RESEARCH PAPER | Medical Science | Volume : 5 | Issue : 4 | April 2015 | ISSN - 2249-555X

Pitfalls in the Cytological Diagnosis of Pleomorphic Adenoma

KEYWORDS: pleomorphic adenoma; salivary gland; fine needle aspiration cytology

Dr. Vikram. Y	Dr. H. Gurubasavaraj	Dr. S. S. Hiremath
Post graduate, Department of Pathology, JJM Medical College,Davangere, Karnataka.	Professor, Department of Pathology, JJM Medical College, Davangere, Karnataka	Professor and Head, Department of Pathology, JJM Medical College, Davangere, Karnataka

ABSTRACT *INTRODUCTION: Salivary glands form the commonest target for fine needle aspiration (FNA). Morphological diversity is the hallmark of pleomorphic adenoma (PA) posing diagnostic difficulties on cytology.*

OBJECTIVE: To list the cytomorphological features of pleomorphic adenoma and to discuss the pitfalls in cytological diagnosis of pleomorphic adenoma.

METHODOLOGY: Prospective study conducted at JJM Medical College, Davangere from July 2012 to June 2014 on 36 salivary gland FNA cases with either cytological and/or histological diagnosis of PA. In 14 cases, histopathological study was made and cytohistopathological correlation was done.

RESULTS: 21 were females and age ranges from 10–88 years (mean 35.97). Majority were located in parotid gland (63.9%). Of 14 cases of available histology, 12 cases correlated well with cytology. Diagnostic accuracy of FNAC in diagnosis of PA was 85.7% with 100% Positive predictive value (PPV).

CONCLUSION: Awareness of cytological variations of pleomorphic adenoma on FNAC helps in avoiding pitfalls leading to accurate diagnosis.

INTRODUCTION:

Fine needle aspiration cytology (FNAC) is a widely accepted tool for the preoperative diagnosis of salivary gland lesions as they are readily accessible. There is perhaps no other organ that presents as many diagnostic challenges and pitfalls as fine needle aspiration (FNA) of salivary glands.[1] Pleomorphic adenoma (PA) is the most common salivary gland tumour. Morphological diversity is the hallmark of PA. A variety of patterns showing varying combinations of epithelial and mesenchymal components are seen on cytology.[2] Problems arise if one component predominates leading to incorrect labeling of the entity.

MATERIALS AND METHODS:

A prospective study of 36 cases with either cytological or histological diagnosis of pleomorphic adenoma. Histology was available in 14 cases with 2 cases having histological diagnosis of pleomorphic adenoma with a different cytological diagnosis were studied during a period of two years from July 2012 to june 2014 in JJM Medical College, Davangere, Karnataka. The aspiration was performed using 22/23 guage needle attached to a 5ml syringe. The air dried smears were stained with May-Grunwald Giemsa (MGG), alcohol fixed smears were stained with hematoxylin and eosin (H&E) and Papanicolaou stains. Surgically resected specimens were subjected to gross examination and fixed in 10% formalin for 24 to 48 hours. After fixation, representative areas were selected for paraffin embedding. Paraffin blocks were prepared and sections of 5-7 µm thick were cut and stained with Hematoxylin and Eosin stain. The cytological and histopathological features were assessed separately and the results of both were correlated to evaluate the accuracy of the procedure using Galen and Gambino method.

RESULTS:

The cases were distributed over a wide age range of 10–88 years, mean age being 35.97 years **(Table 1)**. There were 15 male patients (41.67%) and 21 female patients (58.33%) with M:F ratio of 0.71. The lesions were located in the parotid gland in 23 cases (63.9%), submandibular gland in 7 cases (19.44%) and minor salivary glands (oral cavity) in 6 cases (16.66%).

