ROLE OF PREOPERATIVE CYTOLOGY IN THE MANAGEMENT OF SALIVARY GLAND NEOPLASMS

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BACKGROUND: Salivary gland neoplasms comprise 3-10% of all head and neck neoplasms. Fine Needle Aspiration Cytology (FNAC) is being widely used to establish a diagnosis in the salivary gland masses. **AIM:** The aim of the study is to evaluate the diagnostic accuracy of FNAC in diagnosing salivary gland neoplasms at a tertiary referral center. **MATERIAL AND METHODS:** A retrospective study was conducted between July 2005 and June 2007 in the department of Pathology, Dayanand Medical College & Hospital, Ludhiana. All the patients with salivary gland neoplasms who underwent preoperative FNAC followed by surgical procedure and histo-pathological examination, were included. The FNAC diagnosis was compared with the final histological impression. Considering the histo-pathological diagnosis as gold standard, the diagnostic accuracy of FNAC was calculated. **RESULTS:** 47 cases were included in the study. On FNAC, 35 cases were diagnosed as benign, 10 cases as malignant and 2 cases were identified as neoplastic but suspicious for malignancy. Histopathology diagnosed 35 cases as benign and 12 cases as malignant. FNAC was unable to correctly identify one benign and one malignant neoplasm. FNAC showed a sensitivity of 91.66%, a specificity of 97.14%, a positive predictive value of 91.66%, a negative predictive value of 97.14% and a diagnostic accuracy of 95.74%. **CONCLUSION:** FNAC provides a rapid and accurate modality of diagnosis on OPD basis. It is an important and useful diagnostic tool in the preoperative assessment and management of patients with salivary gland neoplasms.

KEY WORDS: Fine Needle Aspiration Cytology (FNAC), Salivary gland neoplasms, Histopathology

INTRODUCTION: A mass in the salivary gland region often presents a diagnostic challenge with regards to its benign or malignant nature. Identifying malignancy is crucial, for this can have an impact on the type, extent and radicality of surgery. Most malignant neoplasms are not readily distinguishable from their benign counterparts on clinical criteria or radiological imaging alone.

The rapidity for diagnosis, low morbidity and a high diagnostic accuracy makes Fine Needle Aspiration Cytology (FNAC) a popular method for evaluating the salivary gland neoplasms before any surgical intervention. Moreover the superficial location of salivary glands makes them easily accessible for FNAC. The present study was carried out to determine the diagnostic accuracy of FNAC in diagnosing salivary gland neoplasms at a tertiary referral center. We compared the FNAC diagnosis with the final histological impression to determine its diagnostic accuracy.

MATERIAL AND METHODS: A retrospective study was conducted in the Pathology department between July 2005 and June 2007, at Dayanand Medical College and Hospital, Ludhiana. All the patients with salivary gland neoplasms, who underwent preoperative FNAC followed by surgical procedure and subsequent histopathological examination, were included in this study.

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Inclusion criteria: patients of all ages and either gender, having neoplastic lesion on initial FNAC followed by surgical procedure and histopathological examination.

Exclusion criteria: non-neoplastic lesions on FNAC, inconclusive smears on repeat FNAC, patients having neoplastic lesion on FNAC but whose surgical biopsy specimen was not received in the department.

All the aspirations had been performed by a cytopathologist using a 22 gauge needle and the smears were prepared and stained by Giemsa, Papanicolaou and Haematoxylin and Eosin. The results obtained on FNAC were divided into three categories: benign, malignant and suspicious. The cases where the cytology showed atypical cells without having overt features of malignancy were categorized as suspicious. However, for analytical purpose these were included in the malignant category. The sub-typing of the benign and malignant neoplasms was done according to cytological features observed. The FNAC diagnosis was compared with the final histopathological biopsy report. Considering the histopathological diagnosis as gold standard, the diagnostic accuracy of FNAC was determined. The various diagnostic values of the procedure were calculated using the standard formulas.¹

