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Diagnostic accuracy of fine needle aspiration cytology in salivary gland neoplasms-2 year study

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Abstract:

Introduction:
Mass in the salivary gland region often presents a diagnostic challenge. The present study is conducted to diagnose the benign and malignant neoplasms of the salivary glands based on cytomorphology and compare with histopathological diagnosis and to find out the sensitivity, specificity of FNAC of salivary gland lesions, with a note on age, sex, site distribution**. Materials and Methods:** FNAC was performed on salivary gland lesions from June 2011 to May 2013, department of pathology, at tertiary care centre. Smears were made fixed in alcohol, haematoxylin & eosin staining done. For these cases gross & histopathological examination done on partially resected or excised parotid gland neoplasms. Specimens were subjected for routine processing; slides prepared and stained with haemotoxylin and eosin. Total of 75 cases had cytological and histopathological correlation. Appropriate statistical analysis was done to analyse data. **Results:** Of 75 cases, majority (69.3%) of cases involved parotid gland followed by submandibular gland. Pleomorphic adenoma was commonest benign tumor; mucoepidermoid carcinoma commonest malignant tumor. Cystic lesions posed diagnostic difficulty resulting in false negative diagnosis in 4 cases, false positive diagnosis in 1 case. **Interpretation a conclusion:** Salivary gland neoplasms represent wide variety of benign and malignant neoplasms. Tumors most commonly involved parotid gland. Tumors with cystic component posed diagnostic difficulty on FNAC. The overall sensitivity, specificity and accuracy of FNAC in present study were 83.33%, 97.7%, and 92%, which are in concordance with other studies.

Key words: Salivary gland neoplasms, cytological and histopathological correlation, sensitivity, specificity and accuracy

Introduction:

Salivary gland neoplasms represent a wide variety of benign and malignant histological subtypes. Salivary gland neoplasms can arise from major or minor salivary glands. About 64-80% of primary salivary gland tumors occur in parotid gland, 7-11% occurs in submandibular salivary gland, less than 1% occur in sub lingual salivary glands and 9-23% occur in minor salivary glands [1].

The mean age of presentation for malignant salivary neoplasms is 55-65years, while benign tumors develop at least decade earlier, at mean age of 45 years [2].

In files of armed forces pathology institute (AFIP), about 1/3 rd major gland tumors, and half of minor gland tumors are malignant. Ratio of malignant to benign tumors is greatest (>2.3:1) in sub lingual gland, tongue, floor of mouth, retro molar area [3].

Pleomorphic adenoma is most common benign neoplasm accounting to 52.04% of tumors, of which 80% occur in parotid gland. Mucoepidermoid carcinoma is the most common malignant neoplasm, accounting to 4.06% of tumors& it commonly affects major salivary glands, especially parotid gland. Adenoid cystic carcinoma is second most common malignant neoplasm accounting to 1.63% of salivary gland tumors and is seen most commonly in minor salivary glands [4].

Preoperative information about nature of salivary gland neoplasms can be helpful in assessing and establishing a policy toward the neck lymph nodes, achieving wide tumor-free excision margins, preventing treatment delay, and informing patient more appropriately on treatment plan and on possible risk of facial nerve injury. Thus in case of a benign tumor, surgery can be postponed or patient can be followed if general health or other medical conditions pose a major surgical risk.

Preoperatively taken incisional, core biopsies or frozen sections for treatment planning carry risk of tumor spill, bleeding, or inflammation and damage to the facial nerve [5].

Most of salivary glands are easily accessible and there is widespread acceptance FNAC in preoperative diagnosis of salivary gland lesions [5]. In literature, diagnostic accuracy of FNAC ranges from 84% to 99%.[13–19]. Risk of complications is less with FNAC and it is simple, rapid, inexpensive [6].

Materials and Methods:

The study was retrospective and prospective study done at tertiary care centre; between periods of 2011 June to 2013 may (2year study). For cases collected retrospectively details were obtained from case records. For prospective cases FNAC was performed in standard manner. Smears stained with haematoxylin and eosin.

Histopathological specimens included partially resected and excised salivary gland neoplasms. The specimens were subjected for routine processing; slides prepared and stained with haemotoxylin and eosin. Appropriate statistical analysis was done to analyse data.

Results

In this study we analyzed 75 cases of salivary gland aspirates over a period of 2 years; from 2011 June to 2013 may, which had cytological and histological correlation.

Age of patients ranged from 10 to 65 years with maximum no of benign neoplasms observed in age group of 20-50years, maximum number of malignant neoplasms observed in age group of 31-40 years with a mean age of presentation for benign tumors 37.53years, 40.9years for malignant tumors. (Table 1)

Table no 1: Age distribution of salivary gland neoplasms

Age group	No cases of Benign neoplasms	No of cases of malignant neoplasms
0-10	0	2
11-20	7	1
21-30	10	4
31-40	10	10
41-50	10	4
51-60	5	6
61-70	3	3

Among 75 cases observed 44 (58.8%) were females and 31(41.3%) males. Female to male ratio was 1.4:1 (chart no 1). Female predilection observed for benign neoplasms and equal sex incidence for malignant neoplasms.

