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Original Article

Factors Liable for Misinterpretation of Salivary Gland Neoplasms on Fine Needle Aspiration Cytology

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Abstract

Fine needle aspiration cytology (FNAC) is now considered an effective technique for evaluation of salivary gland tumors. However making precise diagnosis, at times, is a challenging job due to diverse morphological alterations and overlapping features of different tumors.

Objective: 1) To determine different factors liable for misinterpretation of salivary gland tumors on fine needle aspiration cytology. 2) To determine overall diagnostic accuracy of fine needle aspiration cytology in salivary gland tumors using histopathology as gold standard.

Design: Cross-sectional study. **Setting:** Department of Pathology, Pakistan Institute of Medical Sciences, Islamabad. **Duration of study:** From 15th October 2009 to 15th October 2010.

Sample size: 51.

Results: The sensitivity and specificity of FNAC came out to be 84.6% and 97.3% respectively with an overall diagnostic accuracy of 98%. Out of 51 cases, 3 were wrongly diagnosed by FNAC. The major factors found responsible for this misinterpretation were; lack of standardization of cellular adequacy in salivary gland cytology smears, indeterminate exact criteria of definite atypia for malignancy and failure to correctly identify different cell types.

Conclusion: FNAC was found to be a useful diagnostic tool in the evaluation of salivary gland tumors because of its simplicity, cost effectiveness, excellent patient compliance and high diagnostic accuracy. The diagnostic pitfalls in salivary gland FNAC, may be avoided by determination of definite predictive atypical nuclear features and identifying non predictive, non relevant nuclear features. Repeat FNAC when required and careful interpretation of slides could avoid and minimize mistakes. Support from special stains may also be quite helpful.

Key words: Fine Needle Aspiration Cytology (FNAC), Salivary gland neoplasm, Diagnostic pitfalls

Introduction

The Fine Needle Aspiration Cytology (FNAC) has now been accepted as the best primary method for evaluation for space occupying lesions of salivary gland region, by head and neck surgeons.[1] It can be performed on an outpatient basis or on patient's bed side, and has an excellent safety record of any method of procuring tissue for morphologic diagnosis.

Salivary glands are a source of wide variety of neoplastic and non neoplastic diseases, both benign and malignant. Therefore a mass in salivary gland region often presents with a diagnostic challenge with regards to its site of origin (sali-

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vary vs. non-salivary), biological behavior (benign vs. malignant) and tissue specific diagnosis[2]. FNAC has gained wide clinical acceptance as a direct approach to morphological diagnosis of salivary gland lesions because most are easily accessible and in most cases diagnostic material is readily available[1], however, sampling and interpretation errors may occur.[2]

Objective of this study was to: 1) determine different factors affecting misinterpretation of salivary gland tumors on fine needle aspiration cytology. 2) Determine overall diagnostic accuracy of fine needle aspiration cytology in salivary gland tumors using histopathology as gold standard.

Materials and Methods

A cross sectional study was conducted in the department of Pathology, from 15th October 2009 to 15th October 2010. Total sample size was 51 and sampling technique used was consecutive (non-probability) sampling. Inadequate and inflammatory samples were excluded from the study.

FNAC was performed using 21 gauge needle. The slides were prepared after aspiration and fixed in 10% alcohol. Slides were stained by H&E and use of special stains was done where necessary. Deeper sections of histopathology slides and cell blocks were obtained where necessary. All FNAC slides were evaluated taking into consideration the following points: Cellularity, cellular pattern, type of cell population, cellular atypia and background.

The data was analyzed using SPSS version 17. Sensitivity, specificity, positive predictive & negative predictive values and overall diagnostic accuracy was determined using 2x2 contingency table.

Results

Age distribution of the study participants ranged from 13 to 92 yrs with a mean of 41.39 ± 17.37. Twenty (39.2%) were males and thirty one (60.8%) were females with a male to female ratio of 1:1.55. Most of the patients (20) were in 21-40 years age group.

