

Can We Confidently Diagnose Pilomatricoma with Fine Needle Aspiration Cytology?

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Abstract

Pilomatricomas can be confidently diagnosed cytologically due to their characteristic cytomorphological features. However, these lesions are rarely encountered by cytopathologists and thus pose a diagnostic dilemma to even experienced individuals, especially when the lesions are focally sampled. We describe two cases of histologically confirmed pilomatricoma. The first case is of a 13-year-old boy with posterior cervical 'lymphadenopathy', and the second one is of a 12-year-old girl with a lower cheek swelling. Both aspirates comprised predominantly atypical basal-like cells, with prominent nucleoli. 'Ghost cells' were readily identified by cell block in case two, but cell block in case one yielded no diagnostic material. In case two, pilomatricoma was accurately diagnosed pre-operatively. A cytological suspicion of a neoplastic process was raised in case one. Despite being diagnostically challenging, pilomatricoma can be diagnosed with careful observation of two unique cytological features of the lesions: (1) pathognomonic 'ghost cells' and (2) irregular, saw-toothed, loosely cohesive basaloid cells, with prominent nucleoli. The role of thorough sampling of the lesion, with multiple passes of various sites, cannot be overemphasized.

Keywords: pilomatricoma, fine needle aspiration, cytology, skin appendage neoplasms

Introduction

Although cutaneous nodules are commonly surgically excised or biopsied in first-line investigations, fine needle aspiration (FNA) cytology of a cutaneous lesion is rarely practiced. Hence, pilomatricoma, a relatively common benign skin appendageal tumour, is rarely encountered in the day-to-day practice of a cytopathologist (1). Although cytomorphological features of pilomatricomas are well described in most cytopathology textbooks, these lesions pose a diagnostic dilemma to even experienced cytopathologists (2). The diagnosis is especially problematic when the lesions are focally sampled, with predominance of one component in an aspirate (2).

We describe two cases of histologically confirmed pilomatricoma. Only one of the cases was correctly diagnosed through a pre-operative cytological assessment. The other case was mistaken for a neoplastic process. In this report, we highlight useful cytomorphological criteria for diagnosing pilomatricoma and potential diagnostic pitfalls in FNA cytology.

Case Report

Case 1

A 13-year-old Malay boy presented with a

two-year history of painful left posterior cervical swelling, which was gradually increasing in size. There were no associated constitutional symptoms or a history of exposure to tuberculosis. Physical examination revealed a 2 cm firm, tender and well-defined nodule at the left posterior upper cervical region at level V. Aspiration was carried out due to the clinical suspicion of lymphoma or tuberculosis involving the cervical lymph node.

Cytological findings

Smears were cellular, comprising predominantly loose cohesive sheets and clusters of atypical basaloid cells. The cells exhibited mild to moderate nuclear pleomorphism and hyperchromatic nuclei, some with one or multiple prominent nucleoli and scanty basophilic cytoplasm (Figure 1a). Occasional foreign body type multinucleated giant cells were noted (Figure 1a). No shadow cells or 'ghost cells' were found. No lymphoglandular bodies were seen in the background to suggest lymphoid tissue. No granulomas were present. A cytological suspicion of a malignant neoplastic process was raised, and excision of the cervical swelling was advised.

Histopathological findings

Subsequent excision biopsy of the swelling showed a cyst-like structure, which contained firm, chalky white material, with a gritty sensation

upon cutting, typical of a calcified epidermal cyst on gross examination. Histological examination revealed features characteristic of pilomatricoma, with aggregates of basaloid cells lining the cyst and eosinophilic cornified material containing anucleated shadow cells or 'ghost cells' in the

centre (Figure 1b). Foreign body giant cell reaction, with areas of calcification, was also noted.

Case 2

A 12-year-old girl presented with progressive enlargement of a swelling on the lower cheek for one year. Examination revealed a firm, well-defined 3 cm nodule on the left lower cheek that clinically mimicked a parotid tumour.