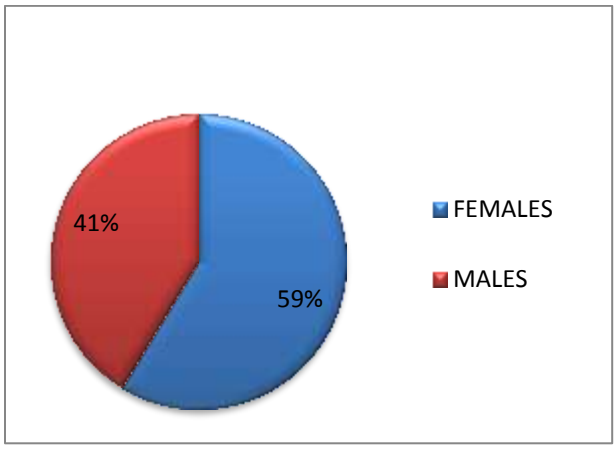

Figure 1: Gender distribution for total cases

Table 2: Site distribution of salivary gland neoplasms

Site	No. of cases	Percentage
Parotid	52	69.3%
Sub mandibular	12	16%
Minor salivary glands	11	14.6%%

Most common site of involvement was parotid gland followed by sub mandibular gland (table no 2)

Diagnosis of salivary gland neoplasms on FNAC:

Cytological diagnosis and their distribution, incidence displayed in table 3

Table 3: cytological diagnosis of salivary gland neoplasms

Cytological Diagnosis	No of Cases	Percentage
BENIGN NEOPLASMS	**49**	**66%**
Pleomorphic adenoma	42	56%
Benign cystic lesion	7	10%
MALIGNANT NEOPLASMS	**26**	**34%**
Mucoepidermoid carcinoma	16	21%
Adenoid cystic carcinoma	6	8%
Salivary duct carcinoma	1	1%
Low grade Spindle cell lesions	3	4%

Diagnosis of salivary gland neoplasms on histopathology:

The histopathological diagnosis, distribution and incidence displayed in table 4

Table 4: Histopathological diagnosis of salivary gland neoplasms

Histological Diagnosis	No of Cases	Percentage
BENIGN NEOPLASMS	**45**	**60%**
Pleomorphic adenoma	44	58.6%
Warthins tumor	1	1.3%
MALIGNANT NEOPLASMS	**30**	**40%**
Mucoepidermoid carcinoma	15	20%
Adenoid cystic carcinoma	7	9.3%
Salivary duct carcinoma	2	2.6%
Acinic cell carcinoma	1	1.3%
Epithelial myoepithelial carcinoma	1	1.3%
Ca ex Pleomorphic adenoma	1	1.3%
Fibro sarcoma	1	1.3%
MPNST	1	1.3%
Aggressive angiomyxoma	1	1.3%

Table 5: Cases with false negative diagnosis

Cytological diagnosis	Histological diagnosis
Benign cystic lesion	Mucoepidermoid carcinoma
Benign cystic lesion	Mucoepidermoid carcinoma
Benign cystic lesion	Mucoepidermoid carcinoma
Benign cystic lesion	Acinic cell carcinoma
Pleomorphic adenoma	Epithelialmyoepithelialcarcinoma

Table 6: Cases with false positive diagnosis

Cytological diagnosis	Histological diagnosis
Mucoepidermoid carcinoma	Warthins tumor

Table 7: Benign neoplasms with inaccurate diagnosis

Cytological diagnosis	Histological diagnosis
Benign cystic lesion	Pleomorphic adenoma
Benign cystic lesion	Pleomorphic adenoma
Benign cystic lesion	Pleomorphic adenoma

Table 8: Malignant neoplasms with inaccurate diagnosis

Cytological diagnosis	Histological diagnosis
Low grade spindle cell lesion	Fibro sarcoma
Low grade spindle cell lesion	Angiomyxoma
Low grade spindle cell lesion	MPNST
Mucoepidermoid carcinoma	Ca ex pleomorphic adenoma
Mucoepidermoid carcinoma	Adenoid cystic carcinoma
Mucoepidermoid carcinoma	Salivary duct carcinoma

Parameters reflecting diagnostic accuracy of FNAC of salivary gland neoplasms in this study are as follows:

Sensitivity: 83.33%
Specificity: 97.7%
Accuracy: 92%
Positive predictive value: 96.1%
Negative predictive value: 89.8%
False positive rate: 2.2%
False negative rate: 16.6%

Discussion

Discussion of individual salivary gland neoplasm:

Pleomorphic adenoma

Cytologically 42 cases were diagnosed as pleomorphic adenoma, Histopathologically 44 cases were diagnosed as pleomorphic adenoma. 3 cases of pleomorphic adenoma were diagnosed as benign cystic lesions cytologically.

One case of epithelial myoepithelial carcinoma was false negatively diagnosed as pleomorphic adenoma. Smears showed two populations of cells spindle and polygonal cells with mild pleomorphism. Pleomorphic adenoma can be considered as possible diagnosis in this case because pleomorphism, spontaneous infarction, presence of necrosis as well as small cells with dark nuclei on cytology mimicking carcinoma and necrosis after FNAC of pleomorphic adenoma (PA) is important features which can cause diagnostic problems on FNAC.

Brachtel EF stated that although fine-needle aspiration biopsy is a highly accurate tool for diagnosis of pleomorphic adenomas, even this common salivary gland neoplasm can be diagnostically challenging and cause pitfalls in cytodiagnosis. In particular, the presence of either cystic degeneration or squamous and mucinous metaplasia can lead to a false positive diagnosis of malignancy [7].

