# Fine-Needle Aspiration Cytology Of Pleomorphic Adenoma: Cytologic Variations And Diagnostic Pitfalls: A Report Of Two Cases.

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**Abstract**: **Introduction:** Fine-needle aspiration cytology (FNAC) of the salivary gland is a sensitive and specific technique used in the diagnosis of lesions of the salivary gland. On FNA, adequately cellular aspirates make distinction easy in most cases. However, sparse cellularity makes diagnosis difficult partly due to lack of observer familiarity with the different patterns. The diagnosis of pleomorphic adenoma (PA) can be made accurately but this common salivary gland neoplasm can be diagnostically challenging, causing pitfalls in cytodiagnosis. **Material And Methods:** A 26-year-old male presented with a firm, painless, mobile slowly-growing mass in the right preauricular region of three years duration. Fine needle aspiration (FNA) was done. A diagnosis of pleomorphic adenoma suspicious of malignancy was given due to the presence of isolated squamous cells, occasional cluster of basaloid cells, occasional giant cells and hyaline globules. Histology confirmed a pleomorphic adenoma with marked squamous metaplasia and keratin cyst formation without evidence of malignancy. A 52-year-old male presented with a firm, painless, mass in the right preauricular region of five months duration. FNAC smears were cellular and showed a hemorrhagic background. Numerous single anucleate and nucleate squamous cells, myoepithelial cell clusters and epithelial cell aggregates were seen. Few foamy cells, giant cells and hyaline globules were noted. Characteristic metachromatic fibrillary chondromyxoid stroma which is usually seen in pleomorphic adenoma was absent. A diagnosis of pleomorphic adenoma suspicious of malignancy was given. The patient was lost to follow up and hence details regarding the histopathological status of his preauricular swelling were not known. **Results:** Here we illustrate that PA with squamous metaplasia, basaloid cells and hyaline globules can be misinterpreted as carcinoma on cytology and discuss the various pitfalls of cytology. **Conclusion:** FNAC is a good pre-operative procedure for the diagnosis of PA. One should be aware of the cytological variations to avoid diagnostic errors. When one is uncertain about classification of a salivary gland tumour the cytopathologist should leave the diagnosis open with a few suggested differential diagnoses rather than issuing a misleading report. [Ramraje S NJIRM 2014; 5(3) :133-137]

**Key Words**: FNAC, diagnostic pitfalls, malignancy, pleomorphic adenoma (PA), squamous metaplasia.

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**Introduction:** Fine-needle aspiration cytology (FNAC) of the salivary gland is a sensitive and specific technique used in the diagnosis of lesions of the salivary gland[1]. On FNA, adequately cellular aspirates make distinction easy in most cases. However, sparse cellularity makes diagnosis difficult partly due to lack of observer familiarity with the different patterns. The diagnosis of pleomorphic adenoma (PA) can be made accurately but this common salivary gland neoplasm can be diagnostically challenging due to histological complexity which is the hallmark of pleomorphic adenoma. Characteristic biphasic pattern comprising of epithelial/ myoepithelial cells and fibro-myxo-chondroid stroma [2] is seen on cytology. The diagnosis of PA can be made accurately by FNAC with a reported reliability of 80-95%[2,3]. Diagnostic difficulty in interpretation of cytological material arises due to sparse cellularity, lack of observer familiarity with the different patterns and limited selective sampling. In the absence of chondromyxoid stroma, squamous metaplasia, basaloid cells and hyaline globules may be misinterpreted as carcinoma.

**Material and Methods**: Case 1**:** A 26-year-old male presented with a firm, painless, mobile slowly-growing mass in the right preauricular region of three years duration. Fine needle aspiration (FNA) was done using a 23 gauze needle attached to a 10 cc syringe. 0.2cc of hemorrhagic material was aspirated. Both alcohol fixed and air dried smears, stained with Haematoxylin and Eosin and Giemsa stains respectively, were examined. The smears showed a cellular aspirate. Against a myxoid background admixed with haemorrhage, epithelial cells singly scattered and in clusters, having well defined cell borders, moderate cytoplasm, round

to oval benign uniform eccentric nuclei and bland chromatin were seen. The stroma showed spindle shaped myoepithelial cells. Isolated squamous cells, occasional cluster of basaloid cells, occasional giant cells and hyaline globules were seen. A diagnosis of pleomorphic adenoma suspicious of malignancy was given [Fig 1, 2]

