Growing Nodule on the Parietal Scalp

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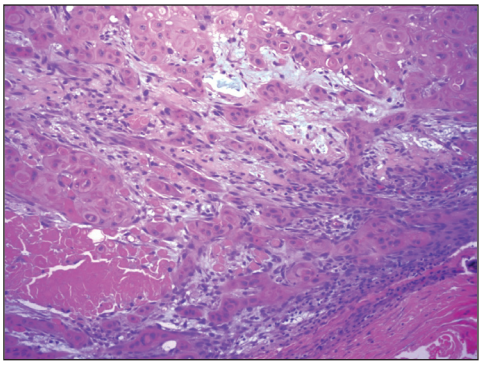
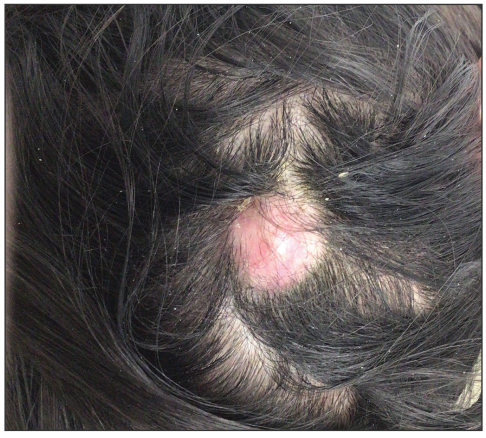


H&E, original magnification ×20



A 38-year-old woman with no notable medical history presented to the dermatology department with a firm enlarging nodule on the scalp of many years' duration. The patient noted there was no drainage or bleeding. Physical examination revealed a mobile, 2.5-cm, subcutaneous nodule on the right parietal medial scalp. An excisional biopsy was performed.

THE BEST **DIAGNOSIS IS:**

a. malignant proliferating trichilemmal tumor
b. pilomatrixoma
c. proliferating trichilemmal cyst
d. squamous cell carcinoma with cystic features
e. verrucous cyst

PLEASE TURN TO PAGE 220 FOR THE DIAGNOSIS

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The authors have no financial disclosures to report.

The eFigures are available in the Appendix online at www.mdedge.com/cutis.

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Cutis. 2025 December;116(6):215, 220-221, E1. doi:10.12788/cutis.1309

THE **DIAGNOSIS:** Malignant Proliferating Trichilemmal Tumor

Biopsy revealed a squamous epithelium with cystic changes, trichilemmal differentiation, squamous eddy formation, keratinocyte atypia, focal necrotic changes, and a focus of atypical keratinocytes invading the dermis (Figure 1). Based on these findings, a diagnosis of malignant proliferating trichilemmal tumor (MPTT) was made.

Malignant proliferating trichilemmal tumor is a rare adnexal tumor that develops from the outer root sheath of the hair follicle. It often arises due to malignant transformation of pre-existing trichilemmal cysts, but some cases occur de novo.[1] Malignant transformation is thought to start from a trichilemmal cyst in an adenomatous histologic stage, progressing to a proliferating trichilemmal cyst (PTC) in an epitheliomatous phase, ultimately becoming carcinomatous with MPTT.[2-4] This transformation has been categorized into 3 morphologic groups to predict tumor behavior, including benign PTCs (curable by excision), low-grade malignant PTCs (minor risk for local recurrence), and high-grade malignant PTCs (risk for regional spread and metastasis with cytologic atypical features and potential for aggressive growth).[1]

More commonly observed in women in the fourth to eighth decades of life, MPTT may manifest as a fast-growing, painless, solitary nodule or as a progressively enlarging nodule at the site of a previously stable, long-standing lesion. Malignant proliferating trichilemmal tumor manifests frequently on the scalp, face, or neck, but there are reports of MPTT manifesting on the trunk and even as multiple concurrent lesions.[1-4] The variability in clinical presentation and the potential to be mistaken for benign conditions makes excisional biopsy essential for diagnosis of MPTT. Histopathology classically demonstrates trichilemmal keratinization, a high mitotic index, and cellular atypia with invasion into the dermis.[4] Malignant transformation frequently follows a prior history of trauma to the area or local inflammation.