Warthin's tumor

Histopathologically one case of warthins tumor diagnosed in 65 year old male patient. Cytologically it is diagnosed as mucoepidermoid carcinoma giving a false positive diagnosis. Aspirated material showed mucoid, granular debris with scant cellularity with cytological details obscured by mucoid debris, few cells showing vacuolated cytoplasm giving a suspicion of mucoepidermoid carcinoma.

Kusum et al reviewed 45 cases with oncocytic preponderance. 5 were oncocytomas and 19 were warthins tumors. They concluded when lymphoid component, mucous was minimal absent warthins tumor can be confused with oncocytomas. In such cases architectural pattern like papillary fragments of acini, multilayered sheets of oncocytes and singly scattered oncocytic epithelial cells favor oncocytoma over warthins tumor [8].

Mucoepidermoid carcinoma:

Cytologically 16, histologically 15 cases were diagnosed as mucoepidermoid carcinoma. 9 cases showed positive correlation. 3 cases of mucoepidermoid carcinoma were falsely diagnosed as benign cystic lesions cytologically. The reason for false negative diagnosis as benign cystic lesion was scant cellularity and aspiration of only cystic contents. One case each of carcinoma ex pleomorphic adenoma, salivary duct carcinoma, adenoid cystic carcinoma, warthins tumor was diagnosed as mucoepidermoid carcinoma cytologically.

In a study done by Hughes et al, one case of mucoepidermoid carcinoma was given as warthins tumor on FNAC. They concluded that presence of abundant dirty background material which is commonly seen in warthins tumor and eosinophilic tumor cells being misinterpreted as oncocytes led to error on diagnosis [9].

Adenoid cystic carcinoma

In the present study 7 cases were given as adenoid cystic carcinoma, cytologically 6 cases were diagnosed as adenoid cystic carcinoma. One case is inaccurately diagnosed as mucoepidermoid carcinoma.

Jesse Jaso et al states that differential diagnosis of AdCC includes tumors that also exhibit tubular and cribriform structures such as polymorphous low-grade adenocarcinoma, tumors with basaloid cellular morphology such as basal cell adenoma and basal cell adenocarcinoma, and tumors with a dual population of ductal and myoepithelial cells such as pleomorphic adenoma[10].

Salivary duct carcinoma

Histologically two case of salivary duct carcinomas were diagnosed, cytologically concordantly one case was given as salivary duct carcinoma; other case was given as mucoepidermoid carcinoma.

Perkins Mukunyadzi et al stated that initial recognition of salivary duct carcinoma as a high grade neoplasm is crucial as this tumor carries a dismal prognosis. High-grade MEC, squamous cell carcinoma, and metastatic breast carcinoma are

important differential diagnosis. MEC consists of a mixture of cell types, including mucous cells, intermediate cells, and cells showing squamous differentiation. Squamous differentiation seen in MEC is subtle and does not usually show full maturation, and degree of nuclear atypia is often mild. Cytoplasm of salivary duct carcinoma cells may appear dense and squamoid, but obvious squamous differentiation and presence of keratin material and high-grade nuclei are more consistent with squamous cell carcinoma [11].

Acinic cell carcinoma

Histologically one case of acinic cell carcinoma was diagnosed it is diagnosed false negatively as benign cystic lesion cytologically. In this case FNAC yielded only hypo cellular fluid with scant cellularity, the cells resembling normal acinar cells with that picture cytologically it was false negatively given as benign cystic lesion.

In a study done by Hughes et al, a case of acinic cell carcinoma was incorrectly diagnosed as normal salivary gland and they found that most likely reason for this error was failure to appreciate the cellularity of the lesion and architecture of acinar structures which were more disorganized and discohesive than those of normal salivary gland [9].

Epithelial myoepithelial carcinoma

One case of epithelial myoepithelial carcinoma was false negatively diagnosed as pleomorphic adenoma cytologically. Because of the presence of different populations of cells spindle cells, plasmacytoid cells and polygonal cells and mild pleomorphism, pleomorphism being a well known phenomenon in pleomorphic adenoma it was given as pleomorphic adenoma.

Diagnosis of epithelial myoepithelial carcinoma is challenging as it can mimic many other salivary gland tumors on cytology. An important diagnostic clue is presence of ductal cells in form of tubules among background sheets of myoepithelial cells.

Carcinoma ex pleomorphic adenoma

Fumio Ide et al states that there is no prototypical carcinoma entity, forms of malignancy found are most common adenocarcinoma not otherwise specified, salivary duct carcinoma and undifferentiated carcinoma. Malignant component is often difficult to sub classify as one of exactly defined carcinoma categories, and more than one phenotype may be present [12].

Malignant peripheral nerve sheath tumor

In our study cytologically a case with spindle cells and mild pleomorphism is diagnosed as low grade spindle cell lesion and histoplathologically that case is diagnosed as malignant peripheral nerve sheath tumor.

Ismet Aslan et al stated that malignant peripheral nerve sheath tumors (MPNST) are among rare tumors of head and neck region and constitute one of the most difficult sarcomas to diagnose due to their cytological variability and architectural pattern. They are often confused with other soft tissue sarcomas [13].

Fibro sarcoma

Histopathologically one case was diagnosed as fibro sarcoma in 40 year old female patient. Cytologically sample yielded spindle cells with mild pleomorphism and diagnosis of spindle cell neoplasm is given.

Mario A. Luna et al states that sarcomas arising in major salivary glands are rare. In his article he presented clinico pathologic features of 11 patients with primary sarcomas of parotid gland and 11 sarcomas were histologically typified as three malignant fibrous histiocytomas and two each of neurosarcomas, rhabdomyosarcoma, fibro sarcomas, and osteosarcomas [14].

