

Original Research Article**Pleomorphic Adenoma of Salivary Glands: Cytomorphological Variation and Diagnostic Pitfalls****Kanika Munish¹, Sneha Vishwasrao Wadhera², Rani Bansal³, Mamta Gupta⁴**

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Abstract

Objective: To study morphological spectrum of Pleomorphic Adenoma and its limitation on fine needle aspiration cytology.

Material and Methods: 40 cases of Pleomorphic Adenoma were evaluated for variations in cytological features. Morphological variables like pattern of epithelial cells, type and extent of mesenchymal matrix, metaplastic cells, nuclear chromatin were evaluated to avoid diagnostic pitfalls.

Result: Female preponderance was noted (62.5%) amongst the total of 40 cases with Male:Female ratio of 0.6. Mean age of 43.8 years was noted with parotid being the commonest site of presentation (77.5%). Most of the cases showed classical picture in form of abundant chondromyxoid stroma with clusters and enmeshed epithelial cells. However, few cases revealed deviation from classical cytological features which could create a diagnostic dilemma.

Conclusion: FNAC is a fairly accurate pre-operative procedure for diagnosis of Pleomorphic Adenoma. Pathologists need to be aware of cytological variations to avoid diagnostic pitfalls.

Keywords: Cytology; Histopathology; Spectrum; Chondromyxoid; Epithelial; Mesenchymal.

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Introduction

Pleomorphic adenoma (PA) is the most common salivary gland tumor and comprises about 79% of the major and 72% of the minor salivary gland tumors [1,2].

Morphologic diversity is the hallmark of this tumor; a variety of patterns showing varying combinations of epithelial and mesenchymal components are seen. FNAC can diagnose a great majority with high level of accuracy if established diagnostic criteria are strictly observed [3,4,5,6]. In most cases, a combination of bland epithelial cells and characteristic fragments of chondromyxoid stroma with spindle cells is diagnostic [3,7].

There is perhaps no other organ that presents as many diagnostic challenges and pitfalls as fine needle aspiration (FNA) of salivary glands. However, in some cases the variations of the morphologic features may cause diagnostic errors [5,8].

The chances of such happening are further enhanced due to limited and selective sampling in FNA. Therefore, it is imperative for the cytopathologist to be cognizant of the variations in the pattern of PA on FNAC smears [9,10]. This study lists the morphological variations encountered in cytologic smears of pleomorphic adenoma that may sometimes pose problem for the cytopathologist and may lead to an erroneous diagnosis.

Fine needle aspiration cytology (FNAC) is a widely accepted tool for the preoperative diagnosis of salivary gland lesions as they are readily accessible [7-11].

Material and Methods

A retrospective and prospective observational study was conducted in the Department of Pathology, Subharti Medical College, Meerut from July 2012 to May 2017. 40 cases diagnosed as Pleomorphic Adenoma on fine needle aspiration cytology were included.

The cytological features like arrangement of epithelial cells in sheets and clusters, amount of chondromyxoid stroma, metaplastic changes, presence of bare nuclei and myoepithelial cells were assessed. Histopathological correlation was done wherever available.

The aspiration was performed using 22 gauge needle attached to 10ml syringe. The air dried smears were stained with May Grunwald Giemsa (MGG) and the alcohol fixed smears were stained with Haematoxylin Eosin (H&E) and Papanicolaou (pap) stains.

Surgically resected specimens were subjected to gross examination after fixation in 10% formalin. Paraffin blocks were prepared and 5µm thick sections were cut and stained with Haematoxylin and Eosin stain.

Statistical analysis to calculate the frequency of cases according to age, sex, site and cytomorphological features was done. Non-concurrence on histopathology was analyzed.

Results

On cytopathology, cases were distributed over a wide range of 20-75yrs of age, mean age being 43.8years. Majority cases of Pleomorphic Adenoma i.e 47.5% belonged to age group between 20-39years. There were 15 males (37.5%), and 25 females (62.5%) with M:F ratio of 0.6. The lesions presented as a parotid swelling in 31/40 cases (77.5%) and submandibular gland in 9/40 cases (22.5%).

Histopathological correlation was available in 8 cases. Majority belonged to age group between 20-39years. There were 3/8 (37.5%) males and 5/8 (62.5%) females. The lesions presented predominantly as a Parotid lesion in 7/8 (87.5%) cases and as submandibular swelling in 1/8cases (12.5%).

