

Pilomatricoma masquerading as metastatic squamous cell carcinoma

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Abstract

We present a case of a 58-year-old woman with a posterior neck mass who underwent fine-needle aspiration of the lesion, with initial cytopathologic evaluation being consistent with metastatic squamous cell carcinoma. However, following excisional biopsy of the tumor, histopathologic evaluation revealed a pilomatricoma. Appreciation of the difficulty in cytologic classification of this benign tumor and its propensity for confusion with more aggressive tumors may help prevent unintended and unnecessary invasive procedures as a result of erroneous diagnoses.

Keywords

Pilomatricoma; neck mass; squamous cell carcinoma.

Introduction

Pilomatricoma is a benign neoplasm derived from cells of the hair follicle matrix and typically presents as a painless, firm, dermal or subcutaneous nodule in the head or neck. They are the second most common superficial mass found in children and are typically diagnosed based on clinical presentation in pediatric patients, however pilomatricomas can occur in patients of any age^[1]. When an adult or elderly patient presents with a firm subcutaneous nodule, particularly in the neck, diagnosis based on clinical findings may be complicated by an appropriate suspicion for a primary malignant neoplasm or metastatic lymphadenopathy^[2]. While histologic confirmation of pilomatricoma following surgical excision of the lesion is relatively straightforward, preoperative diagnosis is complicated by the propensity for falsely positive malignant interpretation of cytopathologic samples. This may lead to preoperative diagnoses of malignancy, typically squamous cell carcinoma (SCC), but less frequently basal cell carcinoma, cutaneous or metastatic neuroendocrine carcinoma and, rarely, melanoma^[3]. It is crucial that otolaryngologists include pilomatricoma in the differential diagnosis of a subcutaneous mass of the head and neck, and be aware of the potential for erroneous cytopathologic interpretation of these lesions in order to avoid overly aggressive surgical intervention for a benign neoplasm.

Here we review the case of a middle-aged woman with a pilomatricoma in the posterior neck originally mistaken for metastatic SCC. We present her case along with a review of the relevant literature, and a discussion of the clinical, cytopathologic, and histological features of pilomatricoma, with emphasis on the pitfalls of cytopathologic diagnosis.

Patient presentation

A 58-year-old woman presented to our tertiary care medical center with a posterior neck mass she had first noted 4 months earlier. The patient had a history of multiple cutaneous basal cell carcinomas of the upper extremities previously excised, but had no prior history of cutaneous lesions of the head or neck. She was entirely asymptomatic and her past medical history was negative for tobacco or alcohol use, family history of malignancies, and radiation exposure. Physical examination was notable for a 0.5-cm firm, mobile, subcutaneous nodule in the left posterior neck, level five. A thorough head and neck examination was negative for other cutaneous or aerodigestive lesions and there was no other palpable lymphadenopathy. Indirect fiberoptic nasopharyngolaryngoscopic examination was negative and a full-body skin examination by her dermatologist was negative for suspicious cutaneous lesions.

The cytopathology department at our tertiary referral center reviewed slides from a fine-needle aspiration (FNA) biopsy of the posterior neck mass. Cytopathologic analysis was initially reported as consistent with metastatic SCC. A positron emission tomography (PET)/computed tomography (CT) scan showed the left posterior subcutaneous neck mass to be 0.5 cm and fluorodeoxyglucose (FDG) avid with a standardized uptake value (SUV) of 2.6, consistent with metastasis to an occipital node. This PET/CT, subsequent magnetic resonance imaging (MRI) of the head and neck, and CT scan of the chest, abdomen, and pelvis failed to identify a primary tumor or distant metastases.

The patient's case was discussed during our multidisciplinary tumor board, which prompted re-examination of the FNA sample. Aspirate smears displayed dispersed squamous cells with dense cytoplasm and prominent nucleoli, as well as ghost cells in a background of neutrophils, lymphocytes, and scattered multinucleated giant cells. The findings were considered consistent with a pilomatricoma on re-examination.

Following the re-interpretation of the FNA specimen, neck dissection was deferred and the patient underwent panendoscopy with excisional biopsy of the posterior neck mass. Panendoscopy was unremarkable and final histopathologic analysis of the specimen confirmed the diagnosis of pilomatricoma with negative margins of resection. The patient has now been followed closely with serial clinical examinations for 2 years; her surgical site has healed well and there are no signs of recurrent disease.

