Pilomatricoma is an uncommon adnexal tumor with heterogeneous features that can mimic various malignancies and contributes to false positive diagnosis on cytology. It is an uncommon, slow-growing, benign skin adnexal neoplasm of hair matrix origin initially described by Malherbe and Chenantais. This tumor is predominantly found in the head and neck region, and presents as a small, asymptomatic, slow-growing dermal, subcutaneous, solitary lesion. More than 50% of these tumors are known to occur in the second decade of life and are often misdiagnosed clinically. Cytological features pose a diagnostic challenge although the histological features are very well delineated. This paper presents the cytological features in two cases outlining the importance of the clinicopathological features that need to be considered for an accurate diagnosis. Awareness of its varied cytologic features and clinical presentation can avoid misdiagnosis.

**Keywords:** Adnexal, Cytology, Pilomatricoma, Skin

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**INTRODUCTION**

Pilomatricoma (PMX), also known as “pilomatricoma” or “calcifying epithelioma of Malherbe,” is a relatively uncommon benign skin adnexal neoplasm of hair matrix origin. It is a slow-growing neoplasm originating from pluripotent cells (outer sheath cell) of the hair follicle root and accounts for 20% of pilar tumors. It was first described by Malherbe and Chenantais as “epithelioma cutis necrotic calcification Malherbe” in 1880. In 1961, Forbis and Helwig proposed the term PMX to avoid the term epithelioma, which could be confused for malignancy. This tumor is predominantly found in the head and neck region, followed by the upper extremities and rarely the lower extremities. It presents as a small asymptomatic slow-growing dermal, subcutaneous solitary lesion. Rarely ulceration and discharge can also be found. It may arise in any age, but about 40% arise in children younger than 10 years and 60% are known to occur in the second decade of life. It is often misdiagnosed clinically. Cytological features pose a diagnostic challenge although the histological features are very well delineated. This paper presents the cytological features in two cases.

**CASE REPORTS**

**Case 1**

A 28-year-old male presented with a painless swelling over the left side of the neck noticed since 1 month and was gradually increasing in size. He was a known case of astrocytoma WHO grade II of the brain treated 14 years ago with surgery and post-surgical radiotherapy. On examination, a firm swelling measuring 3 cm × 1 cm was seen. Clinically suggestive of a lymph node, fine needle aspiration cytology (FNAC) was performed.

**Cytological Findings**

Smears were cellular and predominantly showed sheets and clusters of monomorphic basaloid cells with round to oval nuclei, single nucleoli, and scant cytoplasm. Few clusters of polygonal cells with oval nuclei and abundant cytoplasm were also noted. In addition, the background also showed multinucleate giant cells, foci of calcification along with few ghost cells. A possibility of the cutaneous adnexal tumor was suggested (Figure 1).

**Case 2**

A 27-year-old male presented with a painless swelling over the right ear lobe, which was gradually increasing in size since 3 months. On examination, the swelling measured
about 2 cm × 1 cm. No history of fever, ear discharge or ear pain was noted. FNAC was performed.

**Cytological Findings**
The smears were cellular and showed numerous branching syncytial and few cohesive clusters of monomorphic small to medium-sized cells with scant cytoplasm, round nucleus, many with nucleoli. In addition, spindle-shaped cells some with cytoplasmic melanin interspersed multinucleated giant cells and few small cohesive clusters of monomorphic cells with squamous differentiation were noted. A biopsy was requested to rule out a skin adnexal neoplasm (Figure 2).

**Histopathological Findings**
In both the above cases, a single well circumscribed white nodule was identified with gritty areas of calcification. Microscopy revealed a circumscribed tumor consistent with pilomatricoma. The surrounding stroma showed numerous foreign body giant cells in response to keratin along with areas of calcification (Figures 3 and 4).

**DISCUSSION**
The cytologic diagnosis of PXM is rendered difficult due to various reasons. First, in many centers aspirates are not performed by the cytologist reading the slides. Hence, the clinical information made available (e.g.: neck lymph node in Case 1) can be misleading. Presence of numerous basaloid cells (as occurs in early lesions of PMX and in aspirates from lesional periphery) with very few shadow cells can contribute to cytologic misdiagnosis as malignancy and has been emphasized by many authors (Figures 5 and 6). Further, older PXM with predominant component of shadow cells along with multinucleated giant cells can be interpreted as metastatic cystic squamous cell carcinoma. The cytologic differential diagnosis hence, varies with the predominant cell type detected in the smears (Table 1).