Aggressive angiomyxoma/ low grade fibromyxoid sarcoma

60 year old male patient with left sub mandibular swelling microscopically showed hypo cellular to moderately cellular myxoid or fibromyxoid areas. Curvilinear capillaries with perivascular cell condensation were found. Fusiform tumor cells vary from small and bland to enlarged, bizarre, pleomorphic and multinucleated. The cytoplasm of cells was scant and slightly eosinophilic, and mitoses were infrequent. Histopathologically a differential diagnosis of aggressive angiomyxoma /low grade fibromyxoid sarcoma was given. Cytologically it was given as spindle cell neoplasm without further sub categorization

Table 13: Comparative analysis of sensitivity, specificity, accuracy of FNAC

Study	No of cases	Sensitivity	Specificity	Accuracy
Singh A et al (2011)[15]	56	76.9%	97.1%	
Naeem Sultan Ali et al[16]	129	84%	98%	94%

Neveen Tahoun [17]	82	91.7%	92.5%	92%
SiedZiaodin et al [18]	235	67.27%	91.2%	83.43%
Present study	75	83.3%	97.7%	92%

Conclusion

Salivary gland tumors are relatively less common, and they exhibit a wide variety of microscopic appearances, even within one particular lesion, and this has caused considerable problems in categorization and diagnosis.

Familiarity with the cytological features of rare lesions and morphological variations of the commoner lesions is necessary to avoid misinterpretation. Cystic lesions remain a problematic area for correct diagnosis on cytology

With high diagnostic sensitivity, specificity, accuracy present study reaffirms that FNAC of the salivary glands neoplasms, being a safe quick, safe, and affordable procedure offers an invaluable and highly accurate initial diagnostic approach for the management of patients, whether it is local excision for a benign neoplasm, radical surgery for a malignant neoplasm or alternate treatment.

Figures:

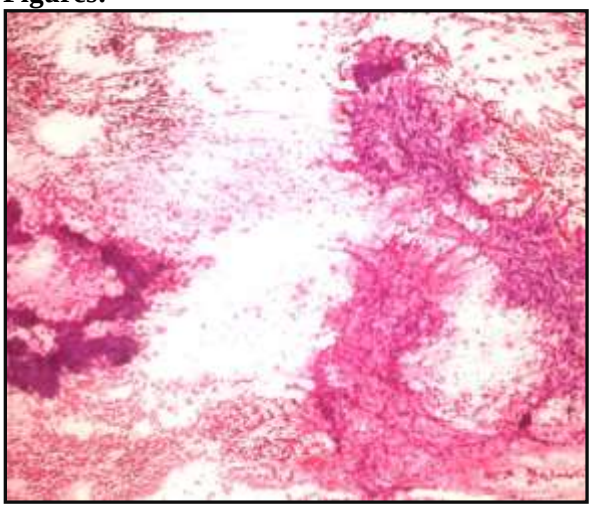

Figure1 (10X, H&E):

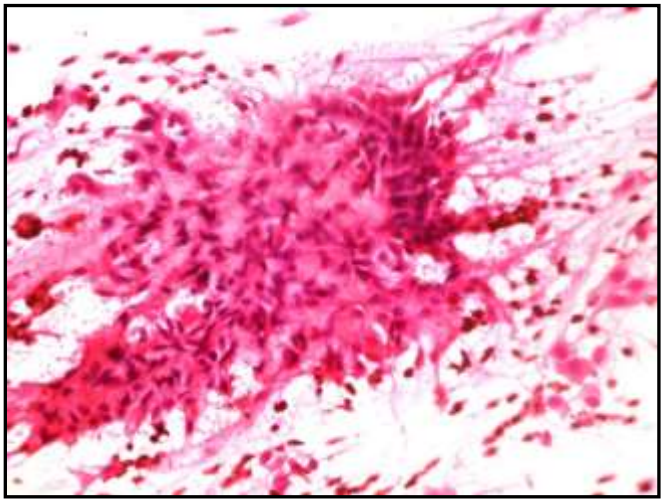

Figure 2 (40X, H&E): Pleomorphic adenoma-Cytosmears showing epithelial and mesenchymal components in fibrillarychondromyxoid background

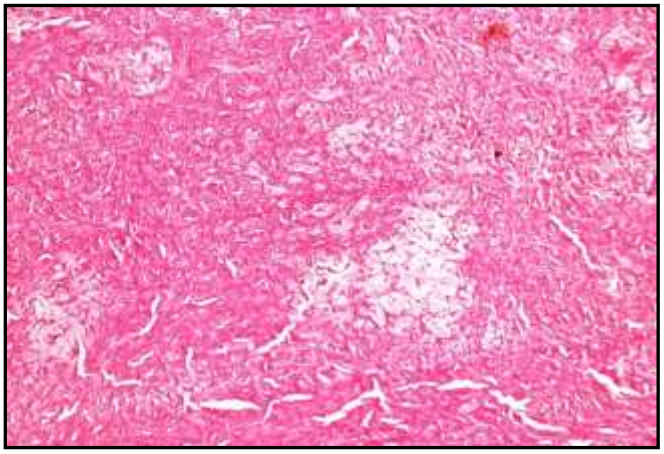

Figure 3 (10X, H&E):