Grossly, aspirates were hemorrhagic in most of the cases with few showing gelatinous consistency. Aspirates were mostly cellular and showed epithelial cells in sheets and clusters on FNA smears in 72.5% (29/40) of the cases of PA. 95% (38/40) of the cases showed bland nuclear chromatin and 92.5% (37/40) presence of bare nuclei in the background. 52.5% (21/40) cases showed plasmacytoid cells as well. 27% (12/40) cases showed epithelial cells entrapped in chondromyxoid stroma (CMS). 5% (2/40) cases showed presence of cystic, oncocytic changes and presence of giant cells/ macrophages/ hyaline globules respectively. Few smears showed squamous cells. Nucleus showed bland granular chromatin and inconspicuous nucleoli. These cells had well defined cell borders and moderate amount of cytoplasm. The fibrillary myxoid background substance was pinkish on Papanicolaou stain and bright magenta on MGG stain (Table 1) (Figure 1,2).

Table 1: Morphological variation seen on FNAC in PA cases N=40

Sl. No.	Cytologic variation	No of cases	% of cases
1	Cellularity	35	
	Richly cellular	35	87.5
	Moderately cellular	3	7.5
	Sparsely cellular	2	5
2	Epithelial cells		
	Sheets and clusters entrapped in CMS	29 12	72.5 30
3	Metaplastic changes		
	Oncocytic change	2	5
	Squamous cells	2	5
4	Nuclear chromatin		
	Bland	38	95
	Hyperchromatic	1	2.5
	Nuclear inclusion	1	2.5
5	Bare nuclei	37	92.5
6	Cystic change	2	5
7	Spindle cells	6	15
8.	Plasmacytoid cells	21	52.5
9.	Other change (giant cells, macrophages ,hyaline globules	2	5

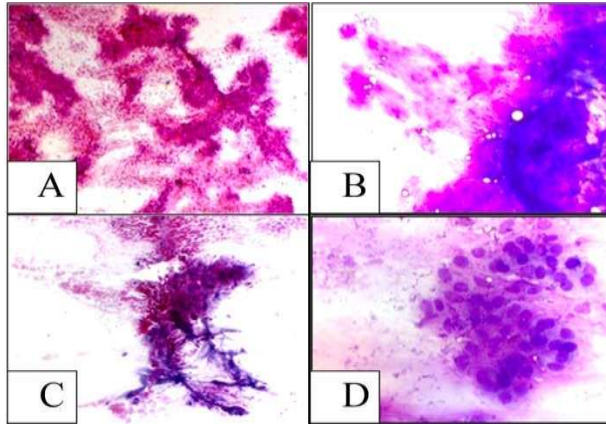


Fig. 1: Pleomorphic Adenoma - Cytomorphology Epithelial cells in clusters, sheets and trabecular pattern surrounded by chondromyxoid background. (A. H&E X,100; B. MGG X,400; Pap X, 100) D: Acinar cells in mucoid background (MGG,X400)

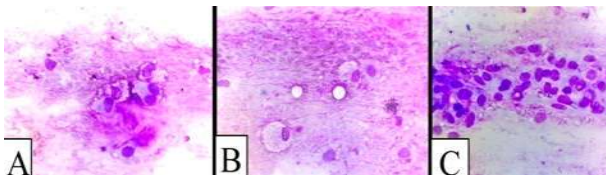


Fig. 2: A. Plasmacytoid cells B. Foamy macrophages C. Nuclear inclusions (MGG,X 400)

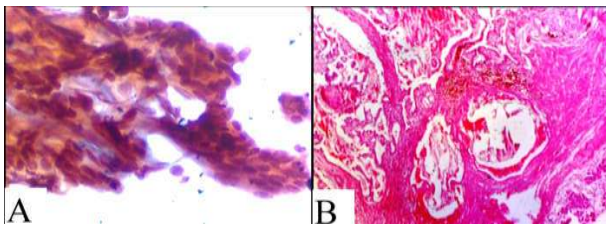


Fig. 3: Non concurrence-cytopathology was reported as (A) Cellular Pleomorphic adenoma (Pap X, 400) while (B) histopathology showed features of Intraductal papilloma(H&E X,100)

In 8 cases correlation between FNAC and histopathology was available. One case reported as Cellular Pleomorphic Adenoma on cytology was diagnosed as Intraductal Papilloma (IDP) on histopathology (Figure 3). Reason for non-concurrance could be rarity of IDP amongst salivary gland tumors and presence of overlapping cytomorphological features of these two entities.