**Figure 1: A Cellular Aspirate Showing A Myxoid Background And Epithelial Cells (H&E, 50x). Inset Showing Uniform Epithelial Cells (H&E, 400x)**

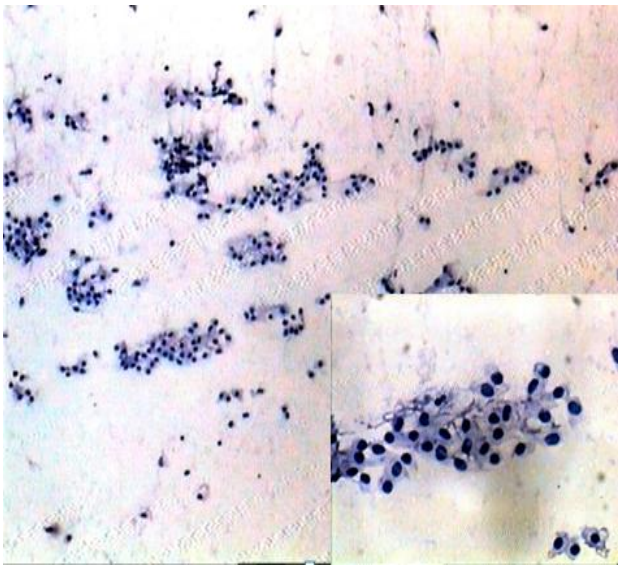
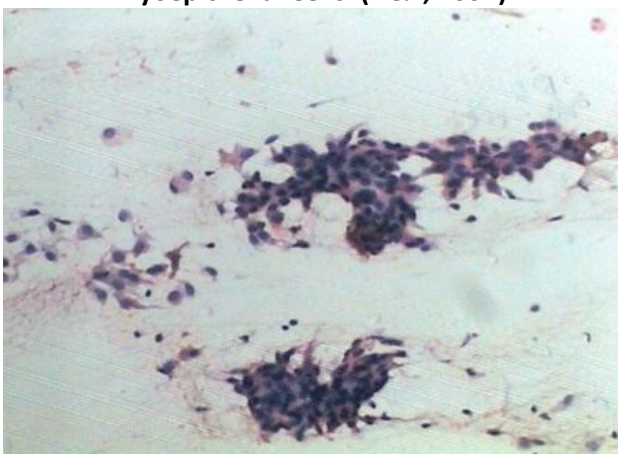


**Figure 2 :Smear Showing Spindle Shaped Myoepithelial Cells. (H&E, 100X)**



**Gross And Histopathological Findings:** Supercificial parotidectomy was done. Gross specimen comprised of an encapsulated nodular, firm mass, measuring 3x2.5x2.5 cm in size. Cut surface of the mass was firm and grey white with no hemorrhagic, necrotic or cystic areas. On histology the tumour was encapsulated showing sheets of squamous cells and multiple keratin filled cysts reminiscent of tricho-epitheliomatous differentiation. The rest of the areas showed features of conventional pleomorphic adenoma i.e. epithelial elements in cords and gland pattern as well as chondromyxoid stroma. Thus histology confirmed a pleomorphic adenoma with marked squamous metaplasia and keratin cyst formation without evidence of malignancy [Fig 3, 4].

