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Orginal Article

Diagnostic Pitfalls in Salivary Gland Cytopathology with Emphasis on Milan System of Reporting

Rini Bishnoi

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Abstract

Salivary gland lesions are relatively less common but challenging because of their marked variability in cytomorphology, clinical features and biologic behavior. Fine needle aspiration cytology (FNAC) is helpful in evaluating suspicious salivary glands lesions due to its their superficial location, easy accessibility, low cost, minimum morbidity, rapid turnaround time, high specificity and sensitivity.

Fine needle aspiration cytology in salivary gland lesions is intriguing for the cytopathologists due to their diverse morphology and overlapping cytological features which lead to the dilemma in diagnosis.

Materials and Methods: Present study was a retrospective analytical study in a tertiary care centre over a duration of 3 years. All the salivary gland FNAC cases were retrieved and divided into various categories as per Milan system for reporting salivary gland cytopathology. Histopathological correlation was done wherever possible.

Results: A total of 152 were included in the study. The percentage of cases in each category was: nondiagnostic 4.5%, nonneoplastic 51.9%, atypical lesions 0.76%, neoplastic category benign neoplasm 21.37%, salivary lesion of uncertain malignant potential 1.52%, suspicious category 2.29%, and malignant category 17.5%. The risk of malignancy for indivdual category was 6.25% (nonneoplastic), 100% (atypical), 3.3% (neoplastic), 0% (benign), 25% (salivary neoplasm of uncertain neoplastic potential), 100% (suspicious for malignancy), and 100% (malignant) categories.

Sensitivity, specificity, positive predictive value, and negative predictive value of FNAC with application of Milan system was 89.4%, 100%, 100%, and 95.74%, respectively.

Conclusion: Salivary gland FNAC when classified toa particular category by Milan system helps to overcome the pitfalls due to congruent features of various diagnostic categories yet provide risk stratification and stochastic information for the doubtful cases.

Keywords: Cytomorphology, Diagnostic accuracy, Fine needle aspiration cytology, Risk of malignancy, Salivary gland.

Author Affiliation: Senior Demonstrator, Government Medical College, Pali, Rajasthan 306401, India.

Corresponding Author: Rini Bishnoi, Senior Demonstrator, Government Medical College, Pali, Rajasthan 306401, India.

E-mail: rini.bishnoi1@gmail.com

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Introduction

Salivary gland neoplasms are heterogenous group of tumours of oral and maxillofacial pathology.

They comprise for 6% of all head and neck tumors.[1] Salivary gland tumours are not put through incisional and needle biopsy techniques due to possible risk of fistula formation and in case of neoplasms, of tumour implantation.[2]

Benign salivary gland neoplasms like pleomorphic adenoma have a tendency to recur after excision. However, there is no evidence of either of these complications occurring with FNA. FNAC is a useful OPD (out patient department) procedure for evaluating salivary glands lesions considering its high specificity, sensitivity, low cost, no morbidity and rapid results. 3 Histopathological examination of the excised salivary gland tissue remains the gold standard diagnostic investigation in the evaluation of salivary gland lesions. FNAC provides a definite diagnosis is a large percentage of cases pre operatively and avoids unnecessary surgery.

In case of highgrade malignancy or of recurrent cancer, a cytological diagnosis allows timely administration of palliative treatment. Due to the heterogeneity of these tumours, different classifications have emerged based on clinical or cytological criteria and to bring uniformity in reporting, experts in cytopathology proposed the Milan system in 2017, which is a risk based stratification system. The present study was conducted to evaluate the efficiency of FNAC in the diagnosis of salivary gland lesions and to discuss and review the morphology and diagnostic challenges in individual Milan categories.

Materials and Methods

This was a retrospective analytical study conducted over a period of 3 years, in a tertiary care center. Ethical committee clearance was obtained from institutional ethical committee. All the cases presenting to cytology department with salivary gland lesions for FNAC were included in the study except for noncooperative cases in which FNAC was not performed. Demographic data and radiologic findings were retrieved from the case records. FNAC was done by using 23 G needle. A maximum of two attempts were done. In the case of large swellings, aspiration was done from multiple areas to minimize sampling error.

The material was spread on slide and 50% were fixed in 90% ethanol for hematoxylin and eosin (H and E) stain and Papanicolaou stain and 50% were air dried for Giemsa stain. All the cases were divided into six categories as per the proposed MSRSGC. Surgical pathology specimens in cases that underwent surgical excision underwent routine processing and cytohistopathological correlation was done. Considering histopathology as gold standard, sensitivity, specificity, positive predictive value, negative predictive value was calculated.