Discussion

Salivary gland lesions account for 2% of all neoplasms. PA are the most common salivary gland tumors constituting 60-70% [1,2,12]. Peak incidence of PA is seen in patients between 30-50 years of age with female preponderance similar to findings noted in present study.

FNAC is a widely accepted, safe and effective technique for pre-operative diagnosis of salivary gland lesions. The

reliability of FNAC in diagnosing PA has been reported as 89.5-96.2% [1,4,5,13,14].

PA is well known for a variety of architectural and cytomorphological patterns. These morphological variations do not often pose a difficulty in histological diagnosis as whole tumour is available for interpretation [8,14,15]. In FNAC only a portion of tumor is sampled, and hence PA can present as a diagnostic dilemma and can be mistaken for several other types of tumors [14,15,16]. It is necessary to adequately re-aspirate or to re-perform FNAC at a later date for further improvement of diagnostic accuracy [15,16].

The cytological diagnosis of PA is relatively simple consisting of a characteristic combination of bland epithelial cells in regular aggregates and metachromatic fragments of fibrillary chondromyxoid stroma with spindle cells [1,3,12]. However, PA is also well known for a variety of architectural and cytomorphological patterns, all of which pose diagnostic problems [14,15,17]. Not only does the proportion between epithelium and chondromyxoid stroma vary considerably, but there are also variations in the appearance of the epithelial cells and the stromal component [7,11,13].

Smears from PA with metaplastic squamous cells, mucoid or mucinous material, cystic changes with sparsely cellular aspirates may be misinterpreted as Mucoepidermoid Carcinoma. PA should be suspected when epithelial & stromal components are identified within mucinous material [7,8,18].

Hyaline globules of basement membrane like material can be found in PA and Adenoid cystic carcinoma, therefore it is not a definite differentiating morphologic feature. In such case, chromatin pattern of tumor cell nuclei must be closely examined. The nucleus of PA cells shows bland chromatin with uniform granularity whereas nuclei of AdCC cells are hyperchromatic, the chromatin is coarse and some may show prominent nucleoli. In addition, presence of stromal fragments with spindle cells favors PA [7,8].

Predominance of epithelial elements may lead to a wrong diagnosis of Basal Cell Adenoma (BCA). Presence of atypical cells having irregular or bizarre nuclei can be degenerative in nature as well. Malignancy should be suspected only when atypical cells are abundant, showing abnormal chromatin and or accompanied by necrosis [1,7,8].

If the myxoid material is abundant & epithelial cells sparse then it can be mistaken for a retention cyst. In contrast to a PA with bizarre cells, the malignant cells of a Carcinoma ex pleomorphic Adenoma (CXPA) are more numerous and are present as clusters as well as dispersed cells with classical features of malignancy, including high N/C ratio, nuclear membrane irregularity and coarse

chromatin pattern. Caution should be exercised while interpreting anisonucleosis and hyperchromasia in PA aspirates as Carcinoma ex pleomorphic adenoma [1,7,8,15].

Conclusion

Present study concludes that the diagnostic accuracy of preoperative FNAC for pleomorphic adenoma of salivary gland is high, it is a safe, easy-to-perform and clinically very useful diagnostic procedure. When performed properly, FNA cytology can provide useful information permitting the clinician to appropriately manage the patient. Extreme care and recognition of limitations of cytology are essential in evaluation of salivary gland lesions. In few cases adequate re-aspiration or re-performing the FNAC at a later date could lead to better diagnostic accuracy. Familiarity with the cytologic features and morphological variations is necessary to avoid misinterpretation. If uncertain, the cytopathologist should leave the diagnosis open with a few suggested differential diagnoses. There still remain few cases that may be inaccurately diagnosed on cytology due to overlapping features and in such cases histopathology is the only modality for final diagnosis.