Cytological findings

Aspirates were cellular, comprising cohesive groups of small basaloid epithelial cells displaying uniform hyperchromatic nuclei, fine granular chromatin and scanty cytoplasm (Figure 2b). There were no identifiable 'ghost cells', leading to an immediate suspicion of a malignant small round cell tumour. A cell block section showed solid nests of basaloid cells, with abrupt trichilemmal keratinisation forming 'ghost cells' (Figure 2b). A diagnosis of pilomatricoma was made and confirmed histologically following subsequent excision (Figure 2c).

Discussion

Pilomatricoma, a benign slow growing skin adnexal neoplasm, may occur at any age. It is frequently seen in children and young adults, with a slight female preponderance (3). Common sites are the hair-bearing areas, with the majority arising in the head, neck and upper extremities (3). Generally, pilomatricoma is located in deep dermal or subcutaneous tissue (3).

The 'tent' sign (tumour shows multiple facets and irregular angles when stretched) is thought to be diagnostic of pilomatricoma clinically. However, this is often obscured, with a wide variety of clinical presentations, which include skin tethering, telangiectasia, cystic consistency and traumatic erosion (4). These lesions are frequently misdiagnosed clinically as basal cell carcinomas, squamous cell carcinomas, sebaceous cysts or dermoid cysts. The lesion in one of the present cases was thought to be a malignant neoplasm. Based on a large case series, Julian and Bowers (4) reported that 74% of pilomatricomas were incorrectly diagnosed pre-operatively. This results in unnecessary, extensive surgery and exposes patients to needless imaging studies and diagnostic workup (5).

Pilomatricoma is characterised cytologically by a combination of two salient features: pathognomonic 'ghost cells' and basaloid cell clusters. These 'ghost cells' typically have a central pale nuclear zone and abundant eosinophilic

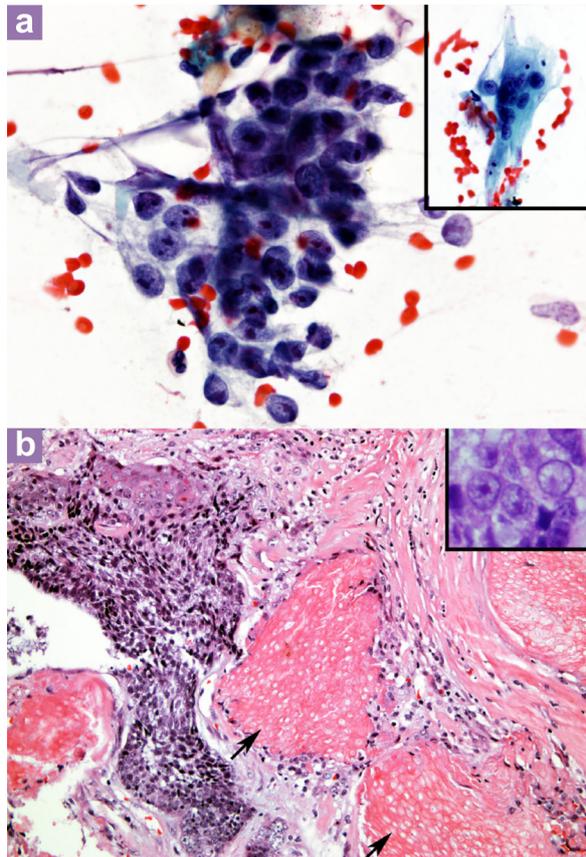


Figure 1: (a) Aspirate shows loose clusters of atypical basaloid cells, displaying mild to moderate pleomorphic hyperchromatic nuclei, some with prominent nucleoli and scanty basophilic cytoplasm (Papanicolaou, 600× magnification). Inset shows foreign body type multinucleated giant cells (Papanicolaou, 400× magnification). (b) Subsequent excision reveals sheets of basaloid cells with abrupt trichilemmal keratinisation towards the centre forming 'ghost cells' (arrows) (hematoxylin and eosin, 200× magnification). Inset shows matrical cells, corresponding to basaloid cells exhibiting prominent nucleoli (hematoxylin and eosin, 400× magnification).