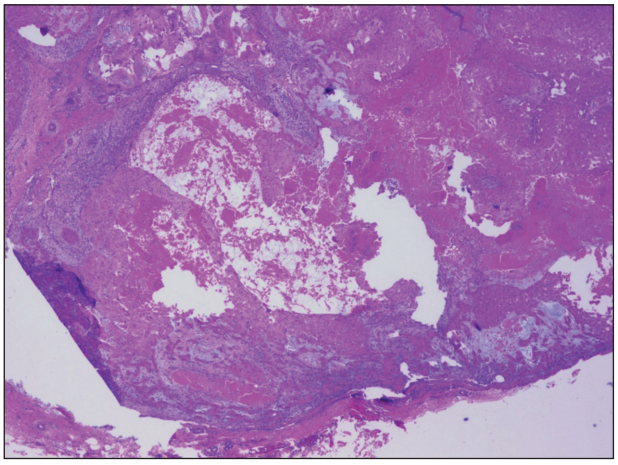


FIGURE 1. Malignant proliferating trichilemmal tumor. Lobulated intradermal mass composed of a squamous epithelium with cystic changes, squamous eddy formation, keratinocyte atypia, trichilemmal differentiation, and focal necrotic changes. Note the nests of atypical keratinocytes invading the surrounding dermis (H&E, original magnification ×4).

Given the locally aggressive nature of MPTT, our patient was referred to a Mohs micrographic surgeon. While both wide excision with tumor-free margins and Mohs micrographic surgery are accepted surgical procedures for MPTT, there is no consensus in the literature on a standard treatment recommendation. Following surgery, close monitoring is needed for potential recurrence and metastases intracranially to the dura and muscles,[5] as well as to the lungs.[6] Further imaging using computed tomography or positron emission tomography can be ordered to rule out metastatic disease.[4]

Pilomatrixomas are benign neoplasms that arise from hair matrix cells and have been associated with *catenin beta-1* gene mutations, as well as genetic syndromes and trauma.[7] Clinically, pilomatrixomas manifest as solitary, firm, painless, slow-growing nodules that commonly are found in the head and neck region. This tumor has a slight predominance in women and occurs frequently in adolescent years. The overlying skin may appear normal or show grey-bluish discoloration.[8] Histopathology shows basaloid cells resembling primitive hair matrix cells with an abrupt transition to shadow cells composed of transformed keratinocytes without nuclei and calcification.[7-8] This tumor can be differentiated by the presence of basaloid and shadow cells with calcification on histopathology, while MPTT will show atypical, mitotically active squamous cells with trichilemmal keratinization (Figure 2).

Proliferating trichilemmal cyst is a variant of trichilemmal cyst (TC) arising from the outer root sheath cells of the hair follicle. While TCs usually are slow growing and benign, the proliferating variant can be more aggressive with malignant potential. Patients often present with a solitary, well-circumscribed, rapidly growing nodule on the scalp. The lesion may be painful, and ulceration can occur, exposing the cystic contents. Histopathologically, PTCs resemble TCs with trichilemmal keratinization but also exhibit notable epithelial proliferation within the cystic space.[9] While there can be considerable histopathologic overlap between PTC and MPTT—including extensive trichilemmal keratinization, variable atypia, and mitotic activity—PTC typically should not demonstrate invasion into the surrounding soft tissue or the degree of high-grade atypia, brisk mitoses, or necrosis seen in MPTT (eFigure 1).[1] Immunohistochemistry may help distinguish