Out of total 51 tumors, 39 were located in parotid gland, followed by submandibular gland (7) and minor salivary glands (5). Surprisingly none of the tumor was found in sublingual gland, making it an unlikely site for salivary gland tumors.

Fine needle aspiration cytology smears were reported on the basis of arbitrary classes labeled as benign, most likely benign, most likely malignant and malignant. Inadequate cases were excluded from the study. The cases labeled as `most likely benign` were those in which although the case was labeled as benign but FNAC was not able to reach the exact tumor entity diagnosis and only a suggestion for the most likely entity diagnosis could be given in some of these cases & vice versa. Total number of such categories picked by FNAC are summarized in Table 1.

Histopathological diagnosis was made and correlated with cytological diagnosis. The final correlation between the two diagnosis was classed as `100% correlation`, `correlation with category only` and `lack of correlation, summarized in Table 2 .

Table 1: Arbitrary categories of Fine needle aspiration cytology used for interpretation of salivary gland lesions

FNAC category	Number of cases (%)
Benign	33 (64.7%)
Most likely benign	7 (13.7%)
Most likely malignant	5 (9.8%)
Malignant	6 (11.8%)
Total	51 (100%)

A strong correlation was found between the diagnosis made by Fine needle aspiration cytology and the final histopathological diagnosis, as shown in Table 3.

In our study the sensitivity of FNAC was found to be 84.6% with a specificity of 97.3%. The positive predictive value was 91.6% and negative predictive value 94.8%. The overall diagnostic accuracy was 98%.

Table 2: Correlation between FNAC and histological diagnosis (n= 51 patients)

Correlation	Frequency (%)
100% correlation	41 (80.4%)
Correlation with category only	7 (13.7%)
Lack of correlation	3 (5.9%)
TOTAL	51 (100%)

Table 3: Cytohistological correlation of study cases (n= 51 patients)

Fine needle aspiration cytology	Histopathology	No. of Patients
Malignant	Malignant	11
Benign	Benign	37
Benign	Malignant	2
Malignant	Benign	1
Total		51

Discussion

Now the role of FNAC in the diagnosis of salivary gland lesions is well established. The sensitivity and specificity of FNAC for salivary gland lesions is high with few pitfalls.[3-,6] Designating the specific type of benign or malignant neoplasm is, however, more problematic. Although FNAC may not give architectural details, but multiple passes give the benefit of cellular representation from the entire lesion.[7]

In our study 38 (74.3%) cases were benign tumors, amongst which pleomorphic adenoma topped the list, constituting about 35(68.6%) of the cases. This observation is similar to seen appreciated in national and international research studies. [8-10] The other benign tumors that were found included benign myoepithelioma, Warthin`s tumor & monomorphic adenoma.

FNAC was able to pick 37 of these benign cases correctly. Out of these thirty seven, 33 had 100% correlation in terms of the benign category and the specific tumor entity diagnosis, whereas in 4 of these, specific entity diagnosis was not reached. Likewise malignant cases overall in this study were thirteen (25.4%), 12 being Mucoepidermoid carcinoma and only one case of Adenoid cystic carcinoma. FNAC was able to pick malignancy in 11 of the cases. However specific entity diagnosis could be provided in only 8.

The features that were studied on cytology slides included cellularity, cell type, cellular pattern, nuclear atypia and background. And it was found that cellularity and some nuclear atypical features may be deceiving in case of salivary gland tumors cytology and should not be used as criterion for delineating benign from the malignant categories.

FNAC specimens from salivary glands are difficult to diagnose for a number of reasons, including problems in sampling as well as difficulty in histological classification. A major roadblock in the histologic classification of salivary gland neoplasms is that the majority of these arise from the same cell lines (epithelial and myoepithelial). Added to this fact is the ability of these cells to undergo a variety of metaplastic changes.