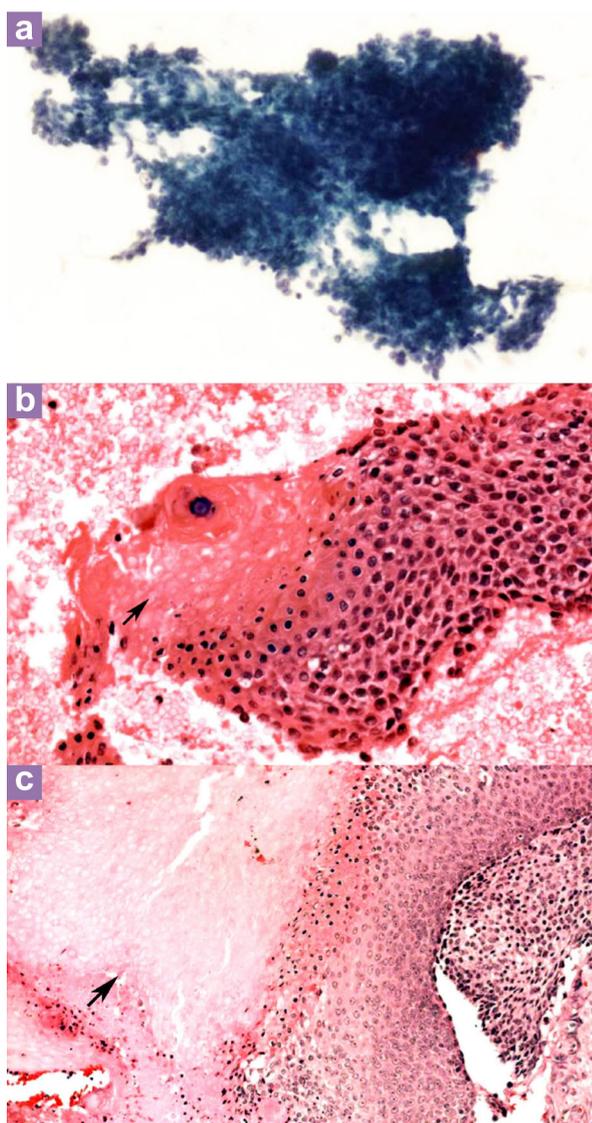


Figure 2: (a) Smear comprises of cohesive clusters of small basaloid epithelial cells displaying uniform hyperchromatic nuclei with fine granular chromatin and scanty basophilic cytoplasm (Papanicolaou, 100× magnification). (b) Cell block section shows solid nests of basaloid cells undergoing abrupt trichilemmal keratinisation forming ‘ghost cells’ (arrow) (hematoxylin and eosin, 200× magnification). (c) Histological section revealed sheets of basaloid cells and ‘ghost cells’ (arrow), characteristic of pilomatricoma (hematoxylin and eosin, 200× magnification).

cytoplasm. The basaloid cells frequently have prominent nucleoli corresponding to matrical cells in histological section and should not be overdiagnosed (6). Other accompanying features are refractile keratin clumps, foreign body giant cell reaction and calcium deposits. The presence of atypical basaloid cells, together with marked nuclear pleomorphism and atypical mitosis, should raise the suspicion of pilomatric carcinoma, especially in an elderly patient presenting with tumour recurrence (4). Attending cytopathologists should be vigilant for frequent mitosis, which is commonly found in pilomatricoma (5).

The histological diagnosis of pilomatricomas is usually straightforward. They often appear on gross examination as lobulated masses, with variable whitish keratinous material on the cut surface (3). Histologically, pilomatricoma is categorised into four sequential evolutionary stages: early, fully developed, early regressive, and late regressive (7). Early lesions are small and cystic. They are composed of basaloid aggregations (i.e. matrical and supramatrical cells) at the periphery, with abrupt trichilemmal keratinisation towards the centre that forms anucleated ‘ghost cells’. Matrical cells are small, display monomorphous round nuclei, with prominent nucleoli and scanty basophilic cytoplasm. In contrast, supramatrical cells are more mature, larger and exhibit oval, vacuolated nuclei, with abundant pale blue cytoplasm. Fully developed lesions are larger than early-stage ones but exhibit similar histomorphology. In early regressive lesions, the bulk of the lesion primarily consists of cornified eosinophilic material containing ‘ghost cells’ which signifies late regressive stage lesions. Variable degrees of calcification or ossification are frequently present (7). In the present cases, both lesions were early regressive stage.