Sensitivity = true positive / true positive + false negative

Specificity = true negative / true negative + false positive

Positive Predictive Value (PPV) = true positive / (true positive + false positive) * 100

Negative Predictive value (NPV) = true negative / (true negative + false negative) * 100

Accuracy = (true positive + true negative) / (true positive + true negative + false positive + false negative) * 100

RESULTS: In this study, we correlated the cytological and histopathological diagnosis for 47 salivary gland neoplasms. The mean age of presentation for a neoplastic lesion was 42 ± 5 years. The benign neoplasms presented in the third decade while the malignant neoplasms predominated in the fourth decade. The overall incidence of neoplastic lesions was marginally higher in males, with a male to female ratio of 1.6:1. On FNAC, 35 cases were diagnosed as benign, 10 cases as malignant and 2 cases as suspicious for malignancy. Table I shows the number and percentage of various neoplasms identified on cytology.

	Diagnosis	Number	%
Benign	Pleomorphic adenoma	33	70.24%
	Warthin's tumor	2	4.25%
	Total	35	74.49%
Malignant	Mucoepidermoid carcinoma	6	12.76%
	Adenoid cystic carcinoma	3	6.38%
	Acinic cell carcinoma	1	2.12%
Suspicious	Suspicious for malignancy	2	4.25%
	Total	12	25.51%
	Grand Total	47	100 %

TABLE I: FNAC DIAGNOSIS OF SALIVARY GLAND NEOPLASMS

On histopathological examination 35 cases were diagnosed as benign and 12 cases as malignant. Two cases reported as suspicious for malignancy on FNAC were diagnosed to be

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mucoepidermoid carcinoma – low grade on subsequent histopathology. Table II shows the number and percentage of various neoplasms identified on histopathology.

	Diagnosis	Number	%
Benign	Pleomorphic adenoma	33	70.24%
	Warthin's tumor	2	4.25%
	Total	35	74.49%
Malignant	Mucoepidermoid carcinoma	8	17.02%
	Adenoid cystic carcinoma	2	4.25%
	Acinic cell carcinoma	1	2.12%
	Carcinoma ex- pleomorphic adenoma	1	2.12%
	Total	12	25.51%
	Grand Total	47	100%

TABLE II: HISTOPATHOLOGY DIAGNOSIS OF SALIVARY GLAND NEOPLASMS

FNAC was unable to correctly identify one benign and one malignant neoplasm. One case reported as pleomorphic adenoma on FNAC, turned out to be carcinoma ex-pleomorphic adenoma on biopsy i.e. it was a false negative. The other case diagnosed as adenoid cystic carcinoma on cytology proved to be pleomorphic adenoma on histopathology i.e. it was a false positive. Table III shows the cyto-histological concordance for the 47 cases.

Cytological diagnosis	Number	Subsequent Histological diagnosis	Number
Pleomorphic adenoma	33	Pleomorphic adenoma	32
		Carcinoma ex-pleomorphic adenoma	1
Warthin's tumor	2	Warthin's tumor	2
Mucoepidermoid carcinoma	6	Mucoepidermoid carcinoma	6
Adenoid cystic carcinoma	3	Adenoid cystic carcinoma	2
		Pleomorphic adenoma	1
Acinic cell carcinoma	1	Acinic cell carcinoma	1
Suspicious for malignancy	2	Mucoepidermoid carcinoma	2
Total	47		47

TABLE III: CYTO-HISTOLOGICAL CORRELATION FOR 47 SALIVARY GLAND NEOPLASMS

The diagnostic values of FNAC were calculated according to the distribution of cases shown in table IV. FNAC showed a sensitivity of 91.66%, a specificity of 97.14%, a positive predictive value of 91.66%, a negative predictive value of 97.14% and a diagnostic accuracy of 94.74%.

