Pilomatrical Carcinoma: Case Report and Review of the Literature

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Pilomatrical carcinoma is a rare malignant tumor that originates from hair matrix cells. Pilomatrical carcinoma may arise de novo as a solitary lesion, or through transformation from its benign counterpart, pilomatrixoma. Differentiation between pilomatrixoma and pilomatrical carcinoma requires close histologic examination and often is difficult. Although uncommon, pilomatrical carcinoma has the potential to metastasize; therefore, prompt diagnosis and appropriate management is essential.

Pilomatrical carcinoma is the malignant counterpart of pilomatrixoma, a benign cutaneous tumor originating from the hair matrix. It is a rare, aggressive tumor with a high probability of recurrence after simple excision, and the potential to metastasize.

We report a case of a 56-year-old white man diagnosed with pilomatrical carcinoma. The patient presented with a 2-month history of an enlarging asymptomatic growth on the cheek. Physical examination revealed a 2-cm, well-demarcated, nontender, moveable, hard subcutaneous nodule on the right mandible (Figure 1). No skin changes or lymphadenopathy was noted. The clinical diagnosis strongly favored a calcified epidermoid cyst or other benign adnexal tumor. An excisional biopsy was performed at the request of the patient.

Sections were evaluated histologically and revealed a multifragmented biopsy of dermal and subcutaneous tissue containing basaloid proliferation with collections of ghost cells, typical of pilomatrixoma (Figure 2).

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In some areas, the lesional cells are relatively bland and noninfiltrative appearing.

However, this case also shows areas with larger more squamoid appearing cells with atypical features, including large nuclei with prominent nucleoli as well as areas of infiltrative appearing cells, features highly concerning for malignancy (Figure 3). In the infiltrative appearing area, there is dense stromal sclerosis associated with highly atypical squamoid and spindle cells, with several mitotic figures found within these cells (Figure 4). In many areas of the biopsy, there is granulomatous inflammation, hemorrhage, and granulation tissue consistent with a reaction to ruptured material from the tumor (Figure 5). While the latter findings often are seen in ruptured pilomatrixoma, the infiltrative areas with atypical spindle cells would not be expected in a benign pilomatrixoma, and the findings are most consistent with a diagnosis of malignant pilomatrixoma (pilomatrical carcinoma).

Multiple laboratory tests using immunohistochemical stains, including p63, cytokeratin 5/6, synaptophysin, p53, and Ki-67 also were reviewed. The tumor cells were strongly and diffusely positive for p63, highlighting the nuclei of the infiltrative and spindle cells, which is positive in most primary cutaneous malignancies including adnexal carcinomas. In addition, results of cytokeratin 5/6 staining also were moderately positive within lesional cells, including the

Figure 1. A 56-year-old white man with a 2-cm, well-demarcated, nontender, moveable, hard subcutaneous nodule present on the right mandible with no skin changes.

infiltrative-appearing spindle cells, which confirmed that these were epithelial, and not mesenchymal, cells. Results of synaptophysin staining were negative and not consistent with a neuroendocrine tumor such as Merkel cell carcinoma. Staining for p53 was weakly but diffusely positive throughout the tumor cell nuclei, including the infiltrative areas, a finding that also favored malignancy. In addition, Ki-67 positivity was high within the basaloid cells and also positive within many of the spindle cells, highlighting up to 10% of the entire lesion. Thus, the overall histologic and immunohistochemical findings supported the diagnosis of pilomatrical carcinoma.

COMMENT

Pilomatrixoma first was described in 1880 by Malherbe and Chenantais[1] as a *calcifying epithelioma* that was thought to originate from the sebaceous gland. In 1949, Lever and Griesemer[2] suggested that the actual origin of the tumor was the hair matrix.[3] Thus, the appropriate term *pilomatrixoma* was adopted, synonymous with calcifying epithelioma of Malherbe, which also is commonly used.