Table 1: Age and sex distribution of cases

Sl. No		Males	Females	Total
1	0-10	1	0	1
2	11-20	1	4	5
3	21-30	2	9	11
4	31-40	6	3	9
5	41-50	1	3	4
6	51-60	2	0	2
7	61-70	2	1	3
8	71-80	0	0	0
9	81-90	0	1	1
	Total	15	21	36

Grossly, aspirates were hemorrhagic in 24, grey white in seven, grey white to gelatinous in one, blood tinged grey white in two, gelatinous in one and oily in one. Aspirates were cellular in 32 and sparsely cellular in four. Aspirates in 33 cases showed epithelial cells in sheets and groups, mesenchymal cells in 31 aspirates and fibrillar ymyxoid background in 33 aspirates. The epithelial cells were small, uniform and had round to oval eccentric nuclei. Nuclei had bland granular chromatin and nucleoli were inconspicuous. These cells had moderate amount of densely stained cytoplasm and well defined cell borders. Mesenchymal cells seen were round to spindle shaped with elongated nuclei. The fibrillary myxoid background substance was pinkish grey in colour with Papanicolaou stain and bright magenta with giemsa stain (Fig 1). Bare nuclei were observed in seven cases, plasmacytoid epithelial cells were noted in four cases, stromal fragments were seen in one aspirate. Background also showed RBCs in 20 aspirates, neutrophils in nine aspirates and mucinous material was seen in one

Volume : 5 | Issue : 4 | April 2015 | ISSN - 2249-555X

aspirate (Table 2).

Table 2: Cytological features

Sl. No	Cytologic features	No of aspirates (36)	Percentage
1	Cellular aspirates	32	88.88
2	Sparse cellularity	4	11.12
3	Epithelial cells in sheets and groups	33	91.66
4	Plasmacytoid epithelial cells	4	11.12
5	Mesenchymal cells	31	86.11
6	Stromal fragments	1	2.77
7	Fibrillary myxoid background	33	91.66
8	Mucoid background	1	2.77
9	Bare nuclei	7	19.44
10	Neutrophils	9	25
11	Red blood cells	20	55.55

Of 14 cases with available histology, agreement of FNAC diagnoses with histological diagnoses was present in 12 cases. In two histologically diagnosed cases of PA and PA with mucus change, cytological diagnosis was myoepithelioma and mucoepidermoid carcinoma respectively **(Table 3)**. Thus, the diagnostic accuracy of FNAC in diagnosis of PA was 85.7% with a Positive predictive value (PPV) of 100%.

Table 3: Cases of PA with variable diagnosis on cytology

Histological diagnosis	Cytological diagnosis	No. of cases
PA	Myoepithelioma	1
PA	Mucoepidermoid carcinoma	1

DISCUSSION:

Fine needle aspiration cytology is widely accepted as a safe and effective technique for preoperative diagnosis of salivary gland lesions.[2] Salivary gland tumours represents about 3% of all neoplasms.[3] Pleomorphic adenomas (PA) are the most common salivary gland tumours constituting 60 to 70% of all parotid tumours, approximately 50% of tumours in the submandibular glands and 40% to 70% of all tumours of the minor salivary glands.[4] PA peaks in incidence in patients between 30 and 50 years of age with a female preponderance, an observation similar to in our study.[5,6,7]

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. However, PA is also well known for a variety of architectural and cytomorphological patterns, all of which pose diagnostic problems. Plasmacytoid appearance of individual tumour cells with abundant cytoplasm is a reliable finding in PA, for differentiating it from adenoid cystic carcinoma (AdCC) on FNA smears, which was observed in few of our smears.[8]

Cystic degeneration and mucin production are common in PA. Low grade mucoepidermoid carcinoma (MEC), Warthin's tumour, acinic cell carcinoma, and benign non neoplastic lesions of salivary glands show cystic change with sparsely cellular aspirates dominated by abundant mucinous material.[2] PA should be suspected when epithelial and stromal elements are identified within mucinous material. Similarly feature led to a misinterpretation of a case of PA as MEC in our study.

Cylindromatous presentation of PA can cause diagnostic dilemma. Such cases may resemble AdCC cytologically **(Fig 2)**. Furthermore, hyaline globules of stromal material can be seen in both the tumors, therefore it is not a fool proof differential morphological feature. In such cases the chromatin pattern of the tumor cell nuclei must be closely examined. The nuclei of PA cells show bland chromatin with uniform granularity whereas nuclei of AdCC cells are hyperchromatic, the chromatin is coarse and some may show prominent nucleoli. In addition, lack of single cell dispersion and presence of stromal fragments with spindled cells favor PA.[2] Similarly cylindromatous presentation was seen in few of our cases.

