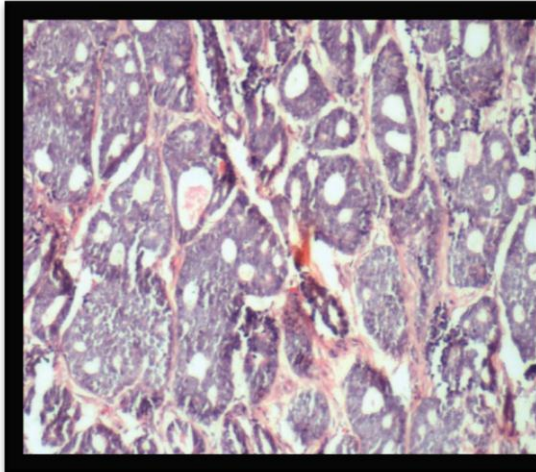


Ductal structures (left) with associated myxomatous background (right)

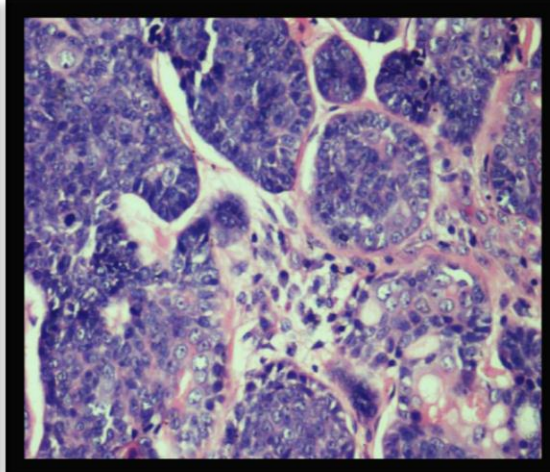


Many of the ducts and myoepithelial cells are surrounded by a hyalinized, eosinophilic background alteration

Adenoid cystic carcinoma



Variable-sized cribriform spaces formed by small deeply basophilic cells imparting Swiss cheese pattern



Variable-sized cribriform spaces formed by small deeply basophilic cells imparting Swiss cheese pattern

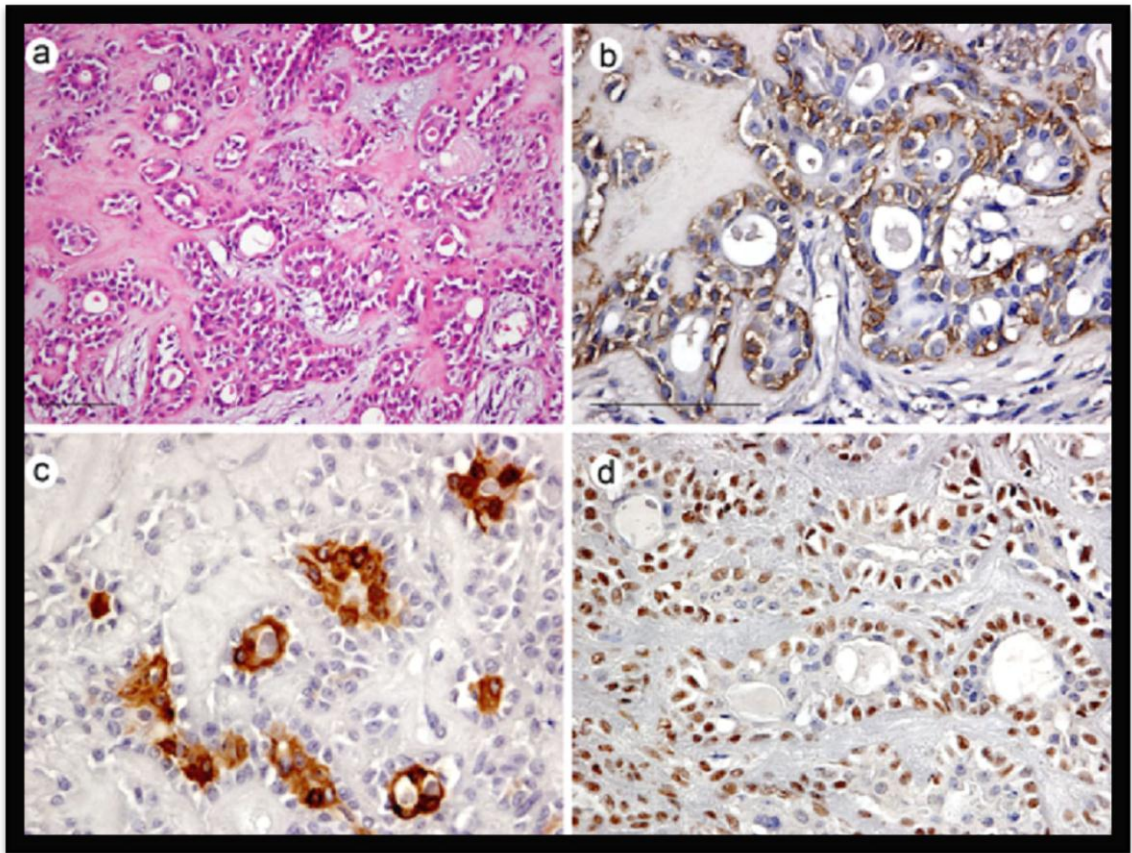
(c)Immunohistochemistry (1,2,8,9,10)

Definition

A technique for identifying cellular or tissue constituents (antigens) by means of antigen-antibody interactions, the site of antibody binding being identified either by direct labeling of the antibody or by use of a secondary labeling method.