Clinically, the tumor is described as a solitary, slow growing, asymptomatic, dermal or subcutaneous mass that most commonly is found in the posterior neck, upper back, and preauricular area. Duration of tumors prior to surgery has been reported to range from 4 months to 10 years.[3] Pilomatrical carcinomas have been reported to range in size from 0.5 cm to 20 cm, with a mean of 3.95 cm, which is slightly larger than its benign counterpart, pilomatrixoma.[4] The consistency

of the tumors may vary from soft and friable to firm. They may have red, yellow, white, and tan skin changes. Lesions cannot reliably be distinguished based solely on clinical appearance, and frequently are mistaken for epidermal cysts. The diagnosis of pilomatrical malignancy is made exclusively by careful histologic evaluation.

Pilomatrical carcinoma has a potential to metastasize in about 10% of cases.[5] Cases of metastasis to the lung, bones, and lymphatics, as well as invasion into the cranial vault, have been reported.[3]

EPIDEMIOLOGY

The epidemiology of pilomatrical carcinoma differs from pilomatrixomas. Pilomatrixomas more often are seen in women (female to male ratio of 3:1) and tend to occur in patients younger than 20 years. The mean age of patients diagnosed with pilomatrixoma is 8.7 years, ranging from 8 months to 19 years.[5] Pilomatrixomas occur most commonly on the head, followed by the upper extremities, neck, trunk, and lower extremities.[3] Involvement of the face has been reported in the frontal, temporal, cheek, periorbital, and preauricular regions.[6] Pilomatrical carcinomas are more predominant in men and more often middle-aged or elderly adults. The mean age of patients with pilomatrical carcinoma is 48 years, ranging from 2 to 88 years, and in this population are more common in the posterior neck, upper back, and preauricular area.[3,4] Approximately 60% of tumors have been located on the head, among which half are in the preauricular region.[7]
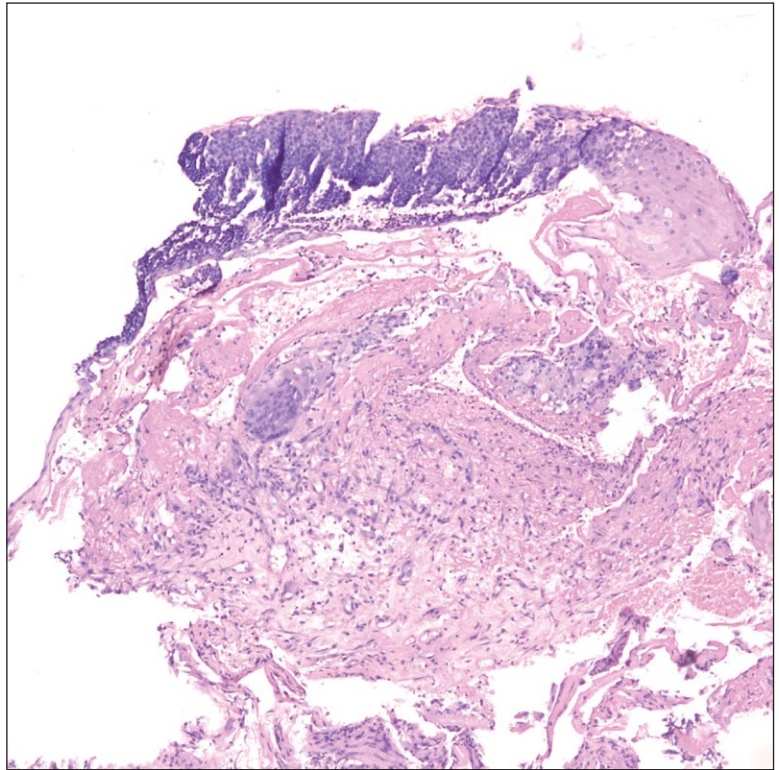
Figure 2. A fragmented biopsy specimen revealed basaloid proliferation and ghost cells (H&E, original magnification ×100).
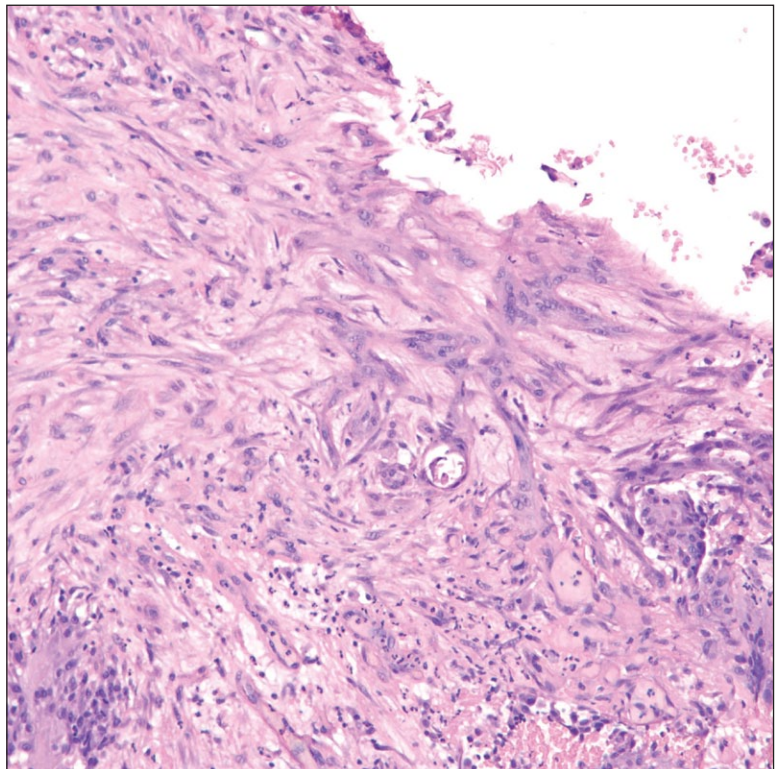