FNAC				
Histopathology		POSITIVE	NEGATIVE	Total
	POSITIVE	(True positive) 11	(False negative) 1	12
	NEGATIVE	(False positive) 1	(True negative) 34	35
	Total	12	35	47

TABLE IV: DISTRIBUTION OF CASES WITH RESPECT TO PRESENCE OF MALIGNANCY ON FNAC AND HISTOPATHOLOGY

DISCUSSION: Salivary gland neoplasms represent about 3- 10% of all the head and neck neoplasms.^{2,3}

The glands have a complex structure composed of secretory cells, acini and a duct system. Therefore the salivary gland neoplasms are rarely homogenous and may present in a variety of combinations and patterns. FNAC is well established as a diagnostic technique and neoplasms of the salivary glands are frequently evaluated by this technique. Majority of these neoplasms occur in the parotid gland (80-85%). The likelihood of a salivary gland neoplasm being malignant is inversely proportional to the size of the gland.⁴ In our study the parotid gland was the most common site for all the neoplasms (64%), followed by submandibular gland (29.8%) and minor salivary glands (6.2 %). The benign neoplasms (74.46%) predominated over the malignant neoplasms (21.27%). Similar findings were recorded in studies conducted by Boccato et al ⁵ and Jayaram and Dashini ⁶.

Pleomorphic adenoma was the commonest benign neoplasm (94.3% cases), as observed in other studies also.⁷⁻⁸ On cytology pleomorphic adenoma shows a biphasic pattern composed of epithelial / myoepithelial cells and fibro-myxochondroid stroma. The components may be arranged in a wide spectrum of microscopic appearances with a potential for errors in cytological interpretation.⁹ It can be a source of confusion with tumors such as basal cell adenoma, adenoid cystic carcinoma and mucoepidermoid carcinoma- low grade on cytology.¹⁰ In our series 32 cases were correctly identified on cytology. One case proved to be carcinoma ex-pleomorphic adenoma on subsequent histopathology. Thus the cyto-histological correlation for pleomorphic adenoma was 97%.

Carcinoma ex-pleomorphic adenoma is a highly aggressive tumor of no specific type.¹¹ It is a malignant transformation in a preexisting pleomorphic adenoma. This transformation occurs in 5 to 25% of untreated patients usually after 15-20 years and warning symptoms are present in many cases.¹² Thus a detailed clinical history should be taken which includes history of previous surgery for pleomorphic adenoma, untreated prolonged swelling, presence of symptoms like pain or sudden increase in size of the swelling. Pathologically, the co-existence of a pleomorphic adenoma and a carcinoma has to be identified to establish the diagnosis of carcinoma ex-pleomorphic adenoma. It is difficult to identify both the components on cytology, probably due to lack of representative sample. The cytological pattern of pleomorphic adenoma may also obscure the presence of a malignant tumor.¹³ According to Klijanienko et al, carcinoma ex- pleomorphic adenoma has the highest false negative rate (35.3%) out of all malignant salivary gland tumors.¹⁴ Collective analysis of other studies also revealed that one third of these cases are missed on cytology.^{11, 15} Thus diagnosing carcinoma ex-pleomorphic adenoma on cytology is a challenge for the pathologists. Careful clinicocytologic correlation and a representative, meticulous sampling and is mandatory. The procedure can be repeated from a different site in doubtful cases. Smears should be well prepared and interpreted with caution.

Warthin's tumor was the second most common benign tumor (5.7%). The three main components that characterize the cytological smears of Warthin's tumor are oncocytes, lymphocytes and a fluid background. We identified two cases of Warthin's tumor with a 100% cyto-histological concordance. Veder et al¹⁶ observed a 95.5% accuracy of FNAC in diagnosing Warthin's tumor.