PMX is a well-recognized skin appendageal tumor. However, the cytological diagnosis of these lesions remains a problem. PMX is basically composed of two
types of cells, basaloid cells, and shadow or ghost cells in varying combination. The basaloid cells have round to oval, hyperchromatic nuclei with visible nucleoli and scanty cytoplasm. Eosinophilic ghost cells, with a distinct border and possess a central unstained area as a shadow of the lost nucleus is the second cell type. Calcification, foreign body giant cells, and keratinization are other notable features.

Basaloid cells of PMX can be interpreted as malignant due to their increase in the nuclear cytoplasmic ratio, slight nuclear hyperchromasia, and nucleoli and is the major pitfall in the cytological diagnosis of PMX. Various authors have mentioned the predominance of basaloid cells in fine-needle aspiration smears, probably be because of easier detachment by the aspiration needle.

Detection of shadow cells/ghost cells has been since it has been considered the most important cytological feature for definitive diagnosis. They appear as sharply outlined masses of refractile keratin, a feature that is recognized mainly on papanicolaou stain. This characteristic has been described by Woyke et al. as eosinophilic clumps and by Chan and McGuire as birefringent keratin material. However, the detection of these cells can be challenging owing to the paucity in cytological smears. Further, clinical information of site of aspirate (e.g.: lymph node in case 1) may mislead the cytologist.

Salivary gland neoplasms like adenoid cystic carcinoma may be considered if the lesions are located in the region of the parotid or submandibular gland. Metastatic neoplasm may also be thought of if history of earlier malignancy is available (as in one of our case).

Table 1: Clinicopathological features to aid the diagnosis of pilomatrixoma

<table>
<thead>
<tr>
<th>Clinical differential diagnosis</th>
<th>Useful clinical clues:</th>
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<tbody>
<tr>
<td>Lymph node without history of prior malignancy</td>
<td>Subcutaneous growth located in the head and neck of young persons should alert the clinician/pathologist of PMX</td>
</tr>
<tr>
<td>Asymptomatic nodular swelling</td>
<td>Clinical data, particularly age and location, past history of malignancy</td>
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<tr>
<td>Basaloid cell predominant smears</td>
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<table>
<thead>
<tr>
<th>Cytologic differentials</th>
<th>Useful cytologic clues:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salivary gland lesions like adenoid cystic carcinoma and pleomorphic adenoma</td>
<td>Lack of identifiable patterns, rosettes, pseudorosettes, molding</td>
</tr>
<tr>
<td>Basal cell carcinoma</td>
<td>Shadow cells are pathognomonic of PMX</td>
</tr>
<tr>
<td>Merkel cell carcinoma</td>
<td>Lack of degenerating singly placed squamoid cells with malignant nuclei, malignant karyopyknosis</td>
</tr>
<tr>
<td>Poorly differentiated or undifferentated cell neoplasm</td>
<td>Absence of background material as hyaline globules</td>
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<tr>
<td>Shadow cell predominant+multi-nuclear giant cells</td>
<td>Both Papanicolaou and Diff-Quik stains may be used</td>
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<tr>
<td>Cystic squamous cell carcinoma</td>
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<td>Epidermal inclusion cyst</td>
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PMX: Pilomatrixoma, FNA: Fine needle aspiration

Figure 6: Gross photomicrograph of pilomatrixoma. Cut section showing a circumscribed lesion with central off white debris

Figure 5: (a and b) Histopathology of pilomatrixoma. Peripheral basaloid cells, ghost cells, and keratin debris are seen (Case 1 and Case 2, respectively) H and E, ×40
Constitutional mismatch repair deficiency (CMMRD) syndrome is a distinct childhood cancer predisposition syndrome due to germline mutations in one of the mismatch repair genes (MLH1, MSH2, MSH6 or PMS2). Both high-grade gliomas and pilomatrixomas are known to occur in these patients. Hence, the possibility of such a syndrome should also be considered when one encounters multiple PMXs or if the patient has a history of gliomas and PMXs. In one of our cases (Case 1), the patient was lost to follow-up, hence genetic workup could not perform to rule out CMMRD.

CONCLUSION

The low clinical accuracy for PMX could be attributed to a possible lack of awareness of the tumor by clinicians. In conclusion, PMX an uncommon adnexal tumor with heterogeneous features can mimic various malignancies and contributes to false positive diagnosis on cytology. Awareness of its varied cytologic features and clinical presentation can avoid misdiagnosis.

REFERENCES