Figure 3. Infiltrative squamoid and spindle cells with atypical features, including large nuclei with prominent nucleoli (H&E, original magnification ×400).

HISTOPATHOLOGY

The histologic differential diagnosis of pilomatrical carcinoma includes pilomatrixoma, squamous cell carcinoma, trichoepithelioma, lymphoepitheliomalike carcinoma of the skin, and mixed tumors of the skin.[7] Pilomatrical carcinomas have the characteristic features of epithelial islands of pleomorphic basaloid cells with vesicular nuclei and prominent nucleoli. Shadow or
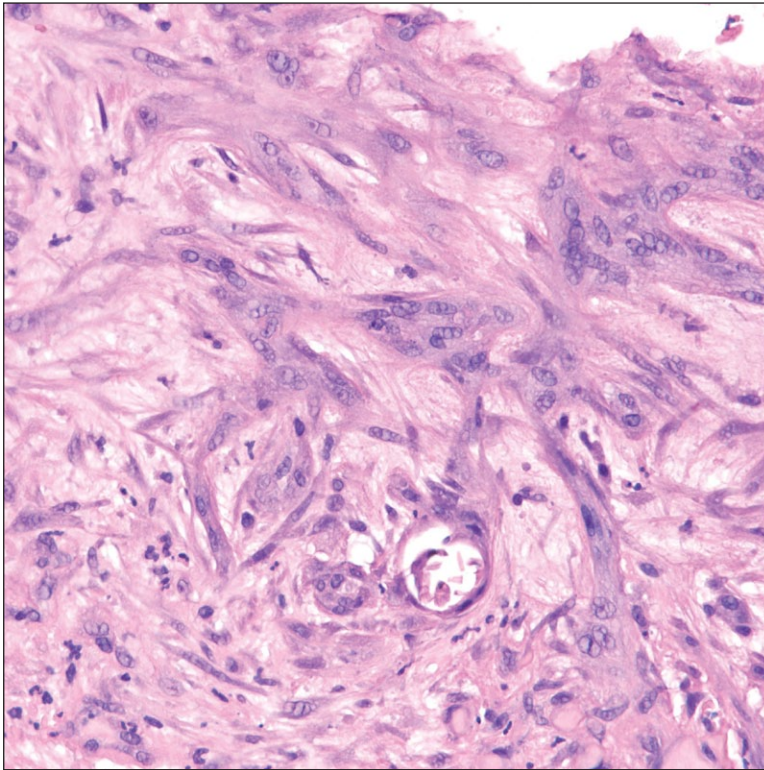
Figure 4. Stromal sclerosis, highly atypical squamoid and spindle cells, and several mitotic figures (H&E, original magnification ×400).
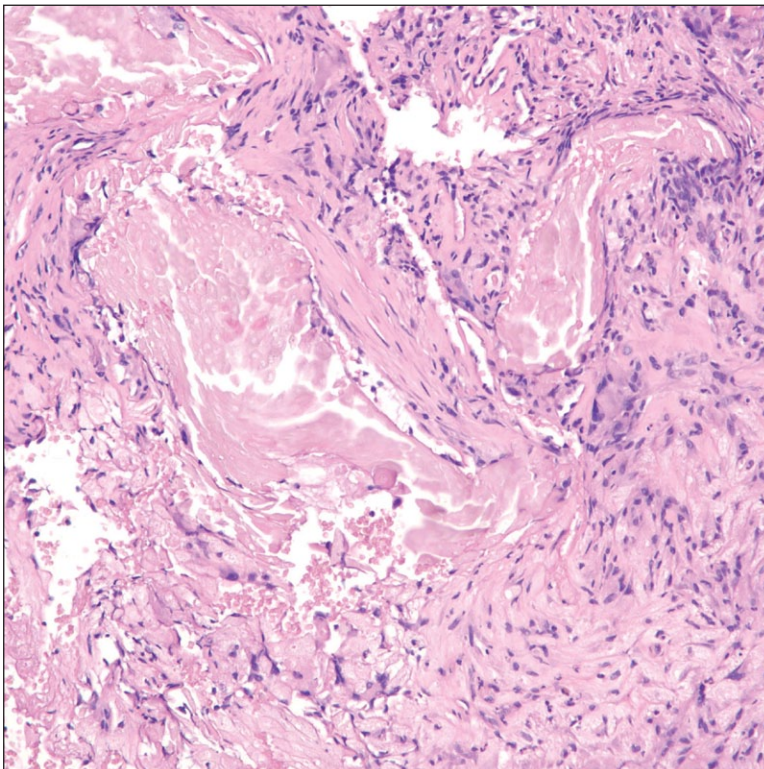

