

Diagnostic Accuracy and Pitfalls in Fine Needle Aspiration Cytology Of Salivary Gland Lesions

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ABSTRACT

Background: Fine Needle Aspiration cytology (FNAC) is an essential diagnostic method used to evaluate salivary gland lesions. However, at times, diverse morphological patterns and overlapping features between benign and malignant lesions becomes challenging and difficult to give a definitive diagnosis.

Aim are to compare the findings of preoperative FNAC with their histopathological types and to discuss the causes for discordancy and identify the potential pitfalls in cytological diagnosis.

Materials and Methods: An observational analytical study was carried out over a 4 year period to review the cases of patients with salivary gland lesions who underwent FNAC in a medical college, hospital. Taking histopathological diagnosis as gold standard, the cytological diagnosis of the cases was compared and the causes of discrepancies were evaluated. Sensitivity, specificity, accuracy, positive predictive value and negative predictive value was calculated.

Results: In the present study, out of 137 cases, cyto- histological correlation was available in 46 cases. Pleomorphic adenoma was the commonest lesion in the study. The diagnostic value of FNAC was: Sensitivity 66.7%, Specificity 97.4%, Positive Predictive Value 80%, Negative Predictive Value 95% and Diagnostic Accuracy 93.3%. False positive diagnosis was rendered in warthin's tumor whereas false negative diagnosis was given in mucoepidermoid carcinoma.

Conclusion: FNAC is useful in the preoperative diagnosis of salivary gland lesions. Pitfalls in cytologic diagnosis were due to errors in sampling, cystic lesions and interpretation of smears .

Keywords: FNAC Salivary Gland , Diagnostic Accuracy, Pitfalls

Introduction

Various lesions of major and minor salivary glands, account for less than 3% of all head and neck tumors. Fine needle aspiration cytology (FNAC) is sensitive and specific technique as compared to incisional biopsy and frozen section in the diagnosis of salivary gland lesions. The main goal of FNA is to determine if a mass is inflammatory and/or reactive, benign or malignant neoplasm and if possible, to render a specific diagnosis. FNA obviates surgery and is beneficial in preoperative information that may play a significant role in appropriate treatment to the patient. However, majority of the salivary gland lesions have varied morphological patterns and overlapping features between non-neoplastic, benign and malignant lesions thus making it difficult to give an accurate diagnosis .^[1-6]

This study aims 1) To determine the diagnostic yield of FNAC of salivary gland lesions and compare it with histopathological diagnosis. 2) To discuss the causes for discordancy and identify the potential pitfalls in cytological diagnosis.

Materials and Methods

An observational analytical study was carried out over a 4 year period to review the cases of patients with salivary gland lesions who underwent FNAC in a medical college, hospital. The study was approved by the institution ethical and research committee.

FNAC was performed using a 22 – 23 gauge needle attached to a disposable syringe under aseptic conditions after prior consent. The material was aspirated and smeared onto a clean glass slides and thin smears were prepared between two slides. The air dried and ethanol fixed smears were stained with MGG (May Grunwald's Giemsa) and Pap (Papanicolau) stain. Forty six (46) patients underwent excision biopsies. After gross examination of specimens, the representative sections were processed and examined by H & E (Hematoxylin and Eosin) methods. Special stains were performed when necessary. Taking histopathological diagnosis as gold standard, the cytological diagnosis of the cases was compared and the causes of discrepancies was evaluated.

Sensitivity, specificity, accuracy, positive predictive value and negative predictive value was calculated.

Results

Among the 137 patients who underwent FNAC, 75 (54.7%) were males and 62 (45.3%) were females (M: F ratio = 1.2:1). The most common gland involved was Parotid gland in 98 cases (71.5%), followed by submandibular gland in 38 cases (27.7%) and a single case involved the minor salivary gland (0.7%).