Discussion

Malherbe and Chenantais first described pilomatricoma in 1880 as a benign subcutaneous neoplasm thought to arise from sebaceous glands, and thus it came to be known as a calcifying epithelioma of Malherbe^[4]. Later this neoplasm was renamed pilomatrixoma or pilomatricoma to reflect its resemblance to cells of the hair follicle matrix^[4].

Pilomatricomas most commonly present in children with over 60% occurring in the first two decades of life and 84% prior to the age of 30 years, however cases have been reported in all ages^[1,5]. There is a female predominance with a male to female ratio of 1:1.6^[5]. Typical clinical presentation is of a non-tender, firm, asymptomatic, subcutaneous mass of the head or neck, which grows slowly over months to years. Frequently the lesion is adherent to the overlying skin. Adherence to deep structures has not been reported and should suggest an alternative malignant diagnosis. Occasionally the epidermis overlying the mass displays a blue or red discoloration and ulceration of the skin is rarely noted. Typically the diameter of the lesion ranges from 1 to 3 cm, however larger masses have been reported^[3].

The clinical differential diagnosis for pilomatricoma in children includes epidermal inclusion cyst, ossifying hematoma, branchial remnant, preauricular sinus, lymphadenopathy, giant cell tumor, chondroma, dermoid cyst, degenerating fibroxanthoma, foreign body reaction, and osteoma cutis^[2]. When located in the preauricular area, pilomatricomas can also imitate lesions of the parotid gland^[2]. In adults and elderly patients, the clinical differential diagnosis also includes metastatic lymphadenopathy as well as primary cutaneous neoplasms. An exceedingly rare malignant variant of these lesions has been reported. Pilomatrix carcinoma is more common

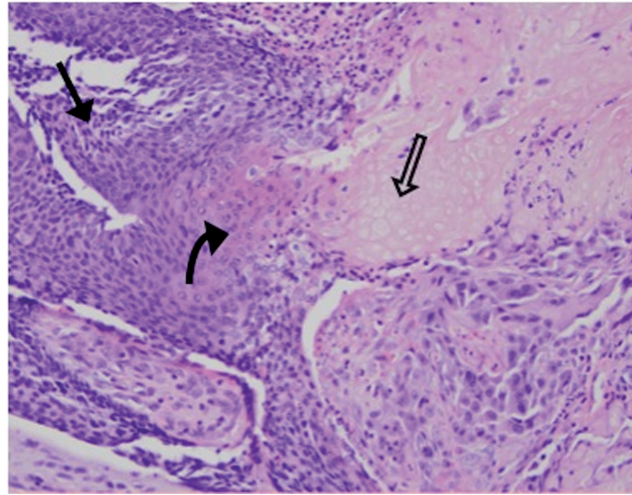


Fig. 1. Hematoxylin and eosin stained histologic section at 400× magnification from the surgically excised posterior neck mass. Characteristic features of pilomatricoma are demonstrated with ghost cells (open arrow), squamous cells (curved solid arrow), and surrounding basaloid cells (solid arrow).

in older men and has a tendency for local invasion and recurrence^[6]. Imaging of pilomatricomas is usually of limited utility, but typically shows a sharply demarcated subcutaneous lesion with various amounts of calcification. The imaging findings can be mistaken for a pathological lymph node. Imaging is occasionally useful in distinguishing a pilomatricoma of the preauricular region from superficial parotid neoplasms^[2]. Ultrasonography may be of some use in evaluation of these superficial lesions as it could provide evidence against the diagnosis of a metastatic lymph node by delineating the depth of the lesion, which in the case of a pilomatricoma would be within the dermal layer of the skin.

Histological diagnosis of pilomatricoma is rarely difficult, with characteristic findings showing islands of ghost cells (also known as shadow cells) surrounded by basaloid cells (Fig. 1). Ghost cells are considered the pathognomonic feature and are anucleate squamous cells with a central unstained region. It is thought that ghost cells represent abortive hair follicles^[3]. The surrounding basaloid cells exhibit deeply staining basophilic nuclei with scant cytoplasm and indistinct cell borders^[2]. Ghost cell areas can show peripheral calcification and a granulomatous reaction including foreign body giant cells^[5].

Treatment for pilomatricoma involves surgical excision en block with or without resection of the overlying skin, depending on the degree of adherence of the tumor to the epidermis. It is widely accepted in the literature that if complete excision is performed recurrence is highly unlikely, with a reported incidence of 0 to 3%^[2].

