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A trichogenic tumor with aggressive features initially diagnosed as basal cell carcinoma

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Abstract
Trichoblastic carcinoma is a rare carcinoma often arising in a pre-existing trichoblastoma. It may resemble basal cell carcinoma, posing a diagnostic challenge. Trichoblastic carcinoma is divided into low-grade and high-grade tumors. Low-grade tumors resemble basal cell carcinomas and are therefore synonymous in some classifications [3, 4]. Similar features such as peripheral palisading of basophilic cells and cells with uniform, ovoid nuclei are often seen in low-grade trichoblastic carcinoma and make distinguishing these lesions from BCC very difficult [5, 6]. Overlap in certain histological features can also be explained in part by the common embryological origin of both BCC and trichoblastic carcinoma. Several studies suggest that BCC, trichoblastic carcinoma, and trichoblastoma all arise from the developing fetal hair follicle [1, 7, 8]. In a study by Schirren et al. [8] examining 30 trichoblastomas and 17 nodular BCCs, both lesions exhibited morphological and immunohistochemical features that were consistent with the fetal hair follicle. The trichoblastic carcinoma described by Regauer et al. [9] demonstrated proliferations of small basaloid cells with large, round nuclei, arising around pre-existing trichogenic structures, underscoring the relationship that trichoblastic carcinoma has to the embryonic hair follicle. Sellheyer et al. observed that BCC, which was described as synonymous with trichoblastic carcinoma, strongly expressed epithelial cell adhesion molecule (Ep-CAM), in a pattern that was similar to the embryonic hair germ [3].

Keywords: basal cell carcinoma, trichoblastoma, trichoblastic carcinoma, trichogenic tumors, hair follicle, skin cancer, dermatopathology

Introduction
Trichoblastic carcinoma is a rare carcinoma often arising in a pre-existing trichoblastoma [1]. It may resemble basal cell carcinoma (BCC), posing a diagnostic challenge [2]. Trichoblastic carcinoma is divided into low-grade and high-grade tumors. Low-grade tumors resemble BCCs and are therefore synonymous in some classifications [3, 4]. Similar features such as peripheral palisading of basophilic cells and cells with uniform, ovoid nuclei are often seen in low-grade trichoblastic carcinoma and make distinguishing these lesions from BCC very difficult [5, 6]. Overlap in certain histological features can also be explained in part by the common embryological origin of both BCC and trichoblastic carcinoma. Several studies suggest that BCC, trichoblastic carcinoma, and trichoblastoma all arise from the developing fetal hair follicle [1, 7, 8]. In a study by Schirren et al. [8] examining 30 trichoblastomas and 17 nodular BCCs, both lesions exhibited morphological and immunohistochemical features that were consistent with the fetal hair follicle. The trichoblastic carcinoma described by Regauer et al. [9] demonstrated proliferations of small basaloid cells with large, round nuclei, arising around pre-existing trichogenic structures, underscoring the relationship that trichoblastic carcinoma has to the embryonic hair follicle. Sellheyer et al. observed that BCC, which was described as synonymous with trichoblastic carcinoma, strongly expressed epithelial cell adhesion molecule (Ep-CAM), in a pattern that was similar to the embryonic hair germ [3].

High-grade trichoblastic carcinoma is often reported in the literature as a lesion with greater malignant potential than BCC that develops in the setting of long-standing trichoblastoma, a benign tumor of follicular germinative epithelium [1]. Some authors use the term malignant trichoblastoma to describe high-grade trichoblastic carcinoma arising from trichoblastoma [9]. Other terms used to describe malignant trichogenic tumors include trichoblastic...
sarcoma, which arises from the stroma, and trichoblastic carcinosarcoma, which arises from the both the epidermis and stroma [6, 10]. The differential diagnosis for high-grade trichoblastic carcinoma is broad and may include Merkel cell carcinoma or other cutaneous adnexal tumors such as sebaceous carcinoma [11, 12]. In a clinical setting, high-grade trichoblastic carcinomas typically present on the scalp in older individuals with a mean age of 75 [8, 13]. However, tumors arising in the setting of Brooke-Spiegler syndrome may present at an earlier age [1, 14]. On histology, high-grade trichoblastic carcinoma is often associated with worrisome and aggressive features including necrosis, irregular nuclei, and a high mitotic rate [1, 9, 14].

In long-standing follicular skin lesions that have recently undergone rapid growth and present with atypical gross morphology, a higher index of suspicion for an aggressive trichogenic tumor is essential. We present a case of a lesion that on shave biopsy showed features consistent with BCC, but on full excision, possessed more worrisome characteristics of trichoblastic carcinoma.

