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. High-grade tumors, which commonly present on the scalp in older individuals or in patients with Brooke-Spiegler syndrome, have been associated with a higher potential for distant metastasis and death. We present a case in which a 73-year-old female had a long-standing scalp nodule for over 30 years that rapidly increased in size. The patient's lesion was initially diagnosed as basal cell carcinoma on shave biopsy, but upon excision, revealed features concerning for trichoblastic carcinoma such as brisk mitotic activity and comedo-like necrosis. Sudden change in an atypical scalp lesion that has been present for many years should increase suspicion for an atypical trichogenic tumor, such as trichoblastic carcinoma.

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

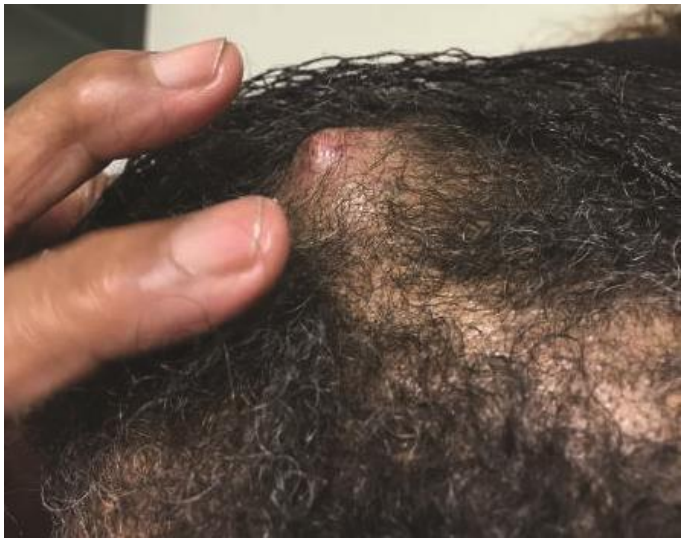

Figure 1. *Image of the gross lesion, located on the scalp.*

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

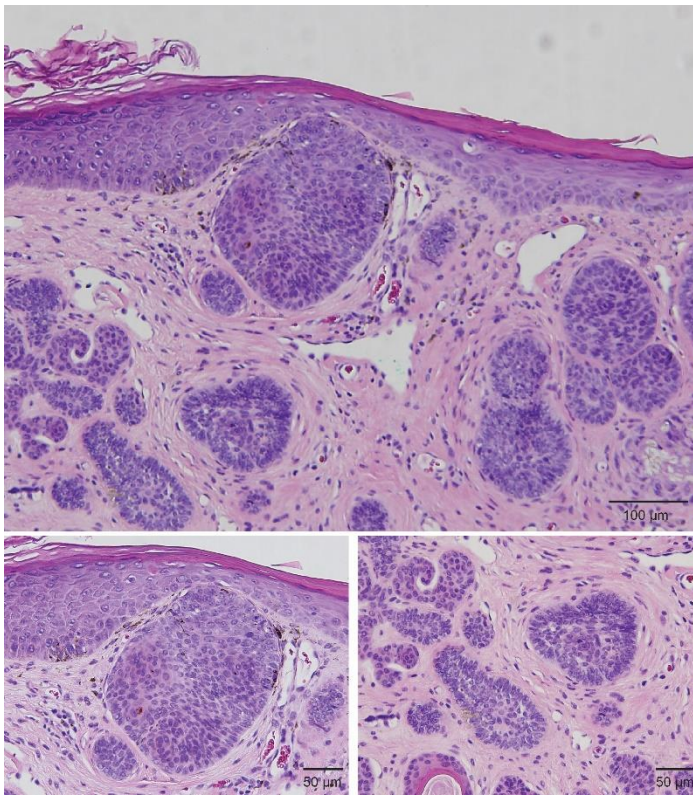

Figure 2. *Initial shave biopsy demonstrating several features of basal cell carcinoma. On low magnification (**A**) nests of basaloid cells with few mitotic figures were observed to be present within a myxoid stroma. Representative images of superficial (**B**) and deep (**C**) sections were also taken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