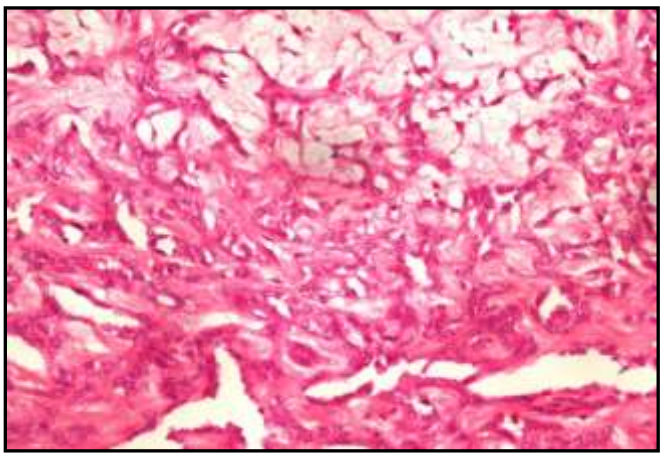

Figure 4 (40X, H&E): Histopathological sections showing epithelial component in loose chondromyxoidstroma in case of pleomorphic adenoma

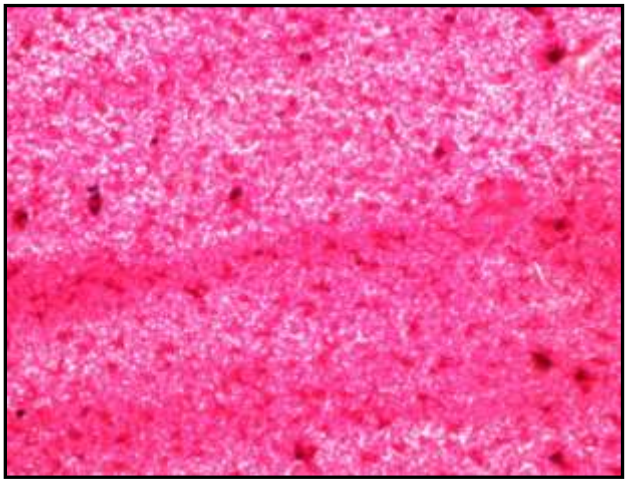

Figure 5(10X,H&E): Cytosmear showing necrotic debri few scattered inflammatory cells and few atypical cells and reported as mucoepidermoid carcinoma later diagnosed as warthin's tumor

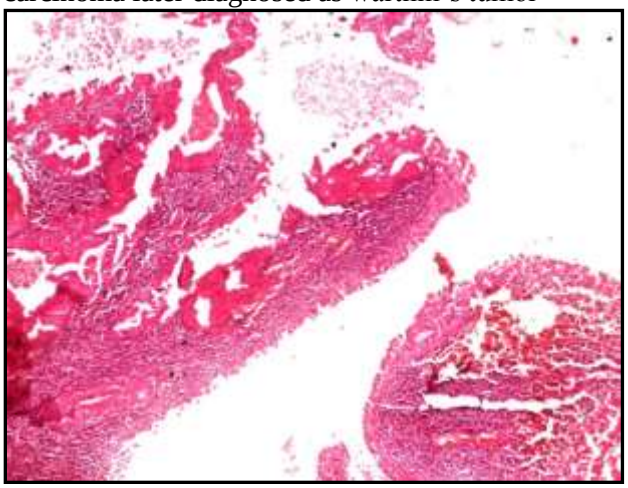

Figure 6(10X,H&E): Histopathological sections showing cystic spaces, with papillary structures projecting into lumina

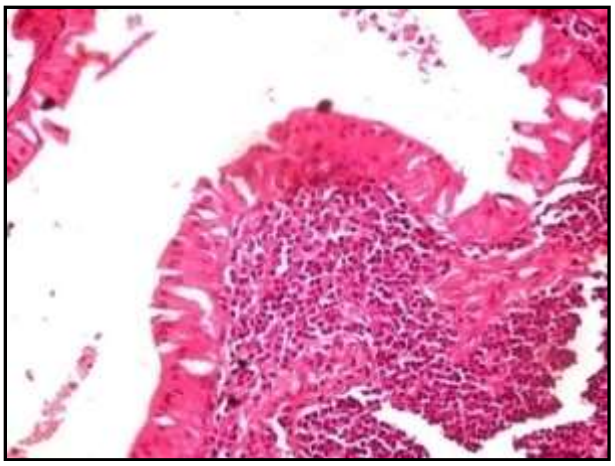

Figure 7:

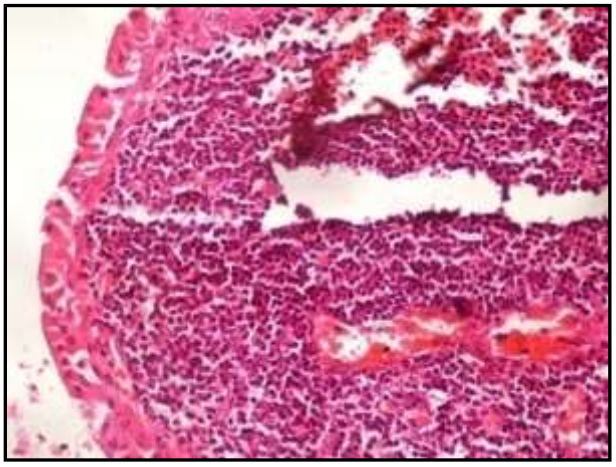

Figure 7, 8 (40X, H&E): Histopathological section showing papillary structure lined by oncocytic cells and flattened basal cells, with underlying lymphoid follicles