Overall gross discrepancy of benign/malignant category between cytology and histopathology diagnosis was found in three cases. In the first case (Figure 1), the FNAC smears revealed many plasmacytoid myopithelial cells of pleomorphic adenoma (Figure 1) These cells were misinterpreted as glandular cells and a diagnosis of ``most likely malignant- suggestive of mucoepidermoid carcinoma`` was generated. Most likely deceiving features were high cellularity, nuclear size variation and hyperchromasia. It must be remembered that it is not uncommon for pleomorphic adenomas to have hypercellular cytolo-

gy smears, and therefore hypercellularity should not be taken as a sign of malignancy. Similarly hyperchromasia is not uncommon in benign cells. Absence of typical myxoid or chondromyxoid stroma might have also contributed to shying away from diagnosis of pleomprphic adenoma. Mistake perhaps could have been avoided if notes were made of smooth nuclear contours, regular nuclear membranes (no dents and no bends) and absence of irregular chromatin distribution. Careful discrimination between predictive and non predictive atypical nuclear responsibility and keeping in view the different morphologies of myoepithelial cells may also have helped.

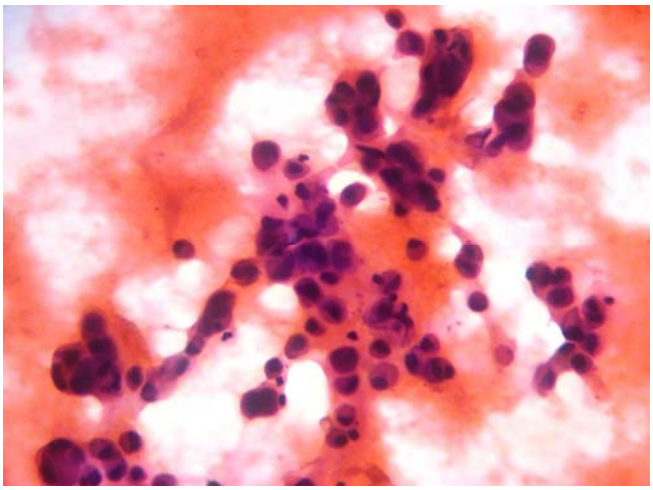

Figure 1: Plasmacytoid myoepithelial cells in aspirate of pleomorphic adenoma, misinterpreted as glandular cells of mucoepidermoid carcinoma. (H&E X 400)

In second case the FNAC smears were hypocellular composed of benign looking epithelial cells with abundant eosinophilic cytoplasm (Fig 2). On the basis of these features diagnosis of ``oncocytoma`` was made, which later on permanent sections proved to be mucoepidermoid carcinoma. In this case misdiagnosis was perhaps made on the basis of low cellularity and ignoring subtle but definite nuclear atypia. The nuclear membrane had subtle breaks and irregularity. The membranes were not sharp, but rather fuzzy due to mucin. Overlapping of the nuclei was also seems to be not considered. Moreover strict criterion for adequacy of aspirates, which is yet to be standardized, should have been observed before rendering a definitive diagnosis. Also for mucoepidermoid carcinoma the nuclear atypia may be quite subtle and one must look for predictive nuclear atypia versus non predictive ones! Nuclear membrane irregularities and irregular chromatin distribution are quite more predictive of malignancy than simple variation in size and hyperchromasia. Option of re-aspiration, list of clinical differential diagnosis and suggestion for tissue diagnosis in cytology report may also play an important role.