Figure 5. Areas of hemorrhage and granulation tissue surrounded by infiltrative atypical spindle cells (H&E, original magnification ×400).

ghost cells, along with zones of necrosis with surrounding stromal desmoplasia also are observed. The basaloid cells have deeply basophilic oval or round nuclei and are found at the periphery of the islands. A transition zone of retained nuclei from basaloid cells to the anucleate, eosinophilic shadow cells often is seen.[8] Tumor necrosis usually is present, as well as frequent atypical mitotic figures. Basaloid cells may infiltrate the entire dermis and

extend into the subcutaneous fat, deep fascia, and skeletal muscle. In pilomatrical carcinoma, the shadow cells tend to form a nested pattern, instead of the flat sheet-like pattern usually observed in benign pilomatrixomas.[3] Histologic criteria for pilomatrical carcinoma include vessel invasion, mitotic index, apoptotic count, as well as molecular markers of cell death and adhesion.[9]

IMMUNOHISTOCHEMISTRY

Immunohistochemical studies have not definitively distinguished the markers that differentiate pilomatrixomas from pilomatrical carcinomas. Lazar et al[10] studied a series of 15 pilomatrical carcinomas and 13 benign pilomatrixomas to assess expression of β_1-catenin using immunohistochemical staining and DNA sequencing of exon 3 from the B1-catenin gene, *CTNNB1*, the defect that leads to the expression of pilomatrixomas. β-Catenin is a downstream effector in the Wnt signaling pathway that signals for proliferation and differentiation. Mutations in the *CTNNB1* gene encoding β-catenin are present in both benign and malignant neoplasms. All cases showed nuclear localization of β-catenin, mutations on exon 3, as well as expression of nuclear cyclin D1. However, 2 pilomatrical carcinomas exhibited accumulation of p53, which was absent in all 13 benign pilomatrixomas.[10] Past studies also have reported high constant expression of CD44v6 and P-cadherin.[11]

TREATMENT

The most widely reported treatment for pilomatrical carcinoma is wide local excision with histologically confirmed clear margins. Because pilomatrical carcinoma is identifiable by hematoxylin and eosin stain, Mohs micrographic surgery also is an excellent treatment option. Currently, there is no consensus on surgical management, and standard excisional margins have not been defined.[8] Adjuvant radiation therapy may be necessary postexcision. Chemotherapy has been used in cases of extensive tumor invasion and in cases of metastasis.