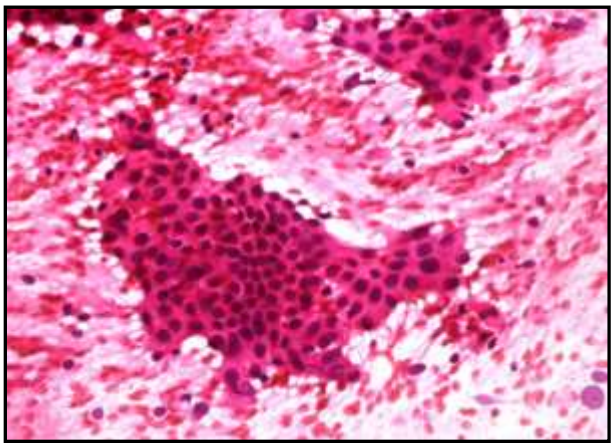

Figure 9 (40X,H&E): Cytosmear of mucoepidermoid carcinoma showing intermediate cells, and basaloid cells in mucoid background.

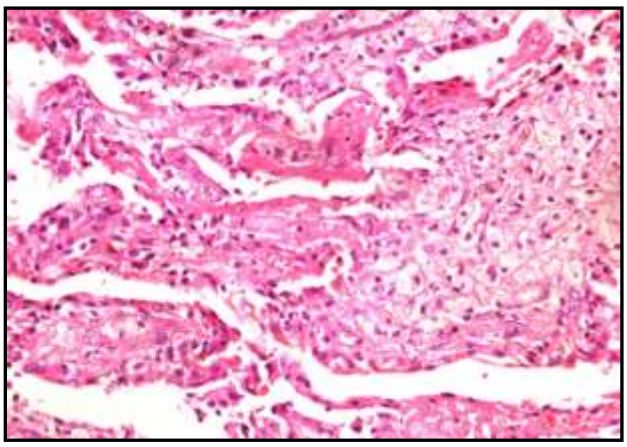

Figure 10 (40X, H&E): Histopathological section showing epidermoid component of mucoepidermoid

carcinoma with clear cells and intermediate cells

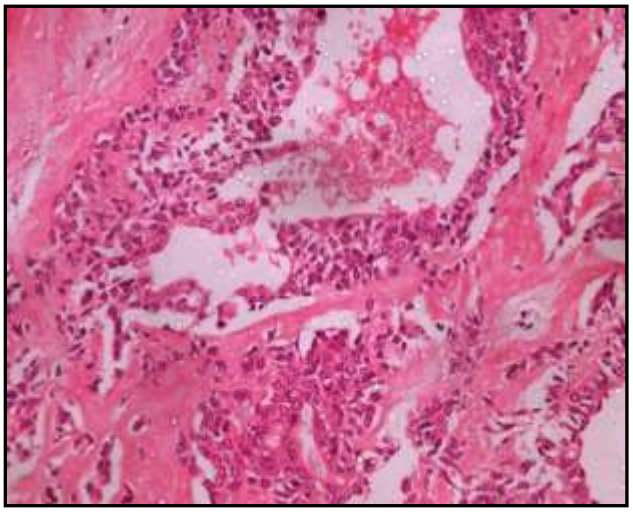

Figure 11(40X,H&E): Histopathological section showing intermediate cells lining cystic spaces

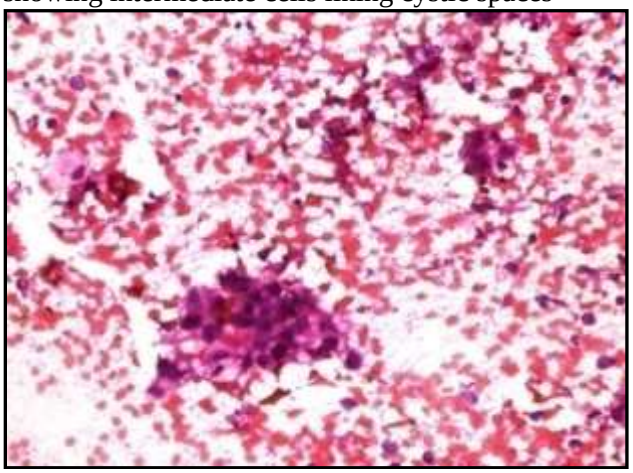

Figure 12(40X, H&E): Cytosmear showing clusters and singly scattered tumor cells admixed with eosinophilic material

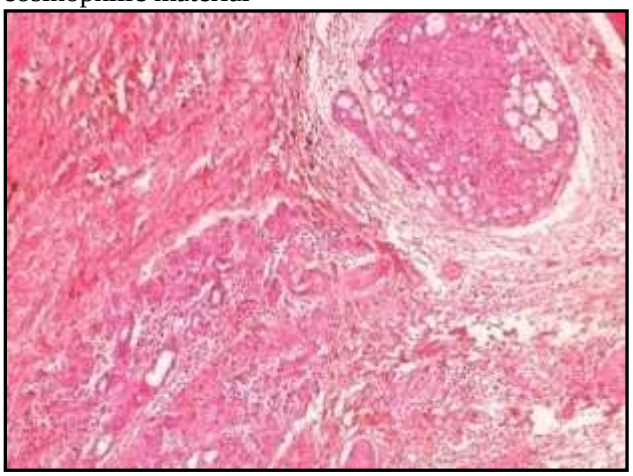

Figure 13(10X, H&E): Histopathological section showing tumor tissue arranged in tubules, solid sheets and cribriform pattern