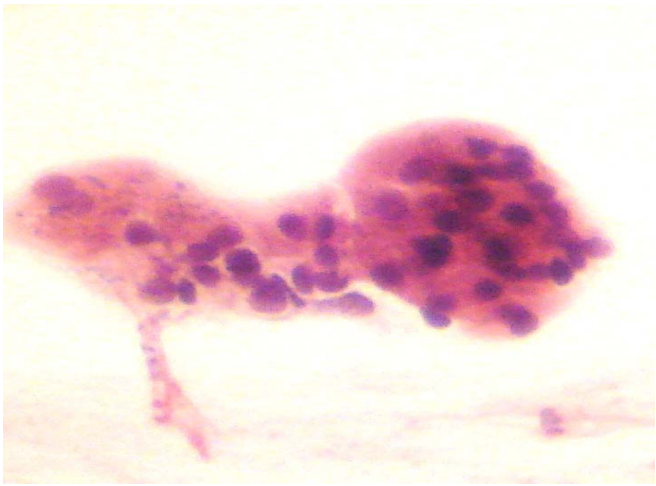

Figure 2: Glandular cells of mucoepidermoid carcinoma misinterpreted as benign oncocytes

Third case revealed moderately cellular cytology smears having basaloid type cells (Fig 3) with high N/C ratio, in a mucoid background. The case was diagnosed as ``suggestive of pleomorphic adenoma``. Later, tissue histopathology revealed mucoepidermoid carcinoma. In this case squamous component of mucoepidermoid carcinoma was missing and perhaps that distracted consideration of this tumor. Sometimes interme-

diate cell population of mucoepidermoid carcinoma closely resembles myoepithelial cells of pleomorphic adenoma, as was seen in the case discussed above. On the other hand, occasional squamous cells and mucous differentiation is common in pleomorphic adneomas. However chondroid differentiation is usually not seen in mucoepidermoid carcinoma and therefore should be a differentiating factor. It also seems that overlapping of the nuclei and soft chromatin texture was ignored! For mucoepidermoid carcinoma, detection of intracellular mucin is a key factor. Romaowsky stain should help in recognition of myxoid stroma, while some stains like PAS-D and mucicarmine would definitely help in detection of intracellular mucin.

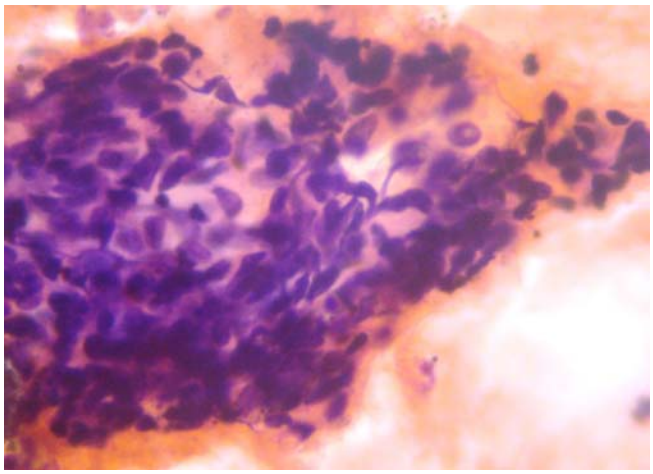

Figure 3: Intermediate cells of mucoepidermoid carcinoma misinterpreted as epithelial cells of Pleomorphic adenoma

Nevertheless in our study the overall sensitivity and specificity of FNAC for salivary gland lesions was found to be 84.6% and 97.3% respectively, with the diagnostic accuracy of 98%. These findings are compatible with those made by Shintanil et al, Jana et al & Cajulis et al.[11-,13]

Our study suggests that individual nuclear abnormalities must be carefully evaluated when examining the cytological smears; some features though more "attractive" may have little value in predicting malignancy e.g. hyperchromasia and nuclear size variation while some subtle features such as irregular membranes, nuclear membrane breaks, dented and fussy nuclear membranes and non uniform thickening and thinning of the membranes!

Conclusion

FNAC was found to be a useful diagnostic tool in the evaluation of salivary gland tumors because of its simplicity, cost effectiveness, excellent patient compliance and high diagnostic accuracy. The diagnostic pitfalls in salivary gland FNAC, may be avoided by determination of definite predictive atypical nuclear features and identifying non predictive, non relevant nuclear features. Repeat FNAC when required and careful interpretation of slides could avoid and minimize mistakes. Support from special stains may also be quite helpful.

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