Despite the well-described cytological features of pilomatricomas, diagnosis of these tumours is often difficult. The diagnosis is particularly problematic when the lesions are focally sampled with limited diagnostic material or contain a predominance of one component (2). In their case series, Ieni et al. (8) reported that pathognomonic ‘ghost cells’ were absent in as many as 40% of FNA biopsies of pilomatricoma. A literature review by Viero et al. (9), of 16 published

articles found that only 21% of FNA biopsies of pilomatricoma were diagnosed correctly, with 25% of cases erroneously regarded as malignant. This reflects the paramount importance of thorough sampling to obtain adequate diagnostic material in an aspirate. It is our opinion that at least three to four passes from various sites of the mass should be performed in all cutaneous lesions. Some authors also suggest the routine use of cell block to minimise diagnostic errors because 'ghost cells' are more readily seen in cell block sections (1,10), as illustrated in case two, although some may dispute this statement.

The differential diagnosis of pilomatricoma is broad cytologically and depends on the proportion of diagnostic components present. In cases where aspirates contain mainly sheets of anucleated and nucleated squamous cells, a pilomatricoma can be confused with an epidermal cyst or trichilemmal cyst. An important differentiating feature is that anucleated squamous cells of epidermal or trichilemmal cysts are singly dispersed, whereas those of 'ghost cells' in pilomatricoma tend to be in cohesive groups (1).

Skin appendageal tumours (e.g. cylindroma, eccrine spiradenoma or hidradenoma) can mimic pilomatricoma, especially when only basaloid cells are present in the aspirates. An important difference is that basaloid cells of skin appendageal tumours are usually arranged in cohesive clusters with a smooth contour, whereas those of pilomatricomas are often irregular, saw-toothed edged, monolayered loose cohesive sheets (10). Unlike skin appendageal tumours, pilomatricomas also exhibit pathognomonic 'ghost cells', foreign body giant cell reaction and calcification.

Foreign body giant cell reaction characterised by multinucleated giant cells is found in many dermatological conditions. The differential diagnosis ranges from non-neoplastic lesions (e.g. ruptured epidermal cysts, ruptured benign cysts and pilomatricomas) to neoplastic lesions (e.g. giant cell tumours and squamous cell carcinomas) (10). Careful observation of the cell components is helpful in making an accurate diagnosis.

Erroneous diagnosis of possible malignancy, such as squamous cell carcinoma or basal cell carcinoma, has been reported in the literature (8–10). 'Ghost cells' are often mistaken for tumour necrosis or disregarded as blood clots. The absence of atypical mitosis and significant nuclear atypia are useful features in excluding squamous cell carcinoma. Likewise, a diagnosis of basal cell carcinoma can be excluded by the absence of

tightly cohesive small, hyperchromatic basaloid cell clusters, with peripheral palisading and sharp borders. Generally, the nucleoli of basaloid cells in basal cell carcinoma are small to inconspicuous (10). In contrast, they are more prominent in pilomatricoma.

In common with the literature, most of the cells in the first case presented here consisted of aggregates of atypical basaloid cells, with prominent nucleoli. Pilomatricoma was not considered in the differential diagnosis due to the clinical impression of a cervical lymph node and the absence of 'ghost cells' in the aspirates. The lesion was mistaken for a possible malignant neoplasm, such as a small round cell tumour. However, the lack of nuclear molding, smudge cells, atypical mitotic figures and background necrotic debris make the diagnosis of a small round cell tumour unlikely. In difficult cases, ancillary tests, such as flow cytometry, immunocytochemistry and molecular cytogenetics, are valuable in arriving at an accurate diagnosis (8–10).

Conclusion

In conclusion, cytological diagnosis of pilomatricomas can be challenging. An accurate diagnosis can be made with careful observation of the presence of two key cytological features of these lesions: 1) pathognomonic 'ghost cells' or shadow cells and 2) basaloid cells, with prominent nucleoli. A pilomatricoma should always be considered when assessing deep dermal or subcutaneous lesions with a long-standing history in the head and neck region of the young. We also found the presence of a foreign body type giant cell reaction helpful. The role of thorough sampling of the lesion, using multiple passes from various sites to increase the chance of obtaining adequate diagnostic materials, cannot be overemphasised.

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Conflict of Interest

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