The predominance of epithelial elements may lead to an erroneous diagnosis of basal cell adenoma (BCA).[9] Sometimes, the presence of atypical cells having irregular often bizarre nuclei have been noted. These elements are probably degenerative in nature. Malignancy should only be considered when the atypical cells are abundant, showing abnormal chromatin pattern and are accompanied by necrosis.[9]

Aspirates from chronic sialadenitis with focal nodules of chronic inflammation consist of epithelial cell aggregates associated with fibrillar fibrous stroma could be mistaken for PA, but the fragments of ductal epithelium with or without squamous metaplasia are cohesive and the stroma is not chondro-myxoid.[9]

If mucomyxomatous component is very abundant it may overwhelm the few epithelial cells present and the lesion may be mistaken for a retention cyst.[6] Aspirates from intraparotid schwannoma can also include tissue fragments resembling the fibromyxoidstroma of PA, but the cellular component is clearly different from the myoepithelial cells of PA.[9] Nerve sheath tumors should always be considered in the differential diagnosis of PA and a diligent search for epithelial elements is recommended.[10]

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 irregularities and coarse chromatin pattern. In fact, a cytologic diagnosis of CXPA is difficult to achieve. One-third of the CXPAs are missed on FNA, with only two thirds diagnosed or suspected.[1,11]

Cytologically, Myoepitheliomas (ME) may simulate cellular PAs, plasmacytomas, spindle cell soft tissue tumours, carcinomas and malignant melanoma.[6,12,13,14] This pitfall was noted in our study, wherein a case of subsequent biopsy confirmed PA had been diagnosed as myoepithelioma on cytology **(Fig 3)**.

Diagnostic accuracy reported in most series range between 80%- 95% which is similar in our study.[15,16,17]

Volume : 5 | Issue : 4 | April 2015 | ISSN - 2249-555X

CONCLUSION:

Awareness of cytological variations of pleomorphic adenoma on FNAC helps in avoiding pitfalls leading to accurate diagnosis.

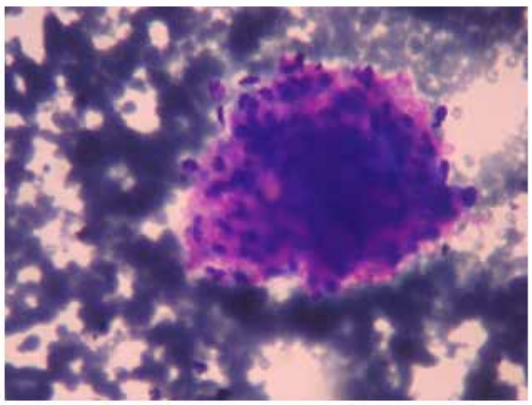

Fig 1: Cytology of PA with fibrillary chondromyxoid matrix (MGG, X400).

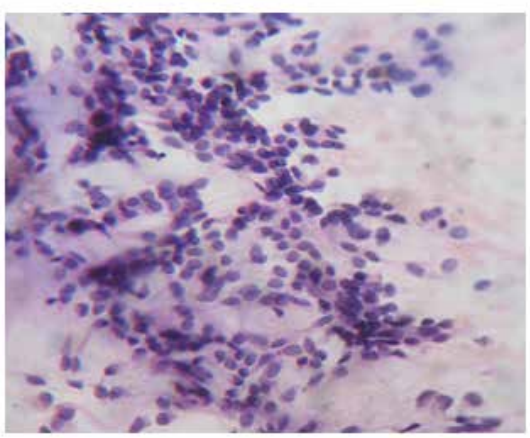

Fig 2: Cylindromatous form of PA (H&E X400).