On FNAC, out of the 137 cases, 3 cases (2.18%) were inadequate due to sparse cellularity, 59 cases (43.06%) were diagnosed as non-neoplastic, while among the 75 cases (54.74%) diagnosed as neoplastic, 65 cases (47.44%) were rendered benign while 10 cases (7.29%) were malignant on cytology.

In this study we analyzed 46 cases (33.57%) of salivary gland aspirates which had cytological and histological correlation of which one was excluded due to sparse cellularity. (Table 1). 06 FNAC cases showed discordant diagnosis in specific typing of the lesion (Table 2).

False negative cases were as follows: Case 01 was cytologically diagnosed as myoepithelioma (Fig 1a), subsequent histology revealed mucoepidermoid carcinoma with spindle cell component (Fig 1b). Case 02 was cytologically diagnosed as WT, while documented histologically as mucoepidermoid carcinoma (Fig 2a). The

aspirate obtained was mucoid. On review of the smears the intermediate cells with eosinophilic cytoplasm was misinterpreted as oncocyctic cells (Fig 2b).

False positive cases were as follows: Case 03 was malignant Squamous neoplasm proved histologically as WT (Fig 3a). FNA showed necrotic debris which appeared as thick, granular material with few clusters and singly dispersed epithelial (squamous) metaplastic cells with atypia, mimicking squamous cell carcinoma (Fig 3b).

Three cases remained benign on histology, however tumor type was changed which were as follows: Case 04 was WT misinterpreted as benign salivary gland cyst. Aspirated 3ml of thick material. FNA showed dirty background with normal acinar cells. Case 05 was pleomorphic adenoma which was incorrectly diagnosed as sialadenitis. The smear showed normal acinar and ductal epithelial cells. Case 06 was chronic sialadenitis incorrectly diagnosed as cellular pleomorphic adenoma. The smear showed abundant normal acinar cells, fibrillary fibrous stroma and occasional lymphocytes.

Taking histology as the “gold standard, the diagnostic value of FNAC after excluding the inadequate cases was as follows: Sensitivity for diagnosis of malignant tumor was 66.7%, Specificity 97.4%, Positive Predictive Value 80%, Negative Predictive Value 95% and Diagnostic Accuracy 93.3%.

Table 1: Relation between FNAC diagnosis and final histopathologic diagnosis.

CYTOLOGICAL DIAGNOSIS	NO.OF CASES	HISTOLOGIC DIAGNOSIS	NO.OF CASES
NON-NEOPLASTIC		8	
Epidermal cyst	1	Epidermal cyst	1
Sialadenitis	1	Pleomorphic adenoma	1
Chronic sialadenitis	4	Chronic sialadenitis	4
Abscess	1	Abscess	1
Benign epithelial cyst	1	Benign epithelial cyst	1
BENIGN TUMORS		32	
Pleomorphic adenoma	21	Pleomorphic Adenoma Chronic Sialadenitis	20 1
Warthin's tumor	8	Warthin's tumor Mucoepidermoid carcinoma	7 1
Cystic lesion	1	Warthin's tumor	1
Myoepithelioma	2	Myoepithelioma Mucoepidermoid carcinoma with spindle cell component	1 1
MALIGNANT TUMORS		5	
Mucoepidermoid carcinoma	1	Mucoepidermoid carcinoma	1
Adenoid cystic carcinoma	1	Adenoid cystic carcinoma	1
Squamous cell carcinoma	1	Warthin's tumor	1
Low grade salivary gland neoplasm with atypical cells	1	Low- grade Mucoepidermoid carcinoma	1
Squamous cell carcinoma /High grade Mucoepidermoid carcinoma	1	Metastatic squamous cell carcinoma (Parotid Lymph Node)	1

Table 2: 06 FNAC Cases of discordant diagnoses in specific typing of the lesion.

