CYTOLICAL VARIATIONS AND DIAGNOSTIC CHALLENGES IN PLEOMORPHIC ADENOMAS

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ABSTRACT

BACKGROUND

Pleomorphic Adenomas are the most common benign neoplasms of the salivary glands and are a diverse group of lesions. Most common site being major salivary glands, of which parotid gland constitutes 64% - 80%. Fine Needle Aspiration Cytology (FNAC) of palpable salivary lesions is accepted as a useful preoperative diagnostic tool worldwide. Cytomorphological and histological diversity encountered in pleomorphic adenomas causes enormous diagnostic difficulty.

Objective- The present study was done to evaluate the cytological features of pleomorphic adenomas with an emphasis on differential diagnoses, challenges encountered during the diagnosis and addressing potential pitfalls.

MATERIALS AND METHODS

This descriptive study was undertaken at the Upgraded Department of Pathology, Osmania General Hospital over a period of one (1) year and nine (9) months, that is from January 2016 to September 2017. Our study included 64 cases of pleomorphic adenoma diagnosed on fine needle aspiration cytology. Rapid Haematoxylin and eosin and Papanicolaou stains were used. Cytological smears were reviewed for nature of aspirate, patterns of epithelial component, type of mesenchymal matrix and degenerative changes like metaplastic and cystic changes. Radiological and histopathological correlation was available in all the cases.

RESULTS

A total number of 116 salivary gland lesions were aspirated, of which Pleomorphic adenomas were 64 (55.1%), chronic sialadenitis were 18 (15.5%), retention cysts were 12 (10.3%), sialadenosis were 8 (08-6.8%) and 3 cases of (03-2.5%) benign neoplasms- out of which two cases were Warthin’s tumour and one case of monomorphic adenoma. Malignant lesions were 11 cases (9.4%).

CONCLUSION

FNAC, though an accurate procedure for diagnosing pleomorphic adenoma, mostly poses diagnostic challenges because of the remarkable degree of cytomorphological diversity, for which pleomorphic adenoma earns a special distinction. Awareness of these variations is needed by the cytopathologist to avoid diagnostic errors.

KEYWORDS

Cellularity, Cytomorphology, Cystic Aspirate, Diversity, Epithelial Cells, Pleomorphic Adenoma, Mesenchymal Matrix, Metaplastic Change, Sialadenitis.

Cytology smears are categorized as classic/stroma rich/cell rich with mandatory presence of epithelial and mesenchymal components for the diagnosis. Uniform crowded epithelial cells with well-defined cytoplasm, singly scattered (myoepithelial cells) plasmacytoid cells and clusters of darkly stained (ductal) cells are seen lying free or intermingled with fibrillary ground substance. Eccentrically placed, bland nuclei, finely reticular chromatin with inconspicuous nucleolus are common findings. Cytoplasm is sharply demarcated, dense and cyanophilic on PAP stained smears. Rarely single cells with atypical nuclei can be seen interspersed in tissue fragments.(4) Epithelial component on the smears can be seen as glandular, adenoid cystic, clear cell, adnexal, cellular, spindle and sebaceous cell patterns. Cystic change, squamous, mucinous and oncocytic metaplasias can occur in 25% of cases.(5)

Objective
The present study was done to evaluate the cytomorphological features of pleomorphic adenomas with an emphasis on differential diagnoses, challenges encountered during the diagnosis and addressing potential pitfalls.

MATERIALS AND METHODS
This study was a descriptive study undertaken at a tertiary care centre over a period of 1 year 9 months from Jan 2016 to Sep 2017. Total numbers of salivary gland lesions encountered during this period of study were 116 cases. 64 cases of pleomorphic adenomas diagnosed on FNAC were included. All the cases were thoroughly reviewed for nature of aspirates, patterns of epithelial component, types of mesenchymal matrix and any degenerative changes were noted.

The cytological smears were alcohol fixed and air dried, stained with routine cytological stains comprising Rapid Haematoxylin and Eosin, Papanicolaou, Giemsa and Toluidine blue stains. Histopathological and radiological correlation was available in most of the cases. Immunohistochemistry was used whenever necessary in diagnostic difficulties.

RESULTS
Out of total 116 cases of salivary gland lesions, Pleomorphic adenomas comprised of 64 (55%), Parotid gland involvement in 38 cases (59.3%) Submandibular gland in 16 cases (25%) and minor Salivary glands in 10 cases (15.7%) (Fig. 1).