References

1. Handa U, Dhingra N, Chopra R, Mohan H. Pleomorphic Adenoma: cytologic variation and potential diagnostic pitfalls. *Diagn. Cytopathol.* 2009;37:11-15.
2. Y Kumar S, Permi H, Paramesha, Kishan, HL Prasad, S Teerthanath, S Jayaprakash et al; Role of fine needle aspiration cytology in salivary gland tumors with histopathological correlation. *Journal of Clinical and Diagnostic Research* 2011 ;5: 1375-80.
3. Orell SR, Klinjanienko J. *Head and neck; Salivary glands.* Orell SR, Strerrett GF. *Fine needle aspiration cytology* 5th ed. Edinburg: Elsevier, 2012.p.38-76.
4. Koirala S, Sayami G, Pant AD. Correlation of FNAC and histopathology in diagnosis of salivary gland lesions. *Journal of Pathology of Nepal.* 2014;4(8):654-7.
5. Panchal U, Shah I, Goswami H. A cytological and histological comparative study of salivary gland lesions at tertiary health care centre *International Journal of Biomedical and Advance Research* 2015; 6(06): 470-74.
6. Lopes ML, Barroso KM, Henriques AC, Dos Santos JN, Martins MD, de Souza LB. Pleomorphic adenomas of the salivary glands: retrospective multicentric study of 130 cases with emphasis on histopathological features *Eur Arch Otorhinolaryngol* 2017;274(1):543-51.
7. Vikram Y, Hiremath S, Gurubasavaraj H. Pitfalls in the cytological diagnosis of Pleomorphic adenoma. In *J App Research.* 2015;5(4):529-31.
8. Verma K, Kusum K: Role of FNAC in diagnosis of pleomorphic adenoma. *Cytopathology* 2002;13:121-27.
9. Palza CM, Jiménez AC, Serrano RT, Mata RG, Molina PC, Muñoz IG. Cyto-histological correlation in parotid gland tumors. *Acta Otorrinolaringologica.* 2010;61(3):184-8.
10. Fonseca FP, de Vasconcelos Carvalho M, de Almeida OP, Rangel AL, Takizawa MC, Bueno AG et al. Clinicopathologic analysis of 493 cases of salivary gland tumors in a Southern Brazilian population. *Oral surgery, oral medicine, oral pathology and oral radiology.* 2012;114(2):230-9.
11. Thangam R, Kotasthane VD, Kotasthane DS, Koteeswaran G, Kannan NS. Cytological and Histomorphological Correlation of Salivary Gland Lesions-An Experience at Rural Tertiary Healthcare Hospital. *Annals of Pathology and Laboratory Medicine.* 2017;4(2):A219-23.
12. Ramraje S, Sisodia S, Goel A. Fine Needle Aspiration Cytology of Pleomorphic Adenoma: Cytologic variations and Diagnostic pitfalls; A report of two cases ; *NJIRM* 2014;5(3):133-37.
13. Bobati SS, Patil BV, Dombale VD. Histopathological study of salivary gland tumors. *Journal of Oral and Maxillofacial Pathology/ JOMFP.* 2017;21(1):46-50.
14. Khetrpal S, Jetley S, Hassan MJ, Jairajpuri Z. Cystic Change in Pleomorphic Adenoma: A Rare Finding and a Diagnostic Dilemma. *Journal of Clinical and Diagnostic Research/ JCDR.* 2015;9(11):ED07-ED08.
15. Gahine R, Sudarshan V, Hussain N, Krishnani C. Pleomorphic adenoma: A diagnostic pitfall in the diagnosis of salivary gland lesions on FNAC: Case reports with review of the literature. *CytoJournal* 2010;7:17.
16. Sushma HM, Shashidhar MR, Meghashree V, et al. Fine needle aspiration of salivary gland lesions- diagnostic pitfalls. *J. Evolution Med. Dent. Sci.* 2017;6(8):600-04.
17. Viguer JM, Jimenez-Heffernan JA, Vicandi B, Lopez-Ferrer P, Navarro M. Cytologic diagnostic accuracy in pleomorphic adenoma of the salivary glands during 2 periods. A comparative analysis. *Acta Cytol* 2007;51:16-20.
18. R Sushma, S Shantilal, G Aprajita. Fine needle aspiration cytology of pleomorphic adenoma: cytologic variation and diagnostic pitfalls: a report of two cases. *NJIRM* 2014; 5(3):133-37.