The risk of malignancy (ROM) was calculated for each category by dividing the number of cancer cases by number of cases with surgical follow-up. Results All the cases presenting to the pathology department with salivary gland lesions for FNAC from January 2017 up to December 2019, that is 152 cases were included in the study. The age of the patients ranged between 10 years to 84 years in the present study, with maximum number of 32 cases seen in age range from 31-40 years. Males were more frequently affected with male to female ratio being 1.7:1.

Parotid was the most frequently involved gland (120/152, 75.9 %), followed by submandibular gland (32/152, 20.2%), palate (4/152, 2.53 %), and sublingual gland (2/152, 1.26%). All the 152 cases were added to their cyto-diagnostic categories of Milan Table 1. (Fig. 1 to 8) Table 2 shows cyto-histopathology correlation of FNAC. Surgical follow-up was obtained in 71.7 % (109/152) cases. Out of these 109 cases, concordance was noted in 91.7% (100/109) cases and the discordant diagnosis was rendered in 9.17% (10/109) cases.

Discussion

FNA of salivary gland is a minimally invasive, safe, low cost, and effective diagnostic technique.[4-6] It proves to be better than frozen sections because it reveals the nature of the lesion before the surgery and thus acts as a useful triage tool preventing patients with nonneoplastic lesions from undergoing surgery.[7-9] In the present study, most frequently encountered lesion in the nonneoplastic category was chronic sialadenitis followed by acute sialadenitis. Chronic sialadenitis might be confused with Warthin'stumour at cytology since both the lesions comprise of lymphoid background.

In the present study, the discordant case in this category was that of chronic sialadenitis which was finally confirmed as Warthin's tumor on histopathology. In the AUS category 05 cases were included which included aspirates containing only mucinous cystic fluid or lymphoid population. Histopathological correlation was not available in these cases. Benign neoplasms constituted to majority of all salivary gland lesions in the present study and pleomorphic adenoma was the commonest lesion which was in accordance with other studies.

Diagnostic accuracy of FNAC for benign lesions in the present study was high (100%), similar to that reported in other studies.[7-11] In the present study, pleomorphic adenoma represented 78.57% of all benign tumours. The cytohistologic correlation

was obtained in all cases, except in one case which showed pleomorphic adenoma with marked atypia and hence was placed in SNUMP category. One case of basal cell adenoma was diagnosed aspleomorphic adenoma as distinguishing pleomorphic adenoma from basal cell adenomamay occasionally be difficult. The FNAC slides were reviewed, it showed highly cellular smears with scant stromal elements and therefore were mistakenly diagnosed as PA. One case of Warthin'stumour was discordantly diagnosed as pleomorphic adenomaon FNAC smears.

Table 1: Distribution of cases in various cyto-diagnostic categories of Milan

Categories		No.	Percentage
Grade 1: Non diagnostic		12	7.89%
Grade 2 : On neoplastic		36	22.70%
Grade 3: Atypia of undetermined significance		5	3.16%
Grade 4: A Benign		62	34.20%
B Snump		6	10.50%
Grade 5: Suspicious for Malignancy		7	4.6
Grade 6	**Malignant**		
Mucoepidermoid Carcinoma	13	24	4.6
Adenoid cystic Carcinoma	6		54.1
Polymorphous low grade carcinoma	1		25
Carcinoma ex pleomorphic adenoma	2		4.1
Epithelial myoepithelial carcinoma	1		8.3
Carcinosarcoma	1		4.1
		152	

The reviewed FNAC slides showed an oncocytic change, which we suspected as epithelial cells with metaplastic change. The lymphoid component was not present in the FNAC slides probably due to a sampling error.(Fig. 1) The present study had 6 cases of salivary neoplasm of uncertain malignant potential (SUMP). One was of basal cell adenoma in which hypercellularity was a cause of concern, hence it was reported as atypical basaloid neoplasm which turned out to be basal cell adenoma at histopathology. (Fig. 2) Another case was reported as pleomorphic adenoma with atypia. However it turned out to be low grade mucoepidermoid carcinoma on histopathology. Several studies have reported the difficulty in distinguishing pleomorphic adenoma with squamous differentiation from mucoepidermoid carcinoma. In this case, mucin was confused with chondromyxoid stroma. Rossi et al.10 in their study, reported eight cases of pleomorphic adenoma at

Table 2: Cytohistological correlation in 109 cases with the associated risk of malignancy and diagnostic accuracy in each category.