Preoperative FNA biopsy of a lesion suspected to be a pilomatricoma is frequently obtained, particularly in older patients for whom the clinical presentation is less straightforward than in children and carcinoma is a diagnostic consideration. However, misclassification of pilomatricoma based on cytologic evaluation is common and misdiagnosis as SCC, epidermal inclusion cysts and giant cell lesions is possible^[7]. Previous reports have highlighted the potential for error with one review showing a rate of correct preoperative cytopathologic diagnosis of only 38%, with 25% of cases thought to be suspicious for malignancy prior to resection^[3]. Features including a highly cellular specimen, presence of primitive-appearing cells with high nuclear to cytoplasmic ratio, prominent nucleoli, nuclear molding and mitotic figures are usually associated with a malignant process. A background rich in debris and inflammatory cells can be confused with the necroinflammatory debris characteristic of malignancy^[8]. Misinterpretation of FNA specimens has been attributed to non-representative samples, predominance of one cellular component over the others in a sample, or lack of awareness of the cytological features of pilomatricoma by pathologists^[7]. Some studies have shown that ghost cells are more apparent on cell block sections obtained from FNA samples than on smears. Thus, preparation of cell blocks from all FNA samples where there is clinical suspicion for pilomatricoma has been recommended. Other studies have found difficulty with identifying ghost cells on alcohol fixed smears, whereas these were more easily identifiable on air-dried smears^[5].

The constellation of cytologic features that support a diagnosis of pilomatricoma include fibrillar pink material surrounding clusters of basaloid cells, anucleate ghost cells, calcification,