Case Synopsis
A 73-year-old female presented to our clinic with an asymptomatic scalp nodule that had been present more than 30 years, but had recently undergone rapid growth. On examination, the lesion of concern appeared as a 3cm subcutaneous, mobile nodule with an overlying 1 cm pink nodule (Figure 1). On dermoscopy, the overlying nodule displayed scattered specks of brown pigment. An oblique shave biopsy was performed to obtain tissue samples from both morphologies.

Biopsy revealed findings consistent with pigmented basal cell carcinoma, nodular pattern (Figure 2). An underlying cystic lesion was noted and interpreted as a follicular cyst. Subsequent excision was performed and revealed features that were concerning for trichoblastic carcinoma (Figure 3). A multilobular proliferation of basaloid cells within a dense fibrous stromal background involving the dermis and subcutis was identified. Atypical and worrisome features included brisk mitotic activity and comedo-like necrosis (Figure 3B). Additionally, the tumor abutted the deep and peripheral margins. Therefore, Mohs micrographic surgery was

Figure 1. Image of the gross lesion, located on the scalp.

Figure 2. Initial shave biopsy demonstrating several features of basal cell carcinoma. On low magnification (A) nests of basaloid cells with few mitotic figures were observed to be present within a myxoid stroma. Representative images of superficial (B) and deep (C) sections were also taken at higher magnification. H&E, image A, 10×; images B and C, 20×.
Case Presentation

Our patient presented with a skin lesion that was initially diagnosed as a BCC on biopsy but on excision showed features concerning for trichoblastic carcinoma (Figure 3). The case demonstrates the need for a higher level of caution in interpretation of pathology of long-standing scalp neoplasms with sudden rapid growth. Despite some of the pathologic features of BCC seen on initial biopsy, complete excision revealed more worrisome features consistent with trichoblastic carcinoma, which, unlike BCC, has been reported to have a higher potential for distant metastasis and death [9]. Although initial pathology was consistent with BCC, the >30 years duration, sudden growth, and atypical clinical features, including a subcutaneous component, should raise suspicion for an alternate diagnosis.

Based on the histologic features of the excised lesions it is possible that the trichoblastic carcinoma and overlying basal cell carcinoma represent distinct entities. As seen in Figure 3, the underlying trichoblastic carcinoma has no connection with the epidermis, whereas the basal cell carcinoma seen in the shave biopsy in Figure 2 directly abuts the epidermis. Furthermore, among the sections that were obtained, there was no evidence of direct connection between the basal cell carcinoma and the trichoblastic carcinoma. Histologic features classically seen in high-grade trichoblastic carcinoma such as high mitotic activity, extensive necrosis, and lack of continuity with the epidermis [6] were seen in the trichoblastic carcinoma upon excision, but not on the BCC seen upon shave biopsy [1, 9].

However, it is also possible that the lesion seen on shave biopsy (Figure 2) actually represents part of the underlying trichoblastic carcinoma. Low-grade trichoblastic carcinoma demonstrates several features consistent with BCC including pseudo-palisading of basaloid cells [9], rare mitoses, monomorphic nuclei, and absence of necrosis [1, 16] all of which were seen on the lesion captured by shave biopsy (Figure 2). On the other hand, the deeper lesion demonstrated brisk mitotic activity, dense fibrotic stroma, and comedo-like necrosis (Figure 3B), consistent with features previously reported in high-grade trichoblastic carcinomas [9, 15].

Considering that high grade trichoblastic carcinoma may resemble other malignant cutaneous adnexal tumors, the diagnosis of a high-grade tumor may rely on the identification of a pre-existing trichoblastoma.
or tricho-epithelioma. The dense fibrotic stroma seen upon excision may represent a perifollicular sheath similar to that of trichoblastoma (Figure 3B), [1]. Other features such as comedo-like necrosis and brisk mitotic activity (Figure 3B), seen in longstanding lesions with sudden, rapid growth are consistent with an aggressive trichogenic tumor [1, 9, 15].

Conclusion
Our report demonstrates that a higher index of suspicion must be exercised in the case of an atypical scalp lesion that has been present for many years and has recently undergone rapid growth. Trichogenic tumors present for extended durations of time that undergo a rapid increase in size have been noted in numerous cases to either demonstrate histologic features more concerning for malignancy [14, 15] or lead to presentation of a patient with multiple systemic metastases [1, 9]. Our case highlights the necessity to biopsy the entire lesion whenever possible to provide dermatopathologists with a complete view and assist in guiding treatment.

References