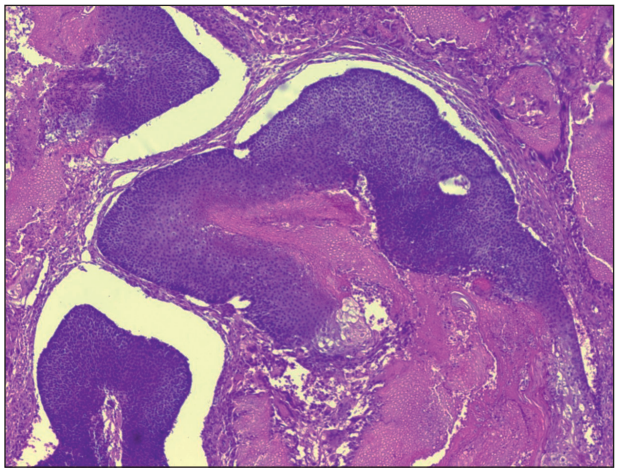


FIGURE 2. Pilomatrixoma. Basophilic matrical cells with scant cytoplasm and hyperchromatic nuclei with occasional normal mitoses transitioning to eosinophilic shadow/ghost cells without nuclei. There often is surrounding granulomatous inflammation with giant cell formation (H&E; original magnification ×10).

PTC from MPTT and squamous cell carcinoma (SCC).[10-11] The pattern of Ki-67 and p53 expression may be helpful with classification of PTC/MPTT into the 3 groups (benign, low-grade malignant, and high-grade malignant) proposed by Ye et al.[1] Other investigators have suggested that Ki-67 expression may correlate potential for recurrence and clinical prognosis.[12] Expression of CD34 (a marker that supports outer root sheath origin) might favor PTC/MPTT over SCC; however, cases of CD34-negative MPTT have been reported, particularly those with poorly differentiated histopathology.

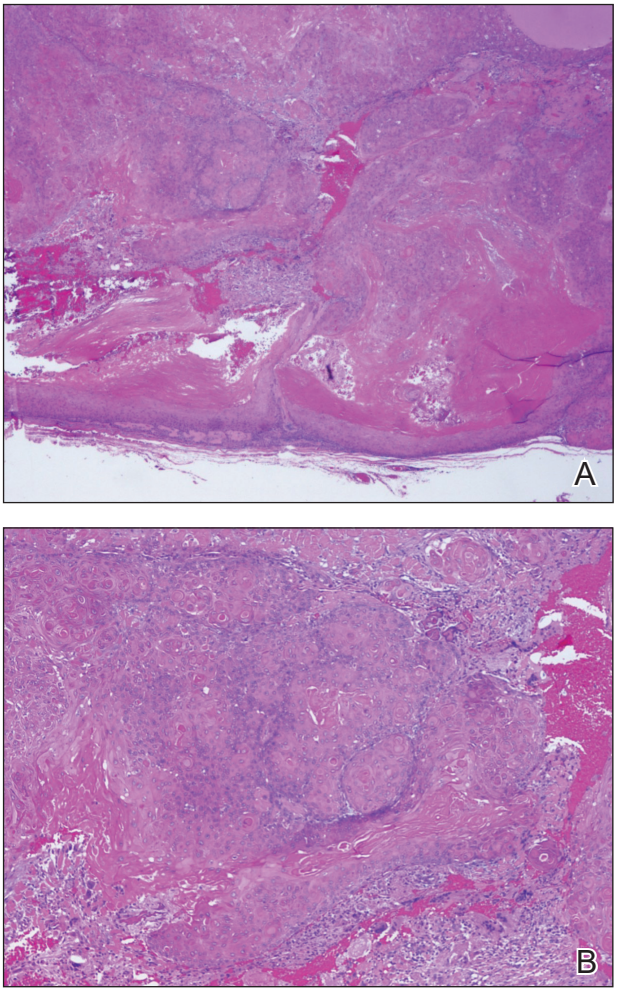
Squamous cell carcinoma with cystic features is a histologic variant of SCC characterized by cystlike spaces containing malignant squamous epithelial cells.[13] Squamous cell carcinoma with cystic features can manifest as a firm nodule with ulceration similar to MPTT or PTC but also can mimic a benign cyst.[14] The diagnosis of invasive SCC with cystic features typically is straightforward and characterized by cords and nests of atypical keratinocytes extending into the dermis with areas of cystic architecture (eFigure 2). While both SCC with cystic features and MPTT may show cystic histopathologic architecture, MPTT typically shows areas of PTC, whereas SCC with cystic features lacks such areas.