**Figure 3: Gross Specimen Comprised Of An Encapsulated, Nodular Mass With A Firm, Grey White, Lobulated Cut Surface**

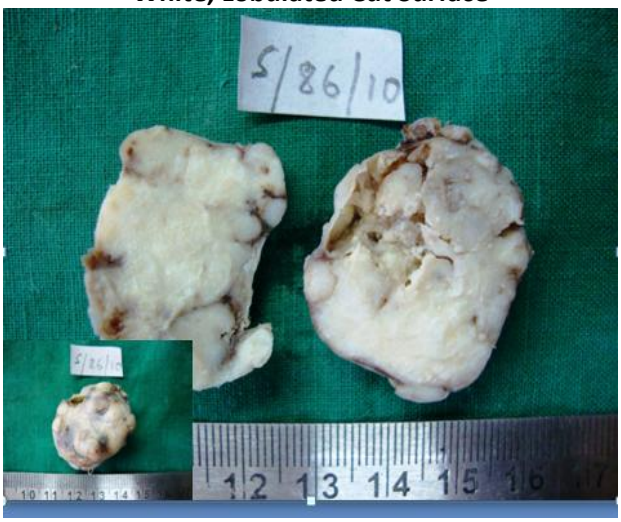
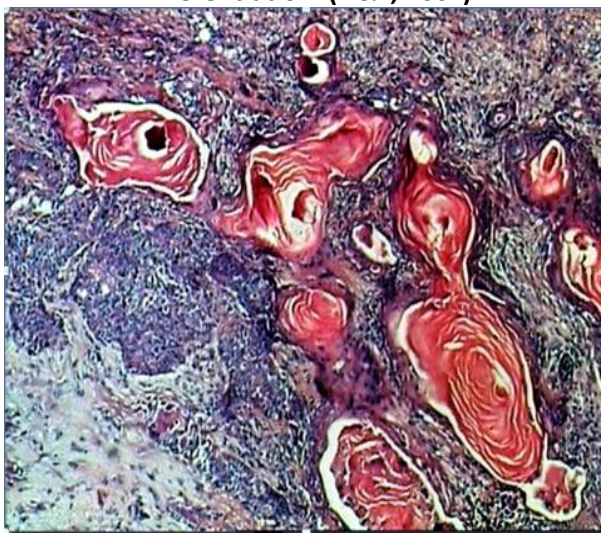



**Figure 4: Multiple Keratin Filled Cysts, Reminiscent Of Tricho-Epitheliomatous Differentiation. (H&E, 100x)**



Case 2: A 52-year-old male presented with a firm, painless, mass in the right preauricular region of

five months duration. FNAC smears were cellular and showed a hemorrhagic background. Numerous single anucleate and nucleate squamous cells, myoepithelial cell clusters and epithelial cell aggregates were seen. Few foamy cells, giant cells and hyaline globules were noted. Characteristic metachromatic fibrillary chondromyxoid stroma which is usually seen in pleomorphic adenoma was absent. A diagnosis of pleomorphic adenoma suspicious of malignancy was given. [Fig 5,6]. The patient was lost to follow up and hence details regarding the histopathological status of his preauricular swelling were not known.

**Figure 5: Myoepithelial Cell Cluster And A Giant Cell (H&E, 200x)**

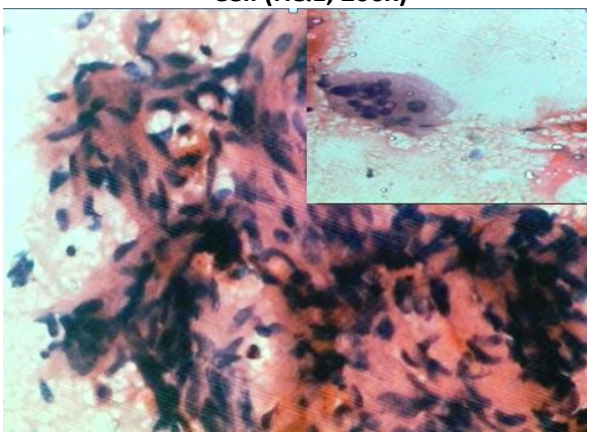
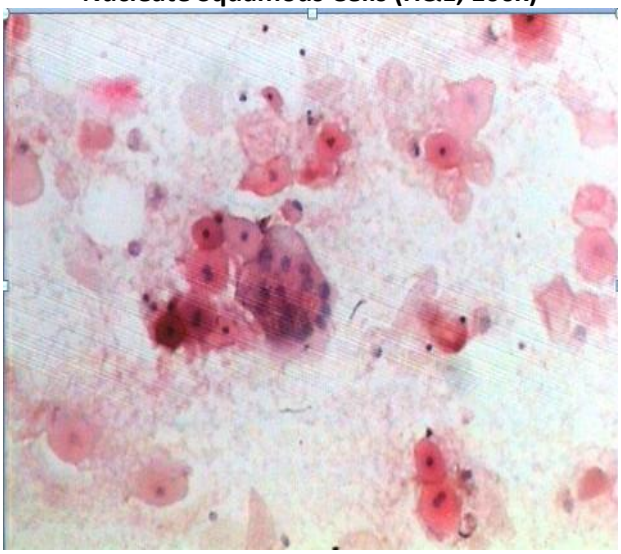


**Figure 6: Numerous Single Anucleate And Nucleate Squamous Cells (H&E, 100x)**



**Discussion:** Histological diversity is the hallmark of pleomorphic adenoma[4].Different parts of the same tumour show a variety of histological patterns[4]. There is a proportional variation between epithelial and chondromyxoid stroma as also metaplastic variations in the epithelial and stromal components[5]. When the whole tumour is available for examination, the diverse morphologic patterns are not a problem in surgical pathology, however, this can lead to misdiagnosis on cytology, due to limited and selective sampling [4,5,6].