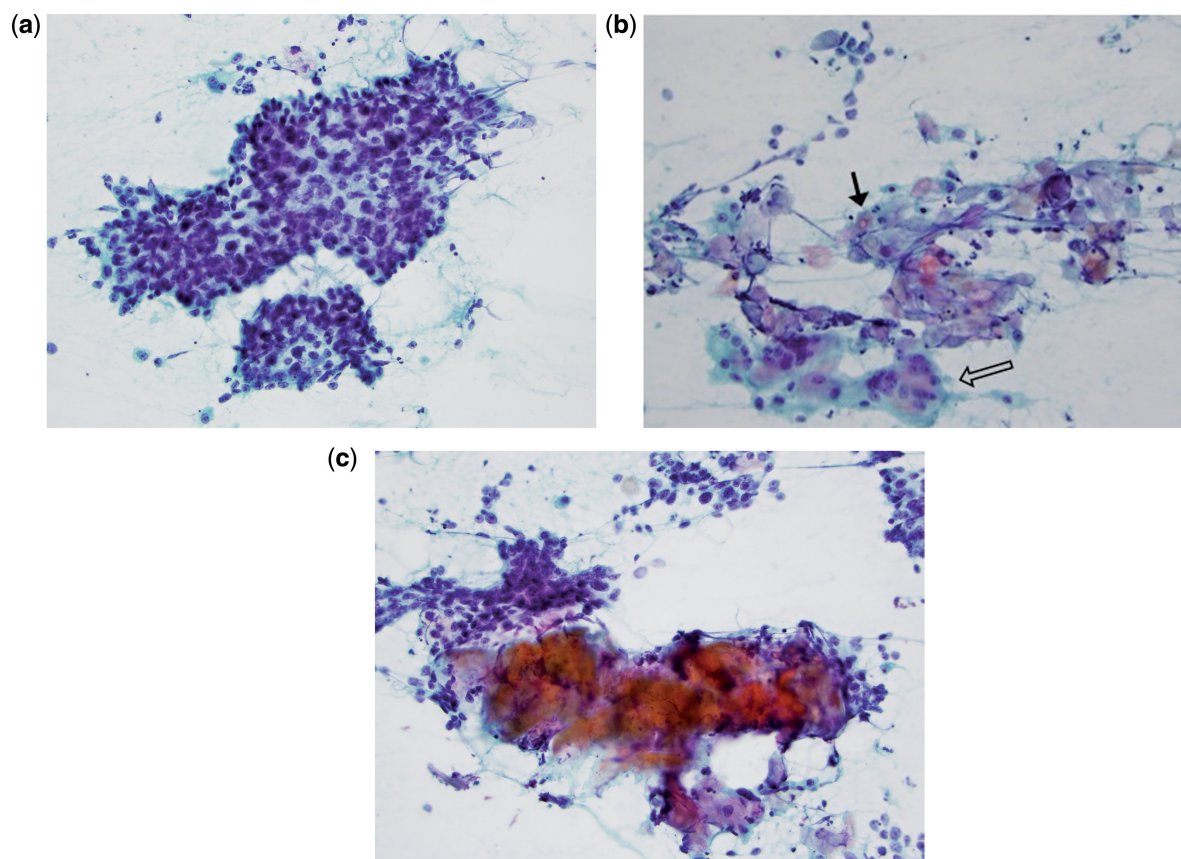


Fig. 2. Cytological smears from FNA of the posterior neck mass at 400 \times magnification showing characteristic findings: (a) basaloid cells with deeply staining nuclei and scant cytoplasm; (b) anucleate ghost cells (solid arrow), multinucleated giant cells (open arrow); and (c) keratin debris, which is non-specific for pilomatricoma, but in combination with basaloid and ghost cells helps to support the diagnosis.

multinucleated giant cells, and keratin debris (Fig. 2). These features help in the distinction between this lesion and malignant tumors^[5]. Awareness of the potential pitfalls in cytologic diagnosis of pilomatricoma may help otolaryngologists correlate any discrepant data in the setting of a clinically indolent lesion. Effective communication and collaboration with their pathology colleagues can assist the clinician in avoidance of unnecessarily aggressive treatment of this benign neoplasm.

Teaching points

1. Pilomatricoma may pose difficulty in preoperative diagnosis on cytological analysis, especially when it presents in an adult patient.
2. Cytological analysis of FNA samples can be misinterpreted for malignant neoplasms, with SCC being the most common misdiagnosis.
3. These patients benefit from a thorough workup and multidisciplinary discussion of the clinical history, imaging studies and pathology to provide pathologists with the appropriate clinical context for cytological analysis.
4. Awareness by both the otolaryngologist and cytopathologist of the clinical presentation of pilomatricoma in the workup of a subcutaneous mass of the head and neck is crucial to the avoidance of unnecessarily morbid treatments for this benign lesion. Table 1 summarizes the clinical, histologic, and cytologic features of pilomatricoma and when this diagnosis should strongly be considered^[5,8].
5. Knowledge by the otolaryngologist of the potential for misdiagnosis on FNA sampling should prompt communication with the cytopathologist when the diagnosis is a consideration.
6. Cytopathologists should consider the diagnosis of pilomatricoma on FNA samples when ghost cells, primitive-appearing basaloid cells with high nuclear/cytoplasmic ratios, multinucleated giant cells, calcification, or nucleated squamous cells are observed.

Table 1. Clinical, cytologic, and histologic features of pilomatricoma

Patient Population	Children	Adults and the elderly
Clinical features	Non-tender, solitary nodule, firm, subcutaneous or intradermal, mobile on underlying tissues, closely associated with or fixed to overlying epidermis. Most commonly found in head and neck, often preauricular	
Differential diagnosis based on clinical examination	Epidermal inclusion cyst, ossifying hematoma, branchial remnant, preauricular sinus, lymphadenopathy, giant cell tumor, chondroma, dermoid cyst, degenerating fibroanthoma, foreign body reaction, osteoma cutis, parotid mass	Same as pediatric, however, also includes: metastatic lymphadenopathy, primary cutaneous SCC, basal cell carcinoma, Merkel cell carcinoma, and small cell carcinoma
Cytopathologic clues that suggest pilomatricoma	Ghost cells ^a , primitive-appearing basaloid cells with high nuclear to cytoplasmic ratio, multinucleated giant cells, calcification, and nucleated squamous cells with evenly dispersed chromatin	
Cytopathologic features that confound analysis	Highly cellular FNA specimen, presence of primitive-appearing cells with high nuclear to cytoplasmic ratio, prominent nucleoli, nuclear molding, and a background rich in debris and inflammatory cells, which can be confused with the necroinflammatory debris characteristic of malignancy. Misdiagnosis is most commonly due to non-representative samples with predominance of one cellular component over the others (especially when ghost cells absent)	
Common misdiagnoses	Epidermal inclusion cyst	Epidermal inclusion cyst, SCC, basal cell carcinoma, giant cell lesions
Histologic features confirming diagnosis	Well demarcated and often surrounded by a connective tissue capsule, cutaneous location, uniform basaloid cells with high nuclear to cytoplasmic ratios surrounding central islands of enucleated ghost cells. Calcification and giant cell reaction are found at periphery of ghost cell islands	

^aPathognomonic finding for the diagnosis of pilomatricoma.

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