Cases	Age	Sex	Site	Cytologic Diagnosis	Histopathological Diagnosis
01	58	M	PAROTID	Myoepithelioma	Mucoepidermoid carcinoma with spindle cell component
02	54	F	PAROTID	Warthin's tumor.	Mucoepidermoid carcinoma
03	47	M	PAROTID	Squamous cell carcinoma	Warthin's tumor
04	53	M	PAROTID	Benign salivary gland cyst	Warthin's tumor
05	58	M	PAROTID	Sialadenosis.	Pleomorphic adenoma
06	61	M	SUBMANDIBULAR	Cellular pleomorphic adenoma	Chronic sialadenitis

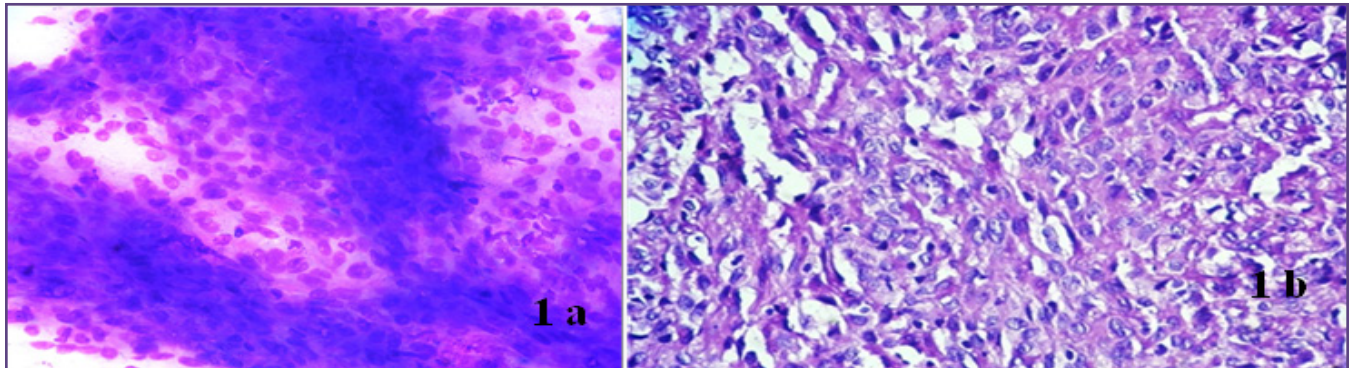


Fig. 1a: Smear shows loosely cohesive spindle cells in a metachromatic fibrillary matrix misinterpreted as myoepithelioma (MGG ,10x) **Fig1b:** Histological section showing mucoepidermoid carcinoma with spindle cell component (H&E,40x).

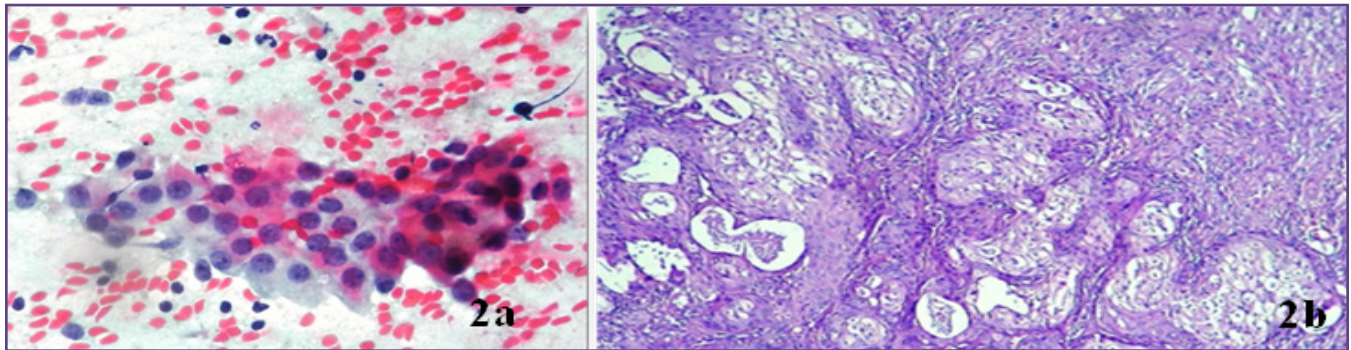


Fig. 2a: Case 2 shows FNA of mucoepidermoid carcinoma showing intermediate cells with eosinophilic cytoplasm misinterpreted as oncocytic cells of WT(Pap, 40x) **Fig 2b:** Histological section showing mucoepidermoid carcinoma with intermediate cells and mucous cells(H&E,40x).