Verrucous cysts refer to infundibular cysts or less commonly pilar cysts or hybrid pilar-epidermoid cysts that exhibit superimposed human papillomavirus (HPV) cytopathic changes. Clinically, a verrucous cyst manifests as a single, asymptomatic, slow-growing, firm lesion most commonly manifesting on the face and back. Histopathologically, the cyst wall may show acanthosis, papillomatosis, hypergranulosis with coarse keratohyalin granules, and koilocytic changes (eFigure 3). These histopathologic features are believed to be induced by secondary HPV infection. While HPV-related change, characterized by koilocytic alteration, papillomatosis, and verruciform hyperplasia, more commonly affects epidermal cysts, occasionally trichilemmal (pilar) cysts are involved. In these cases, verrucous cysts should be distinguished from MPTT. Verrucous cysts may contain rare normal mitotic figures, but do not contain atypical mitosis, marked cellular pleomorphism, or an infiltrating pattern similar to MPTT.[15]

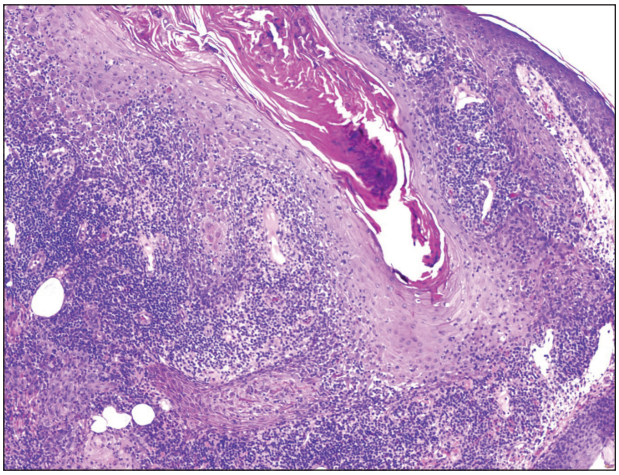
REFERENCES

1. Ye J, Nappi O, Swanson PE, et al. Proliferating pilar tumors: a clinicopathologic study of 76 cases with a proposal for definition of benign and malignant variants. *Am J Clin Pathol*. 2004;122:566-574. doi:10.1309/0XLEGFQ64XYJU4G6
2. Saida T, Oohara K, Hori Y, et al. Development of a malignant proliferating trichilemmal cyst in a patient with multiple trichilemmal cysts. *Dermatologica*. 1983;166:203-208. doi:10.1159/000249868
3. Rao S, Ramakrishnan R, Kamakshi D, et al. Malignant proliferating trichilemmal tumour presenting early in life: an uncommon feature. *J Cutan Aesthet Surg*. 2011;4:51-55. doi:10.4103/0974-2077.79196
4. Kearns-Turcotte S, Thériault M, Blouin MM. Malignant proliferating trichilemmal tumors arising in patients with multiple trichilemmal cysts: a case series. *JAAD Case Rep.* 2022;22:42-46. doi:10.1016/j.jdcr.2022.01.033
5. Karamese M, Akatekin A, Abaci M, et al. Unusual invasion of trichilemmal tumors: two case reports. *Modern Plastic Surg.* 2012;2:54-57. doi:10.4236/MPS.2012.23014
6. Lobo L, Amonkar AD, Dontamsetty VV. Malignant proliferating trichilemmal tumour of the scalp with intra-cranial extension and lung metastasis-a case report. *Indian J Surg.* 2016;78:493-495. doi:10.1007/s12262-015-1427-0
7. Jones CD, Ho W, Robertson BF, et al. Pilomatrixoma: a comprehensive review of the literature. *Am J Dermatopathol*. 2018;40:631-641. doi:10.1097/DAD.0000000000001118