Diagnostic category	FNAC	Histopathology		ROM
		Concordant	Discordant	
Inadequate	12	NA	NA	0%
Non -neoplastic	36	18	1	5.50%
Atypia of undetermined significance	5	NA	NA	NA
Benign	62	59	3	5.04%
Salivary neoplasm of Unknown malignant potential	6	1	5	83.30%
Suspicious for malignancy	7	6	1	100%
Malignancy	24	24	0	100%
Total	152	109		

FNAC, which were diagnosed as malignant on surgical follow up leading to a high false positive rate of 17.4%.

Two cases of SUMP were diagnosed as pleomorphic adenoma with atypical features on cytology which turned out to be Carcinoma ex pleomorphic adenoma on histopathology. The FNAC smears which were studied showed epithelial cell clusters which revealed a prominent nuclear enlargement and atypia with clusters of benign epithelial cells and myxoid stroma. (Fig. 3) Lewis et al reported that carcinoma ex pleomorphic adenoma arises from a pre-existing benign mixed tumor.[12] One case of SUMP category was diagnosed as basal cell adenoma with atypia but turned out to be adenoid cystic carcinoma on histopathology.

The cytology slides were reviewed and showed relatively cohesive clusters of basaloid cells with scant stroma.(Fig. 4) In the current study, the Risk of malignancy for SUMP category was 83.3 % which was significantly higher to that reported by Rohilla et al. A case of epithelial myoepithelial carcinoma was reported as pleomorphic adenoma with atypia in cytology, hence placed in SUMP category. Review of the slides showed cellular smears, comprising of epithelial cell clusters in a chondromyxoid background. Orell et al[13] states that the cytological diagnosis of epithelial myoepithelial carcinoma is challenging due to the difficulty in discerning the biphasic pattern and recognizing the myoepithelial cells as clear cells in smears. Histopathology revealed characteristic biphasic epithelial and myoepithelial components with mild nuclear pleomorphism. The suspicious category in the this study included seven cases, 6 of which showed a cytohistologic correlation.

The ROM was 100%, higher than that reported in previous literature, which was, 60%, 79% and 83% by Milan system, Rossi et al, Griffith et al[14] Amita et al[15] respectively. Three cases of low grade mucoepidermoid carcinoma depicted features of malignancy but due to lack of significant atypia these lesions were classifiedas suspicious rather than malignant category. (Fig. 5) One case of mucopidermoid carcinoma was misdiagnosed as poorly differentiated squamous cell carcinoma on FNAC due to absence of mucous and intermediate cells in the aspirate.

Another case in suspicious category was of acinic cell carcinoma which was misdiagnosed as cystic lesion on FNAC.(Fig. 6) Due to inadequate sampling from areas of predominant cystic areas lead to erroneous diagnosis of benign cystic lesion. The FNAC slides were reviewed, which showed plenty of foamy macrophages and degenerated epithelial cells against a myxoid background. Postema et al6 also observed similar findings when diagnosing cystic lesions, and concluded that cytologic diagnosis of "cysts" should be interpreted with caution. On histology cells of well differentiated acinic cell carcinoma resemble normal salivary acinar epithelial cells but do not form discrete round acini defined by a basement membrane.

A case of malignant epithelial neoplasm diagnosed on FNAC turned out to be carcinosarcoma on histopathology. The cytology smears showed numerous single malignant epithelial cells that had irregular nuclear membrane , increased NC ratio, and coarse chromatin pattern with prominent nucleoli. Histopathology revealed the malignant sarcomatous component comprised of moderately differentiated spindle cells and the malignant epithelial component was poorly differentiated squamous cell carcinoma. Kyon et al[16] and Sironi et al[17] reported that Carcinosarcomas (true malignant mixed tumors) of the salivary glands are rare biphasic tumors that exhibit both carcinomatous and sarcomatous elements. These tumors are thought to develop de novo in the salivary gland, and contain malignant stromal and epithelial elements. The carcinomatous component varies, in the form of of adenocarcinoma, squamous cell carcinoma, or undifferentiated carcinoma.

They may also show specific salivary carcinoma phenotypes, including salivary duct carcinoma or adenoid cystic carcinoma. Sarcomatous elements can also be variable, including chondrosarcoma, osteosarcoma, fibrosarcoma, and malignant fibrous histiocytoma. Most frequently, the sarcomatous component dominates, though the two elements can be found in an intermixed pattern. The overall prevalence of malignancy in present study was 15.7 %, well within the range observed by other authors (15–32%). In the present study, mucoepidermoid carcinoma was the most common malignancy accounting for 54% of all malignant lesions followed by adenoid cystic carcinoma (25%). Many studies report similar incidence rates.