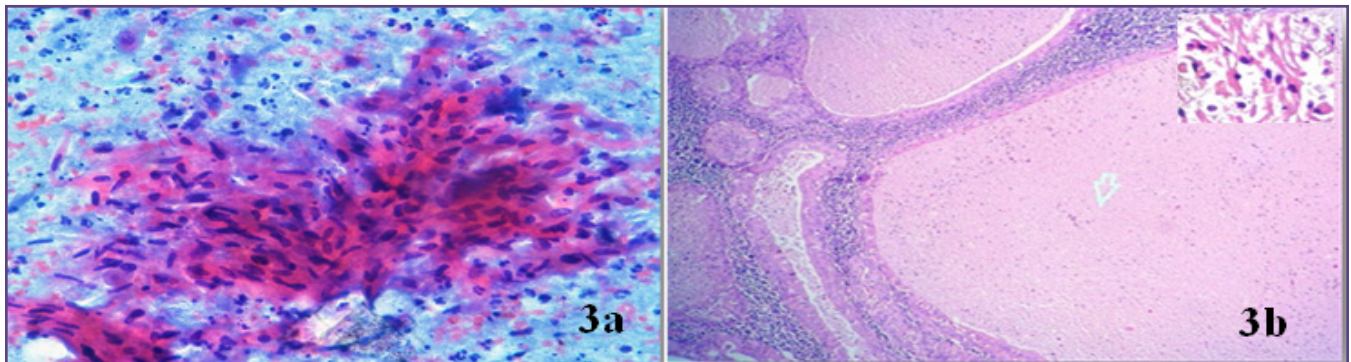


Fig. 3a: FNA of WT, squamous metaplastic cells with atypia , mimicking squamous cell carcinoma (Pap,40x) **Fig 3b:** Histological section of WT showing cystic spaces with squamous metaplastic cells (H&E,40x) .Inset showing squamous metaplastic cells (H&E,100x).

Discussion

FNAC of salivary gland lesions is very useful, quick, reliable and minimal invasive, however various interpretation challenges are encountered^[1,21]. Sensitivity, specificity and accuracy of FNA diagnosis of salivary glands obtained in this study is comparable with the data obtained in similar studies done previously (Table 3).

FNA of salivary lesions is difficult in cytology due to heterogeneity of benign and malignant tumors and the overlapping cytomorphological features which account for the indeterminate or “suspicious” diagnose^[3,13]. False positive and false negative diagnoses were pointer towards problems and pitfalls in cytologic interpretation.

The false negative results reported in literature ranged from 0-37%^[2]. In our work it was 4.44%, this was due to misdiagnosis of 2 cases, one case each of myoepithelioma and WT misdiagnosed as mucoepidermoid carcinoma. According to Orell et al^[5] a definitive diagnosis of mucoepidermoid carcinoma requires the coexistence of mucin-secreting cells and cells with squamous differentiation. The challenge is not only in relation to cytodagnosis but also in cytological typing^[12]. False-negative diagnoses usually occur due to fluid causing dilution of tumour cells, inflammatory cells and debris obscuring the tumor cells. Rarely the bland-looking intermediate cells being misinterpreted as benign cells^[6,19] as in our case.

Spindle cell component in a mucoepidermoid carcinoma is however rare as seen in our case and only a few case reports have been reported. On review of the smears only spindle cell component was seen which led to an erroneous diagnosis of myoepithelioma. Neoplastic myoepithelium in salivary gland tumors, is prone to assume a spindle cell configuration and has been reported to undergo dedifferentiation^[7].