8. Sharma D, Agarwal S, Jain LS, et al. Pilomatrixoma masquerading as metastatic adenocarcinoma. A diagnostic pitfall on cytology. *J Clin Diagn Res*. 2014;8:FD13-FD14. doi:10.7860/JCDR/2014/9696.5064
9. Valerio E, Parro FHS, Macedo MP, et al. Proliferating trichilemmal cyst with clinical, radiological, macroscopic, and microscopic orrelation. *An Bras Dermatol*. 2019;94:452-454. doi:10.1590/abd1806-4841.20198199
10. Joshi TP, Marchand S, Tschen J. Malignant proliferating trichilemmal tumor: a subtle presentation in an African American woman and review of immunohistochemical markers for this rare condition. *Cureus*. 2021;13:E17289. doi:10.7759/cureus.17289
11. Gulati HK, Deshmukh SD, Anand M, et al. Low-grade malignant proliferating pilar tumor simulating a squamous-cell carcinoma in an elderly female: a case report and immunohistochemical study. *Int J Trichology*. 2011;3:98-101. doi:10.4103/0974-7753.90818
12. Rangel-Gamboa L, Reyes-Castro M, Dominguez-Cherit J, et al. Proliferating trichilemmal cyst: the value of ki67 immunostaining. *Int J Trichology*. 2013;5:115-117. doi:10.4103/0974-7753.125599
13. Asad U, Alkul S, Shimizu I, et al. Squamous cell carcinoma with unusual benign-appearing cystic features on histology. *Cureus*. 2023;15:E33610. doi:10.7759/cureus.33610
14. Alkul S, Nguyen CN, Ramani NS, et al. Squamous cell carcinoma arising in an epidermal inclusion cyst. *Baylor Univ Med Cent Proc*. 2022;35:688-690. doi:10.1080/08998280.2022.207760
15. Nanes BA, Laknezhad S, Chamseddin B, et al. Verrucous pilar cysts infected with beta human papillomavirus. *J Cutan Pathol*. 2020;47:381-386. doi:10.1111/cup.13599

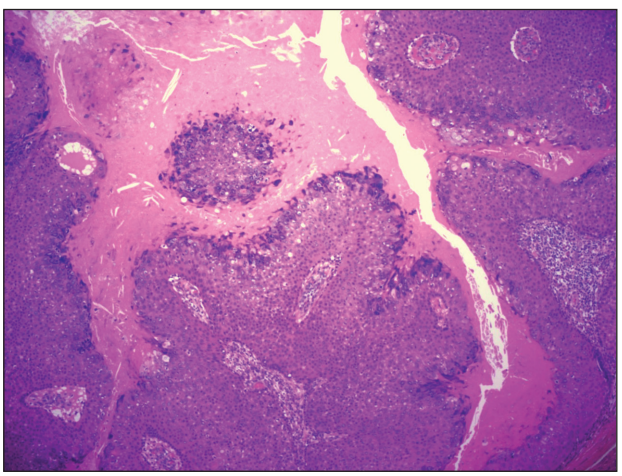
APPENDIX



eFIGURE 1. Proliferating trichilemmal cyst. A, Well-circumscribed dermal tumor with a pushing border that exhibits abrupt trichilemmal keratinization and has extensive epithelial proliferation within the center of the cystic space (H&E, original magnification ×4). B, Epithelial proliferation with minimal cytologic atypia (H&E, original magnification ×10).



eFIGURE 2. Squamous cell carcinoma with cystic changes. Invasive cords and nests of atypical keratinocytes extend into the dermis with an overlying epidermal connection. The center of the tumor shows cystic architecture (H&E; original magnification ×10).



eFIGURE 3. Verrucous cyst. Note the cyst wall with acanthosis, papillomatosis, orthokeratosis and parakeratosis, hypergranulosis with coarse keratohyalin granules, and koilocytic changes (H&E; original magnification ×10).