Location of the Tumour

Most common age group was 21 to 30 years with median age of 25. A female preponderance with 44 cases was observed in our study (Fig. 2).

Age Incidence of Pleomorphic Adenoma

Other pathologic lesions included were chronic sialadenitis 18 (16%), retention cysts 12 (10%), malignant lesions in 11 (9%), sialadenosis 8 (7%) and other benign neoplasms 3 cases (3%) (Fig. 3).

Spectrum of Lesions

Other pathologic lesions included were chronic sialadenitis 18 (16%), retention cysts 12 (10%), malignant lesions in 11 (9%), sialadenosis 8 (7%) and other benign neoplasms 3 cases (3%) (Fig. 3).
Figure 5. H and E X40- Cytosmear with Mucinous Material, Few Plasmacytoid Cells- PA with Mucus Cells

Figure 6. H and E X40- Cytosmear with Mucinous Material, Tumour Cells with Vacoulations

Figure 7. H and E- Cytosmear with Dispersed Myoepithelial Cells and Clusters of Atypical Cells

Figure 8. H and E X40- Cytosmear of Carcinoma Ex-Pleomorphic Adenoma, Scant Stroma

Figure 9. H and E Stained Smear X40- Acinar Groups of Atypical Cells- Cellular PA

Figure 10. H and E X40- Sheets of Squamous Metaplastic Cells with Few Myoepithelial Cells, Scant Stroma
DISCUSSION

The global annual incidence of all salivary gland tumours is 0.4 - 13.5 cases/100,000. Incidence differs in various ethnic groups and geographic variations are also noted. Pleomorphic Adenoma is the most common benign tumour involving parotid gland in 64% to 80%. Superficial lobe being the preferential location. Bilateral synchronous involvement occurs infrequently. Sublingual gland is the least involved (<1%). Pleomorphic Adenoma is thought to be derived from pluriotent reserve cells of intralculated duct. Differential diagnostic difficulties arise when secondary changes like cystic change, oncocytic metaplasia and squamous metaplasia as seen in other benign tumours like Warthin’s tumour or malignancies like Squamous Cell Carcinoma.

Epithelial component shows varied patterns like Cylindromatous pattern as seen in Basal cell carcinoma, Adenoid cystic carcinoma and Adenoid cystic carcinoma. Cellular pattern, myoepithelial pattern as seen in myoepithelial cell carcinoma and epithelial-myoepithelial carcinoma. Clear cell pattern as seen in Renal cell carcinoma, Thyroid carcinoma and Melanoma metastases. However, cellular atypia, complex patterns with absence of stroma is diagnostic of malignancy. Neoplasms with cystic change or partially cystic, bloody aspirates or non-bloody aspirates need to be centrifuged and the cellular element of the fluid need to be concentrated onto a manageable slide area. Cautious and systematic approach is needed, particularly in cystic lesions with metaplastic changes. Presence of squamous cells with necrotic debris in cystic aspirates and tumours which form keratin filled cysts pose diagnostic difficulties with differential diagnosis of malignancies like Squamous cell carcinoma and Mucoepidermoid carcinoma. Ischaemic infarction in tumours can also mimic malignancy. Keratoepithylomas and dermoid cysts of parotid are other differentials. Puzzling mixture of necrosis, keratin, inflammation, adenexal differentiation like trichoepitheliomatous differentiation are also rarely seen. Recurrent Pleomorphic Adenoma is common in parotid gland. Diagnostic factors are presence of high mesenchymal content, chondroid and myxoid stroma. Incidence is more in younger patients with Multinodularity. Malignant change occurs in 2% - 7% of cases in association with multiple recurrences. Tumours are seen more in elderly males in the deep lobe of the gland. A well-differentiated myoepithelial carcinoma, ex-pleomorphic adenoma can show mild cytologic atypia with diagnostic problems.

Mucoceles are often misdiagnosed as Pleomorphic Adenoma. Wispy mucus is often misinterpreted as chondromyxoid stroma, leading to erroneous conclusion. Schwannian differentiation in pleomorphic adenoma is a rare entity. We reported one such case. However, Nerve sheath tumours should always be considered in differential diagnosis of pleomorphic adenoma with spindle cell rich stroma and diligent search for epithelial elements is recommended in diagnosing schwannomas in head and neck areas. MPNST is misdiagnosed as PA in the presence of eosinophilic stromal material with spindle cells, which is mistaken for chondromyxoid stroma and myoepithelial cells. Metastasising mixed tumour of parotid is a rare tumour with rapid growth and extensive metastasis occurring to bones, CNS, liver, lungs, lymph nodes, sphenoid sinus, maxilla and skin. This tumour is thought to be due to immunosuppression. Immunohistohemical expression of ER, PR, (receptors) P53, BCL-2, Ki-67, CD 105 and P21 positivity are seen.