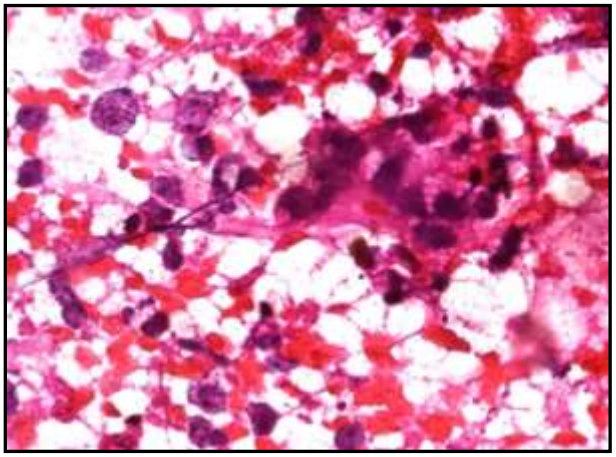

Figure 14(40X, H&E): Cytosmear of salivary duct carcinoma showing obviously malignant epithelial cells

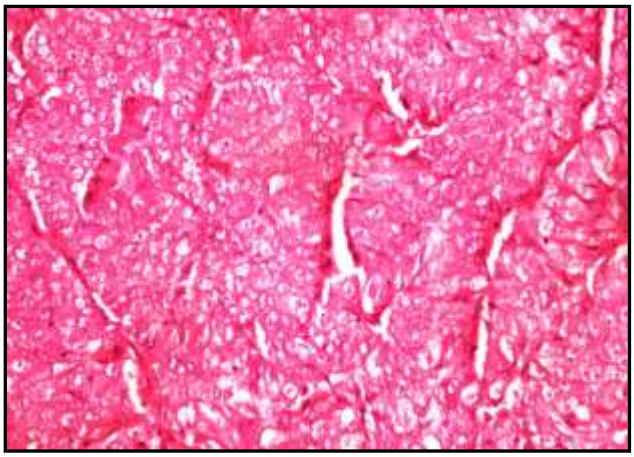

Figure 15(40X, H&E): Histopathological section of salivary duct carcinoma

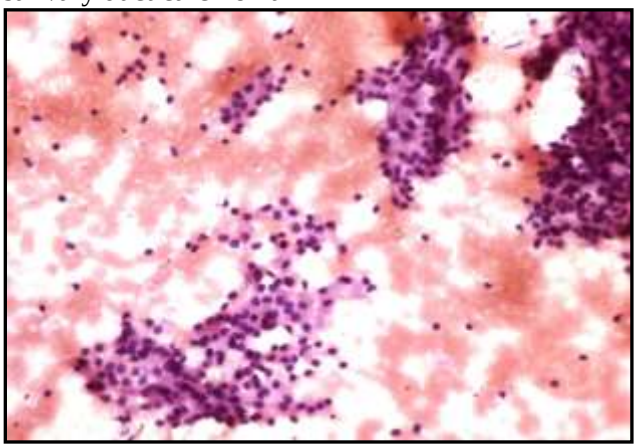

Figure 16(10X, H&E): cellular cytosmear of acinic cell carcinoma showing cells with vacuolated cytoplasm, bland nuclei

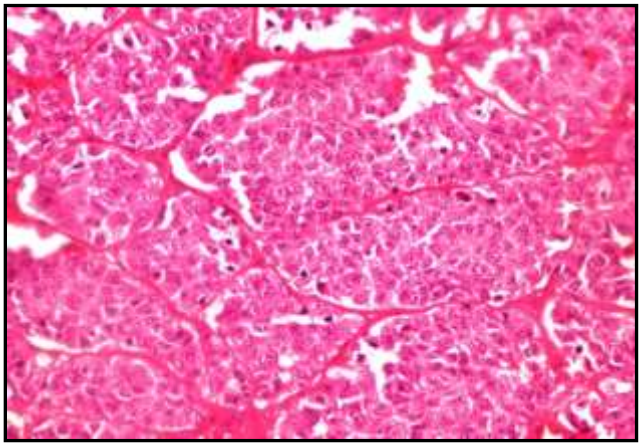

Figure 17 (10X, H&E): Histopathological section of acinic cell carcinoma

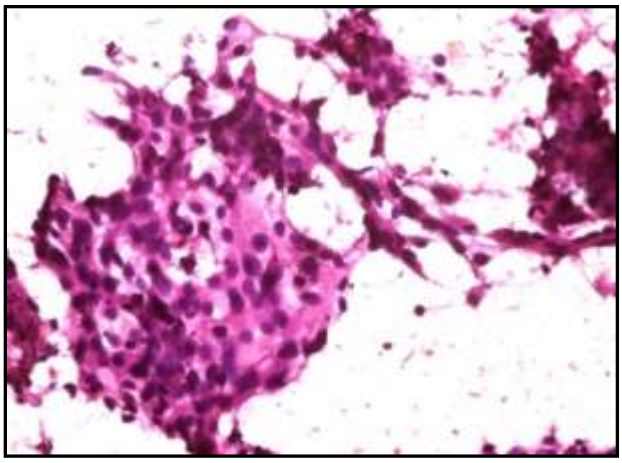

Figure 18(40X, H&E): Cytosmear showing pleomorphic cells in a case of carcinoma ex pleomorphic adenoma