Aspirates from PA show cell clusters with a "sunburst" appearance caused by peripheral spindled cells streaming into a fibrillar myxoid stroma. About 25% of pleomorphic adenomas show focal squamous metaplasia. Florid squamous metaplasia is also reported[7]. Adenexal differentiation in the form of extensive keratin filled cysts, reminiscent of tricho-epitheliomatous differentiation, as seen in our case, has been reported in literature [8-10]. Squamous metaplastic changes, when extensive may be misdiagnosed as metastatic well-differentiated squamous cell carcinoma on FNAC, particularly in the neck region[11, 7.]

Pleomorphic adenoma can be misdiagnosed as mucoepidermoid carcinoma on cytology due to squamous and basaloid cells which are close mimics of squamous and intermediate cells of mucoepidermoid carcinoma. Presence of mucoid material, vacuolated histiocytic cells, sebaceous/mucinous metaplastic cells and absent metachromatic fibrillar stromal material so characteristic of pleomorphic adenomas on aspiration cytology [2,,8, 9] often cause confusion[12].

Near similar features in our cases also led to the cytological misdiagnosis of carcinoma. There are literature reports, wherein pleomorphic adenoma was misdiagnosed as mucoepidermoid carcinoma. In a case report by Hamdan et al, a misdiagnosis of mucoepidermoid carcinoma was made on frozen section [13]. An important feature of pleomorphic adenoma is chondromyxoid stroma [5]. Smears should be closely scrutinised for fragments of chondromyxoid stroma to avoid misinterpretation of pleomorphic adenoma in the presence of squamous metaplasia as a mucoepidermoid carcinoma on cytology. We reviewed our case slides again after the histological diagnosis was

made and found occasional fragments of stroma. Also, keratinisation, especially of the extracellular type, is rare in mucoepidermoid carcinoma [8]. Even if the features diagnostic of pleomorphic adenoma are identified, the differential diagnosis should still include a mucoepidermoid carcinoma arising in a pre-existing pleomorphic adenoma. However, mucoepidermoid carcinoma ex pleomorphic adenoma is exceedingly rare and is usually a high grade malignancy[8,9]. Thus, on cytology, a number of differential diagnoses can be considered depending on the varied morphology of PA. The tumour may be confused with and needs to be differentiated from monomorphic adenoma, myoepithe-lioma and adenoid cystic carcinoma if the epithelial pattern predominates. Metaplastic squamous cells and scant mucoid material may be misinterpreted as mucoepidermoid carcinomas. A retention cyst can be mistaken if the myxoid material is abundant and epithelial cells sparse. Occasional PA shows hyaline globules of basement membrane-like material which is also a feature of adenoid cystic carcinoma.

One has to exercise caution while interpreting anisonucleosis in aspirates from pleomorphic adenoma since carcinoma ex pleomorphic adenoma is well recognized but is exceptional. Confusion with adenoid cystic carcinoma, acinic cell carcinoma or mucoepidermoid carcinoma is seen. Also, histologically documented PA can be misdiagnosed even after reviewing the slides.

On cytology, nodular fasciitis also can be mistaken for pleomorphic adenoma, leading to unwarranted surgical treatment. Though they share common morphological features, fuzzy cytoplasmic borders, one-to-multiple fragile cytoplasmic processes and prominent nucleoli seen in nodular fasciitis should be looked for in spindle and plasmacytoid cells which help in differentiating it from pleomorphic adenoma[14].

**Conclusion:** Thus besides experience, sampling and genuine problems in typing the tumour also play a role in the misclassification of salivary gland neoplasms. FNAC is a good pre-operative procedure for the diagnosis of PA. One should be aware of the cytological variations to avoid diagnostic errors [15].When one is uncertain about classification of a salivary gland tumour the cytopathologist should leave the diagnosis open with a few suggested differential diagnoses rather than issuing a misleading report.

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