Appropriate laboratory testing includes liver function tests, calcium levels, and chest x-ray examination. If aggressive local invasion is suspected, a computed tomography scan or magnetic resonance imaging should be performed to define tumor extension.[7] Past studies have found that the radiologic findings of pilomatrixoma typically demonstrate a well-circumscribed lesion with homogeneous or sandlike calcifications on plain radiograph and computed tomography studies.[12] Niwa et al[4] reported a case of pilomatrical carcinoma of the axilla, which demonstrated a diffuse inhomogeneous mass with cystic changes on magnetic resonance imaging. Areas of low signal intensity corresponded to calcifications, while the inhomogeneous signal intensities related to varying degrees of tumor proliferation. High signal intensity was attributable to cystic spaces forming in areas of tumor necrosis.

Pilomatrical carcinoma is a rare malignant form of pilomatrixoma, which arises from hair matrix cells. Careful histologic evaluation is necessary to distinguish benign pilomatrixoma from pilomatrical carcinoma. Pilomatrical carcinoma may arise de novo or from a preexisting benign pilomatrixoma, which may be clinically indistinguishable. In cases where previously excised or curetted pilomatrixomas recur, a reexcision with careful histologic evaluation is indicated.[7]

Pilomatrical carcinoma occurs more often in middle-aged to older individuals, more commonly in men, and has a predilection for the posterior neck, upper back, and preauricular area. Pilomatrical carcinomas frequently recur; however, treatment with wide local excision or Mohs micrographic surgery has been shown to lower the rate of recurrence.[4,5]

Distant metastases have been reported in up to 10% of cases.[5] Due to the potential for metastasis, prompt diagnosis followed by wide local excision or Mohs micrographic surgery and close clinical and radiologic follow-up is recommended.

REFERENCES

1. Malherbe A, Chenantais J. Note sur l'epitheliome calcifie des glandes sebaces. *Prog Med*. 1880;826-837.
2. Lever WF, Griesemer RD. Calficying epithelioma of Malherbe; report of 15 cases, with comments on its differentiation from calcified epidermal cyst and on its histogenesis. *Arch Derm Syphilol*. 1949;59:506-518.
3. Sau P, Lupton GP, Graham JH. Pilomatrix carcinoma. *Cancer*. 1993;71:2491-2498.
4. Niwa T, Yoshida T, Doiuchi T, et al. Pilomatrix carcinoma of the axilla: CT and MRI features. *Br J Radiol*. 2005;78:257-260.
5. Scheinfeld N. Pilomatrical carcinoma: a case in a patient with HIV and hepatitis C. *Dermatol Online J*. 2008;14:4.
6. Yencha MW. Head and neck pilomatricoma in the pediatric age group: a retrospective study and literature review. *Int J Pediatr Otorhinolaryngol*. 2001;57:123-128.
7. Barbosa A, Guimaraes N, Sadigursky M. Pilomatrix carcinoma (malignant pilomatricoma): a case report and review of literature. *Anais Brasileiros de Dermatologia*. 2000;75:581-585.
8. Sassmannshausen J, Chaffins M. Pilomatrix carcinoma: a report of a case arising from a previously excised pilomatrixoma and a review of the literature. *J Am Acad Dermatol*. 2001;44(suppl 2): 358-361.
9. Omidi AA, Bagheri R, Tavassolian H. Pilomatrix carcinoma with subsequent pulmonary metastases: a case report. *Tanaffos*. 2006;5:57-60.
10. Lazar AJ, Calonje E, Grayson W. Pilomatrix carcinomas contain mutations in *CTNNB1*, the gene encoding beta-catenin. *J Cutan Pathol*. 2005;32:148-157.
11. Bassarova A, Nesland JM, Sedloev T, et al. Pilomatrix carcinoma with lymph node metastes. *J Cutan Pathol*. 2004;31:330-335.
12. De Beuckeleer LH, De Schepper AM, Neetens I. Magnetic resonance imaging of pilomatricoma. *Eur Radiol*. 1996;6:72-60. ■