The cytohistologic correlation for this category was 100%. ROM was 100% which was similar to that proposed by MSRSGC and reported by Rossi et al., Griffith et al. and Nagel et al.[18] The diagnostic efficacy of the Milan system in present study was similar to that reported in the literature. High efficacy of FNAC was obtained in the present study, when MSRSGC was applied which confirms

the usefulness of this scheme in reporting salivary gland lesions.

In the present clinical scenario risk based stratification is necessary to assist and alert the clinician about the subsequent management plan and the ROM.

References

1. Barnes L, Eveson JW , Reichart P. , Sidransky D : Pathology and genetics of head and neck tumors in World Health Organization Classification of Tumors, P. Kleihues and L. H. Sobin, Eds., IARC Press, Lyon, France 2005 ; 210
2. A. A. Choudhury, T. Sultana, B. H. Siddique, and A. S. A. Amin, "Diagnosis of parotid gland mass by the fine needle aspiration cytology (FNAC) and its histopathological correlation—2 years study in BSMMU, Dhaka," Bangabandhu Sheikh Mujib Medical University Journal, vol. 4, no. 2, pp. 65–69, 2011.
3. Frable MAS and FrableWJ :Fine-needle aspiration biopsy of salivary glands Laryngoscope,1991; 101: 245–249.
4. Mairembam P, Jay A, Beale T, et al. Salivary gland FNA cytology: role as a triage tool and an approach to pitfalls in cytomorphology. Cytopathology. 2016; 27: 91- 96.
5. Rajwanshi A, Gupta K, Gupta N, et al. Fine-needle aspiration cytology of salivary glands: diagnostic pitfalls—revisited. DiagnCytopathol. 2006; 34: 580-584.
6. Kim BY, Hyeon J, Ryu G, et al. Diagnostic accuracy of fine needle aspiration cytology for high-grade salivary gland tumors. Ann SurgOncol. 2013; 20: 2380- 2387.
7. Pastore A, Borin M, Malagutti N, et al. Preoperative assessment of salivary gland neoplasms with fine needle aspiration cytology and echography: a retrospective analysis of 357 cases. Int J ImmunopatholPharmacol. 2013; 26: 965- 971.
8. Postema RJ, van Velthuysen ML, van den Brekel MW, Balm AJ, Peterse JL. Accuracy of fine-needle aspiration cytology of salivary gland lesions in the Netherlands Cancer Institute. Head Neck. 2004; 26: 418- 424.
9. Stewart CJ, MacKenzie K, McGarry GW, Mowat A. Fine-needle aspiration cytology of salivary gland: a review of 341 cases. DiagnCytopathol. 2000; 22: 139-146.
10. Rossi ED, Wong LQ, Bizzarro T, Petrone G, Mule A, Fadda G, et al. The impact of FNAC in the management of salivary gland lesions: Institutional experiences leading to a risk based classification scheme. Cancer Cytopathol 2016;124:388 96.
11. Rohilla M, Singh P, Rajwanshi A, Gupta N, Srinivasan R, Dey P, et al. Three year cytohistological correlation of salivary gland FNA cytology at a tertiary center with the application of the Milan system for risk stratification. Cancer Cytopathol 2017;125:767 75
12. Lewis JE, Olsen KD, Sebo TJ. Carcinoma ex pleomorphic adenoma: pathological analysis of 73 cases. Hum Pathol. 2001;32:596–604
13. Orell S, Sterrett G. Orell, Orell and Sterrett's Fine Needle Aspiration Cytology. London: Elsevier Health Sciences UK; 2011.
14. Griffith CC, Pai RK, Schneider F, Duvvuri U, Ferris RL, Johnson JT, et al. Salivary gland tumor fine needle aspiration cytology: A proposal for a risk stratification classification. Am J ClinPathol 2015;143:839 53.
15. Amita K, Rakshitha HB, Singh A, Shankar SV. Evaluation of accuracy of milan system for reporting salivary gland cytology: Review of morphology and diagnostic challenges in each category. J Cytol 2020;37:18-25.
16. Kwon MY, Gu M. True malignant mixed tumor (carcinosarcoma) of parotid gland with unusual mesenchymal component. A case report and review of the literature. Arch Pathol Lab Med 2001; 125:812–5.
17. Sironi M, Isimbaldi G, Claren R, et al. Carcinosarcoma of the parotid gland: cytological, clinicopathological and immunohistochemical study of a case. Pathol Res Practice2000;196:511–517.
18. Nagel H, Laskawi R, Büter JJ, Schröder M, Chilla R, Droese M. Cytologic diagnosis of acinic cell carcinoma of salivary glands. DiagnCytopathol 1997;16:402 12