The IHC technique includes the following steps:

- Deparaffinization of tissue sections
- Quenching of endogenous enzymes,
- Antigen retrieval.
- Blocking of nonspecific binding sites.
- Binding primary antibody
- Binding with biotinylated secondary antibody.
- Detection method using peroxidase –Anti peroxidase method.
- Addition of chromogen substrate, usually DAB.
- Counterstaining, dehydrating and cover slipping the



Immuno histochemical profiles for podoplanin in glandular structures of pleomorphic adenoma (a) Immunoperoxidase stain for podoplanin, (localized in outer structures of Pleomorphic adenoma), (b) Keratin (k)19 also positive for p63, (c) and p63, (indicating duct epithelial like differentiation and the inner cells were positive for k19) (d) indicating myo epithelial differentiation.

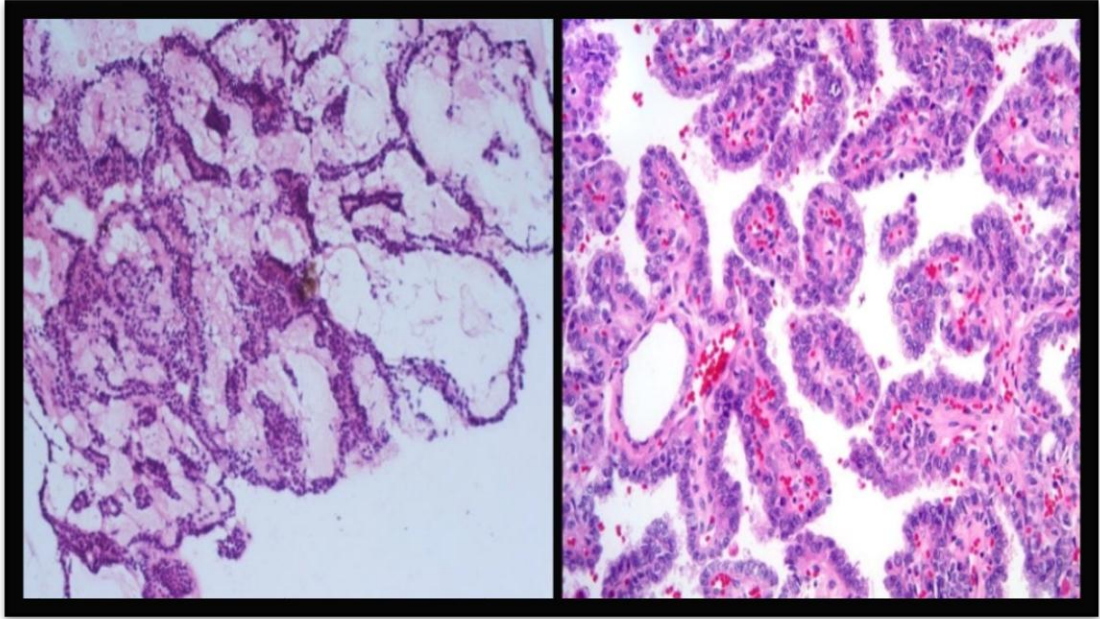
(d) FROZEN SECTION: (1,2)

Frozen section procedure is a pathological laboratory procedure to perform rapid microscopic analysis of a specimen, the technical of the name this procedure is cryosection.

The Frozen technique includes the following steps:

- Select the representative area of tissue trim no longer than 2x2x2
- Place it on specimen holder with the embedding medium
- Freeze by keeping on the cryostat base (-15 to -20)
- Fix the specimen holder and check if properly placed and locked
- Retract the specimen holder position till the knife touches the block

- Position the anti role plate
- Cut sections, Fix the sections on slide and stain it



a) frozen section, b) Routine H&E Section, (Poor morphology of frozen section when compared to routine section)

Merits:

Fastest of all methods
 Excellent for IHC, IF, ISH
 Often easiest to section depending upon the tissue

Demerits:

More prone to freezing artifact
 Poorest morphology

Conclusion

Salivary gland pathologies may be neoplastic, non-neoplastic, inflammatory, or non-inflammatory. Early surgical intervention after a good clinical, radiological, and histopathological diagnosis is need of an hour to minimize the postoperative complications. Early diagnosis and management with recent advanced technologies is the key factor in achieving excellent prognosis of the disease.

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