The false positive rates reported in the literature ranged from 0-10%. In our series, it was 2.22%, this was due to misinterpretation of WT on FNAC as squamous cell carcinoma. WT have a characteristic cytomorphologic appearance represented by three main components - oncocytes, lymphocytes, and the fluid background. Cytological difficulties can be divided into three areas:

1.) Absence of one or more diagnostic components; 2.) Squamoid pattern; and 3.) Mucinous metaplasia. The fluid imparts a dirty background appearance that may be confused tumor necrosis^[8,10,15].

Mucoepidermoid carcinoma, squamous cell carcinoma, and oncocytoma are commonly misdiagnosed as WT. In the present case, FNA showed dirty necrotic background and squamous metaplastic cell clusters with atypia. However, oncocytes and lymphocytes were not visualized in the smears which was misleading and lead to the diagnosis of squamous cell carcinoma. It has been shown that metaplastic/reparative changes can occur in benign salivary gland neoplasms due to physical trauma induced by FNA which include squamous metaplasia, infarction, necrosis, subepithelial stromal hyalinization, acute/chronic hemorrhage, inflammation with multinucleated giant cells, granulation tissue with subsequent fibrosis, cholesterol cleft formation, pseudoxanthomatous reaction and microcystic degeneration^[9]. Squamous metaplasia in our case could be attributed to previous FNA.

In one case (case 4) WT, a non specific diagnosis of cystic lesion was made in cytology as the smears showed mainly fluid and benign acinar cells even on repeated aspiration. On histology it turned out to be WT with predominant cystic change. Histologically, WT characteristically consists of cystic and solid areas. The cystic area is lined by layers of tall columnar oncocytic luminal cells and flattened or cuboidal basal cells, while the stroma consists of lymphocytes^[10-12]. The cytological diagnosis of cystic salivary gland lesions is rather difficult due to the wide range of lesions that enter the differential diagnosis which include chronic sialadenitis, WT, acinic cell carcinoma, pleomorphic adenoma and mucoepidermoid carcinoma^[4,21].

In one case (case 5) pleomorphic adenoma was reported as sialadenitis on FNA. The smear showed only acinar and benign ductal epithelial cells. The error was mainly due to sampling which highlights the importance of multiple sampling especially in a small sized lesion.

In another case (case 6), a histologically proven chronic sialadenitis was misinterpreted as cellular pleomorphic adenoma on FNAC. This was mainly due to cellular

Table 3: Comparative analysis of sensitivity, specificity, accuracy of FNAC.

Study	No of Cases	Sensitivity	Specificity	Diagnostic Accuracy	Ppv	Npv
Present study	46	66.7%	97.4%,	93.3%.	80%	95%
Yadi Rama Raju etal ¹⁴	75	83.3%	97.7%	92%	96.1%	89.8%
StramandinoliRTetal ¹⁶	79	82.3%	68.2%	87.7 %	68.2%	87.7%
Iqbal M et al ¹⁷	49	62.5%	96.97%	96.4%		
Rehman H et al ¹⁸	50	53.28%	88.57%	78%	72.7%	79.9%

smears and lack of acini with only ductal epithelial cells. Usually clinical correlation solves the problem. Tumor like nodules caused by focal chronic inflammation is seen in chronic sialadenitis. Presence of epithelial cell aggregates associated with fibrillary fibrous stroma could be mistaken for pleomorphic adenoma, but the fragments of ductal epithelial cells are cohesive and stroma is not chondromyxoid^[5].

Our experience shows that FNA cytology of salivary gland lesions is a valuable diagnostic method. Accuracy depends on experience, and this method provides superior advantages for the clinicians and the patients.

Conclusion

FNAC is recommended as a safe and reliable technique in diagnosis of salivary gland lesions. Despite of high sensitivity, there are certain pitfalls due to the misleading diagnostic yields. A cautious approach towards salivary gland lesions is recommended. Pitfalls in cytologic diagnosis were due to errors in sampling, cystic lesions and interpretation of smears.

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