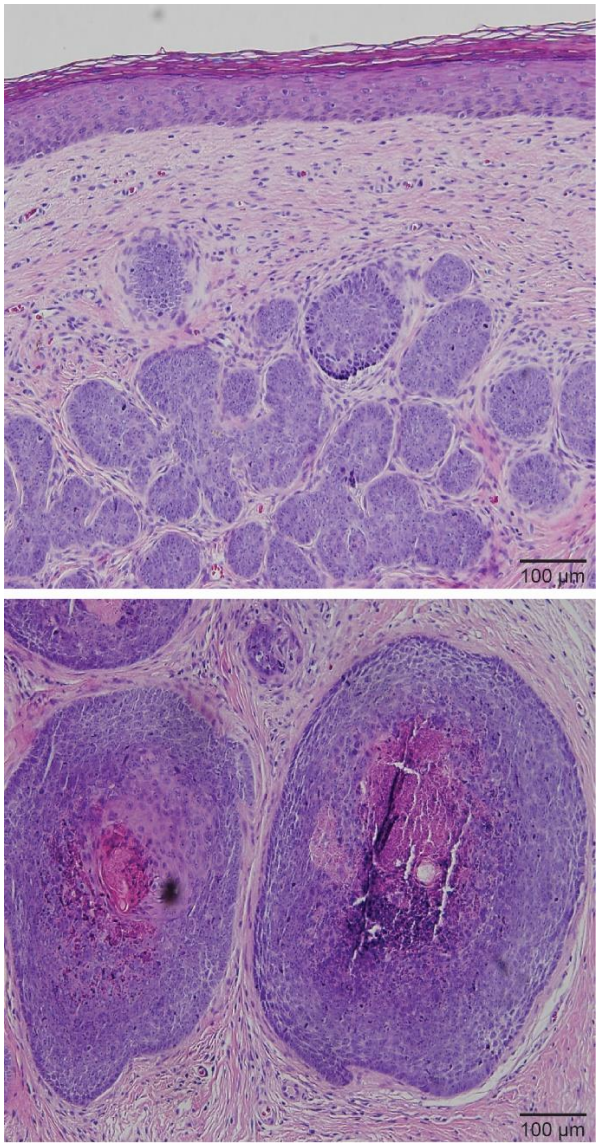

Figure 3. *Excisional biopsy demonstrating a lesion that extends from the dermis (A) into the sub-cutis and contained numerous mitotic figures, dense fibrotic stroma, and comedo-like necrosis (B), H&E stain, images A and B, 10×.*

recommended to ensure complete removal, which was performed without complication and with clear margins.

Case Discussion

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 long-standing 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

1. Schulz T, Proske S, Hartschuh W, et al. High-grade trichoblastic carcinoma arising in trichoblastoma: a rare adnexal neoplasm often showing metastatic spread. *Am J Dermatopathol.* 2005;27(1):9-16. [PMID: 15677970].
2. Ackerman AB, Reddy VB, Soyer HP. A critique of current classifications of proliferations with follicular differentiation. In: Ackerman AB, Reddy VB, Soyer HP, editors. Neoplasms with follicular differentiation. 2nd ed. New York: Ardor Scribendi; 2001. p. 95-105.
3. Sellheyer K, Krahl D. Basal cell (trichoblastic) carcinoma common expression pattern for epithelial cell adhesion molecule links basal cell carcinoma to early follicular embryogenesis, secondary hair germ, and outer root sheath of the vellus hair follicle: A clue to the adnexal nature of basal cell carcinoma? *J Am Acad Dermatol.* 2008;58(1):158-67. [PMID: 18158927].
4. Tebcherani AJ, de Andrade HF, Jr., Sotto MN. Diagnostic utility of immunohistochemistry in distinguishing trichoepithelioma and basal cell carcinoma: evaluation using tissue microarray samples. *Mod Pathol.* 2012;25(10):1345-53. [PMID: 22684216].
5. Hua C, Velter C, Osio A, et al. Locally Aggressive Trichoblastic Tumours (Low-grade Trichoblastic Carcinomas): Clinicopathological Analysis and Follow-up. *Acta Derm Venereol.* 2018;98(1):126-7. [PMID: 28421230].
6. Kazakov DV, Kempf W, Michal M. Low-grade trichoblastic carcinosarcoma of the skin. *Am J Dermatopathol.* 2004;26(4):304-9. [PMID: 15249861].
7. Rofagha R, Usmani AS, Vadmal M, Hessel AB, Pellegrini AE. Trichoblastic carcinoma: a report of two cases of a deeply infiltrative trichoblastic neoplasm. *Dermatol Surg.* 2001;27(7):663-6. [PMID: 11442619].
8. Schirren CG, Rutten A, Kaudewitz P, et al. Trichoblastoma and basal cell carcinoma are neoplasms with follicular differentiation sharing the same profile of cytokeratin intermediate filaments. *Am J Dermatopathol.* 1997;19(4):341-50. [PMID: 9261468].
9. Regauer S, Beham-Schmid C, Okcu M, Hartner E, Mannweiler S. Trichoblastic carcinoma ("malignant trichoblastoma") with lymphatic and hematogenous metastases. *Mod Pathol.* 2000;13(6):673-8. [PMID: 10874673].
10. Rosso R, Lucioni M, Savio T, Borroni G. Trichoblastic sarcoma: a high-grade stromal tumor arising in trichoblastoma. *Am J Dermatopathol.* 2007;29(1):79-83. [PMID: 17284968].
11. Jakobiec FA, Mendoza PR. Eyelid sebaceous carcinoma: clinicopathologic and multiparametric immunohistochemical analysis that includes adipophilin. *Am J Ophthalmol.* 2014;157(1):186-208.e2. [PMID: 24112633].
12. Ratner D, Nelson BR, Brown MD, Johnson TM. Merkel cell carcinoma. *J Am Acad Dermatol.* 1993;29(2 Pt 1):143-56. [PMID: 8335732].
13. Mann B, Salm R, Azzopardi JG. Pilar tumour: a distinctive type of trichilemmoma. *Diagn Histopathol.* 1982;5(3):157-67. [PMID: 7140503].
14. Kirby JS, Siebert Lucking SM, Billingsley EM. Trichoblastic carcinoma associated with multiple familial trichoepithelioma. *Dermatol Surg.* 2012;38(12):2018-21. [PMID: 22849566].
15. Sau P, Lupton GP, Graham JH. Trichogerminoma. Report of 14 cases. *J Cutan Pathol.* 1992;19(5):357-65. [PMID: 1282133].
16. Schirren CG, Burgdorf WH, Sander CA, Plewig G. Fetal and adult hair follicle. An immunohistochemical study of anticytokeratin antibodies in formalin-fixed and paraffin-embedded tissue. *Am J Dermatopathol.* 1997;19(4):335-40. [PMID: 9261467].