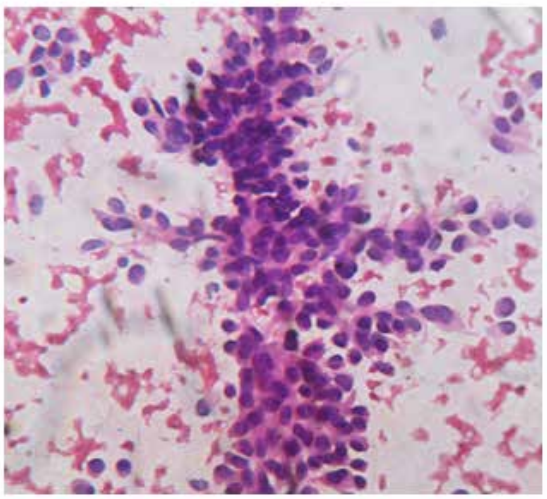

Fig 3: PA mimicking myoepithelioma (H&E X400).

REFERENCE

1. Boerner SL. Patterns and pitfalls in fine needle aspiration of salivary gland. Curr Diagn Pathol 2003;9:339-54. | 2. Handa U, Dhingra N, Chopra R, Mohan H. Pleomorphic adenoma: Cytologic variations and potential diagnostic pitfalls. Diagn Cytopathol 2009;37:11-5. | 3. Rehman HU, Khan MS, Whid FI, Ahmad WI. A profile of parotid gland tumours from a tertiary care hospital in Peshawar. J Postgraduate Medical Institute 2011;02:158-162 | 4. Elhosseiny A. Salivary glands. In: Koss LG, Melamed MR, editors. Koss' diagnostic cytology and its histologic basis. 5th ed. Philadelphia: LWW;2006.p.1229-61. | 5. Gnepp DR, El-Mofty SK. Salivary glands. In: Damjanov I, Linder J, editors. Anderson's Pathology. 10th ed. Missauri: Mosby;1996.p.1616-46. | 6. Kocjan G, Shah KA. Salivary glands. In: Gray W, Kocjan G, editors. Diagnostic Cytopathology. 3rd ed. Edinburgh: Churchill Livingstone;2010.p.231-252. | 7. Kumar SY, Permi HS, Paramesha, Kishore, Prasad HL, Teerthanath S et al. Role of fine needle aspiration cytology in salivary gland tumours in correlation with their histopathology. J Clin Diagn Res 2011;5:1375-80. | 8. Das DK, Anim JT. Pleomorphic adenoma of salivary gland: to what extent does fine needle aspiration cytology reflect histopathological features?. Cytopathology 2005;16:65-70 | 9. Orell SR, Klijanienko J. Head and neck; salivary glands. In: Orell SR, Sterrett GF, editors. Fine needle aspiration cytology. 5th ed. Edinburgh: Churchill Livingstone;2012.p.38-76. | 10. 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 | 11. Klijanienko J, El-NaggarA K, Vielh P. Fine-needle sampling findings in 26 carcinoma ex pleomorphic adenomas: diagnostic pitfalls and clinical considerations. Diagn Cytopathol 1999;21:163-6. | 12. Tabbara SO. Salivary glands. In: Sidawy MK, Ali SZ, editors. Fine needle aspiration cytology, a volume in the series foundations in diagnostic pathology. 1st ed. Edinburgh: Elsevier;2007.p.1-36. | 13. Khademi B, Kazemi T, Bayat A, Bahranifard H, Danesh Y, Mohammadianpanah M. Salivary gland myoepithelial neoplasms. Actacytol 2010;54:1111-7. | 14. Kumar PV, Sobhani SA, Monabati A, Hashemi SB, Eghtadari F, Hamidi SA. Myoepithelioma of the salivary glands: fine needle aspiration biopsy findings. Acta Cytol 2004;48(3):302-8. | 15. Verma K, Kapila K. Role of fine needle aspiration cytology in diagnosis of pleomorphic adenomas. Cytopathology 2002;13:121-127 | 16. Stewart CJ, MacKenzie K, McGarry GW, Mowat A. Fine needle aspiration cytology of salivary gland, a review of 341 cases. Diagn Cytopathol 2000;22:139-46 | 17. Kapadia SB, Dusenbery D, Dekker A. Fine needle aspiration of pleomorphic adenoma and adenoid cystic carcinoma of salivary gland origin. Acta Cytol 1997;41:487-92