Mucoepidermoid carcinoma was the predominant malignant neoplasm (67%). Sousa and Desa¹⁷ and Khandekar et al¹⁸ also observed mucoepidermoid carcinoma to be the commonest malignancy in the salivary glands. The cytological smears from a mucoepidermoid carcinoma show

presence of mucus producing cells and intermediate cells in a dirty mucoid background. The cells exhibit varying degree of atypia according to which the tumor is categorized as low, intermediate and high grade. Low-grade tumor accounts for about 80% of all mucoepidermoid carcinomas and is characterized by a cystic growth pattern.¹⁹ It is well recognized for its potential false-negative diagnostic pitfall. Aspiration of a low-grade tumor usually yields mucoid fluid and the smears are typically hypocellular having bland cytologic features.¹⁹ A low grade tumor has to be differentiated from Warthin's tumor, benign salivary gland cyst, branchial cleft cyst, sialolithiasis and pleomorphic adenoma.¹⁹ A careful search for mucus-producing goblet cells is imperative in these cases. In our study, 6 cases reported as mucoepidermoid carcinoma on cytology were confirmed on histology. Two cases reported as suspicious for malignancy on cytology were confirmed to be mucoepidermoid carcinoma – low grade on subsequent histopathology. Kljianienko et al²⁰ reviewed 50 cases of mucoepidermoid carcinoma and suggested that FNAC is an accurate technique for diagnosing high or intermediate grade tumors but unsatisfactory in detecting low grade tumors.

Adenoid cystic carcinoma was the second most common malignant tumor (17%). Aspirates from adenoid cystic carcinoma usually show two components: epithelial cells and acellular basement membrane material seen as homogeneous spherical structures. A major diagnostic problem is its differentiation from pleomorphic adenoma. The hyaline globules of basement membrane or a predominant epithelial pattern can be seen in pleomorphic adenoma as well.²¹⁻²⁴ We observed one false positive case, in which the smears were mainly composed of epithelial cells arranged in a cylindromatous pattern with no chondromyxoid material in the background. Thus the cyto-histological concordance for adenoid cystic carcinoma in our study was 67%. Viguer et al²⁵ listed cellular atypia (20.6%), cystic transformation (7%), and the presence of cylindromatous pattern (5%) as common variations in pleomorphic adenoma that are responsible for majority of misdiagnosis. The cytological distinction between these two tumors can be made if the smears are adequately cellular so that the distinctive relationship between the epithelial and extracellular matrix can be recognized.²¹ The tumor cells in pleomorphic adenoma have a plasmacytoid appearance with abundant cytoplasm as compared to the cells adenoid cystic carcinoma.²²

We identified one case of acinic cell carcinoma with a 100% cytohistological concordance. Cytological diagnosis depends on the identification of acinar cells and/or recognition of the acinar-glandular arrangement.¹⁹

The overall accuracy of FNAC in diagnosis of salivary gland neoplasms has been reported to be 87% to 100%.²⁶ A review of literature suggests that FNAC is the mainstay of diagnosis of salivary gland neoplasms, but it cannot always be relied upon in isolation.²⁷ Table V compares the diagnostic accuracy of FNAC in studies conducted by various authors.

Study	Sensitivity	Specificity	PPV	NPV	Accuracy
Fernandes & Pandit (2000) ²⁸	90.3%	80%	66.66%	89.65%	87.5%
Haberal et al (2003) ²⁹	80%	92.86%	57.14%	97.50%	91.49%
Postema RJ (2004) ³⁰	88%	99%	95%	97%	96%
Stramandinoli RT (2010) ³¹	68.2%	87.7%	68.2%	87.7%	82.3%
Vaidya et al (2011) ³²	81.8%	100%	100%	95.9%	96.6%
Jain et al (2013) ³³	92.8%	93.9%	81.2%	98.4%	93.75%
Present study (2013)	91.66%	97.14%	91.66%	97.14%	95.74%

TABLE V: DIAGNOSTIC ACCURACY OF FNAC IN STUDIES CONDUCTED BY VARIOUS AUTHORS

CONCLUSION: FNAC is an important and useful diagnostic tool in the preoperative assessment and management of patients with salivary gland neoplasms. Adequate sampling, high quality smear preparation and established diagnostic criteria can help to diagnose majority of common benign and malignant salivary gland neoplasms with a high level of accuracy. The findings of FNAC should be read in conjunction with clinical findings and in doubtful cases the true nature of the lesion should be confirmed by biopsy examination.

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