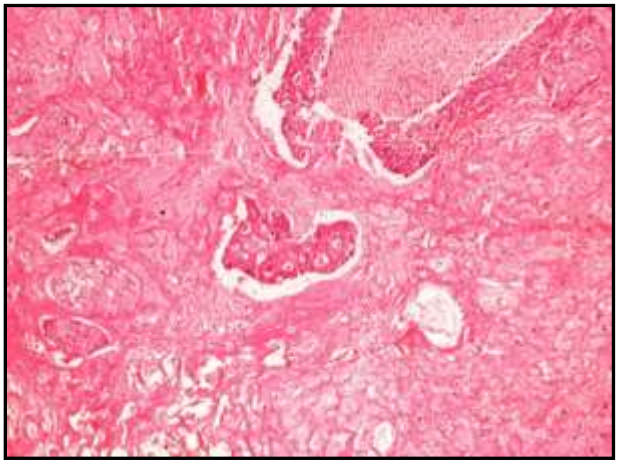

Figure 19 (10X, H&E): Histopathological section showing malignant component adjacent to myxoid mesenchymal component

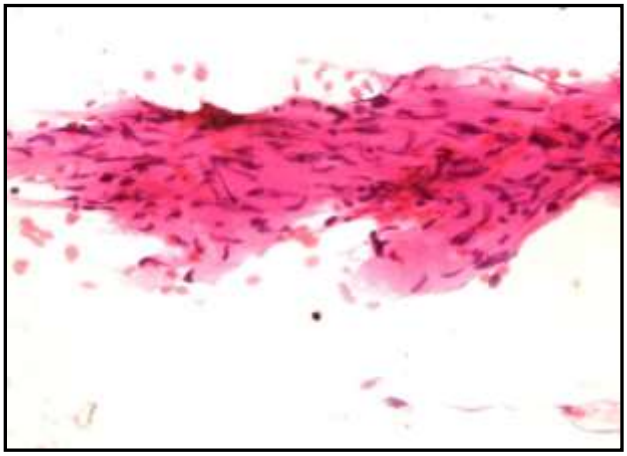

Figure 20 (40X, H&E): Cytosmear showing pleomorphic spindle cells

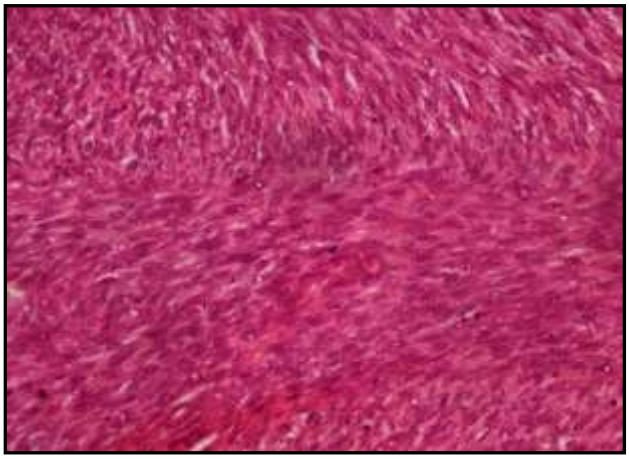

Figure 21 (40X, H&E): Histopathological section showing pleomorphic spindle cells arranged in bundles and fascicles

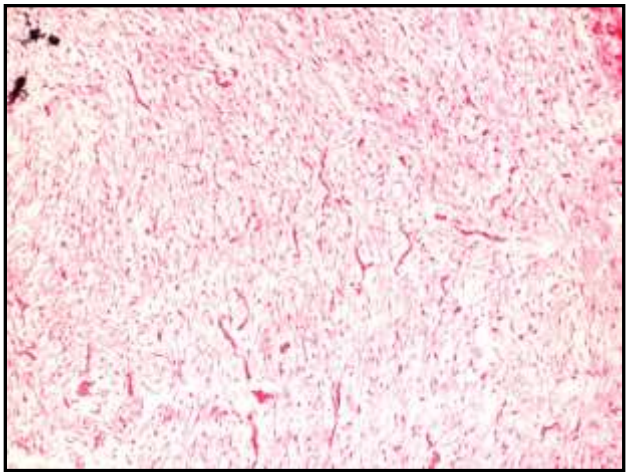

Figure 22:

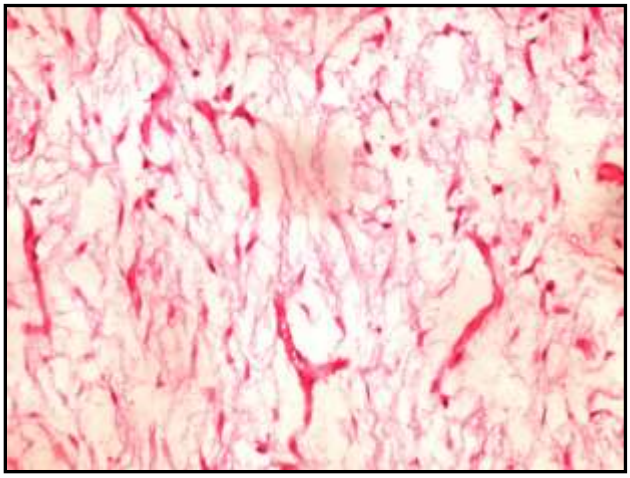

Figure 22 (10X, H&E), 23 (40X, H&E): low grade fibromyxoid sarcoma

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