Matrix producing tumours of parotid are Pleomorphic adenoma, Carcinoma ex-PA. Adenoid cystic carcinoma (ACC), Basal cell adenoma (BCA), epithelial-myoepithelial carcinoma and polymorphous low-grade adenocarcinoma. In presence of cribriform cell clusters in pleomorphic adenomas differential diagnosis of ACC is to be considered. Both can exhibit significant cyto logical variations and overlap. Treatment is different in both, so differentiation is necessary. Carcinoma- ex-PA accounts for 3.6% of salivary gland tumours. The common malignancies occurring in PA are Adenocarcinoma NOS (42.4%) and salivary duct carcinomas (32.8%). Uncommon varieties are adenosquamous, adenoid cystic, undifferentiated, myoepithelial, epithelial-myoepithelial and sarcomatoid carcinomas. Mucoepidermoid carcinoma in pleomorphic adenoma is a rare event. To avoid false negative diagnosis, at least 3 passes are recommended from different areas. Mammary analogue secretory carcinoma is a recently described tumour with translocation (12; 15). FNA smears are cellular with bland epithelial cells admixed with extracellular secretory material.

Adnexal differentiation with keratin filled cysts formation is rare. Radiation induced carcinogen exposure are the inciting factors. Differential diagnoses are SCC, Collision tumour consisting of SCC and Carcinoma ex-PA. Cutaneous leiomyoma originating along with Pleomorphic adenomas in parotid associations are rare. History of previous FNAC and awareness of its effects on histology of the subsequent surgical specimen are necessary to avoid misdiagnosis of malignancy. Ex: Squamous metaplasia, infarction, necrosis, stromal hyalinisation, haemorrhage, inflammation, giant cell reaction, fibrosis, granulation tissue, cholesterol cleft formation, pseudo-xanthomatoid reaction, pseudocapsular invasion and microcystic change.

Sometimes, Sialosis which is a salivary gland enlargement by hypertrophy can also be mistaken for Pleomorphic adenoma. Differentiating features are abundant acinar and ductal tissue is seen in a clean background. Other rare D/D’s with adipocyte clusters in the aspirates are Lipomatous PA, Sialolipoma, Oncocytic lipoadenoma, Lipomatosis and Spindle cell lipoma. Tuberculous involvement of parotid is extremely rare, can present as indolent parotid enlargement and generally overlooked. Presence of granulomas and AFB stain positivity helps in diagnosis. Nodular fascitis mimicks Pleomorphic adenoma with presence of spindle and plasmacytoid cells. Clumping of intercellular stromal and myxoid matrix material and myoepithelial cells show fuzzy borders, fragile cytoplasmic processes and nucleoli. IHC shows Vimentin, SMA and MSA positivity. Masses in the lower pole of parotid can have difficulties with D/D-intraparotid lymph node lesions. In case of lateral neck masses, secondary tumours are the commonest (20%). Of these metastasis from parotid is most common. PTC, Adenocarcinoma lung, RCC, Breast carcinoma, Melanoma, SCC can metastasise to salivary gland parenchyma or into the lymph nodes in and adjacent to the gland. IHC helps in tumours with cytopathological unequivocal findings. Metastatic Pleomorphic Adenoma is a curiosity, only sporadically reported. IHC markers like CK-19, CK-14, EMA and CEA for the Ductal component and Keratin, actin, myosin, S-100
CONCLUSION

Majority of salivary gland nodules are benign. Pleomorphic adenomas offer some difficulty in diagnosis on cytological examination. But presence of squamous cells, clear cells, lymphoid cell and abundant stroma in the smears can pose problems. FNA otherwise demonstrates well most of the histopathological features of PA and can be used as a diagnostic tool in the initial assessment of the tumour. Mandatory presence of all three elements is needed for a diagnostic dilemma. Familiarity with the variable aspirate components. Most frequent problem involves variations in diagnostic challenge. Indian J Pathol Micro 2012;56 :- 4802, pISSN 2278-4784/ eISSN 2278-4748/ Vol. 7/ Issue 14/ Apr. 02, 2018

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