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Case Report

A Diagnosis of Trichoblastic Carcinoma Using Immunohistochemistry

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INTRODUCTION

Trichoblastic carcinoma is a rare cutaneous adnexal neoplasm that primarily develops de novo (87.1%), though it also can arise from a preexisting tumor, such as a trichoblastoma (12.9%).[1] Trichoblastic carcinoma often is misidentified as basal cell carcinoma and is challenging to distinguish based solely on histopathology. From June 2000 to October 2020, only 93 cases have been documented in the literature.[1,2] Notably, nearly one in four cases were initially misdiagnosed as basal cell carcinoma.[1] This frequent misclassification suggests that many cases of trichoblastic carcinoma may go undetected. Given the differences in prognosis and metastatic potential between trichoblastic carcinoma and basal cell carcinoma, a more systematic approach to trichoblastic carcinoma identification is critical. In this report, we detail the diagnostic method used to identify trichoblastic carcinoma in an unusually young patient who presented with a tumor measuring 12×13 cm.

CASE REPORT

A 38-year-old man presented to the clinic with a large, ulcerative lesion on the right parietal scalp (Figure 1). The patient first noticed the mass at age 35, and it grew periodically over the next three years. The lesion was painful, with frequent bleeding and serosanguinous discharge. He had no notable medical history, was not on any medications, and had not received prior treatment for the lesion. A shave biopsy initially identified the lesion as a moderately well-differentiated squamous cell carcinoma. Consequently, the patient was referred for wide excision and staging of the malignancy. Pre-operative computed tomography (CT) imaging suggested metastasis to a right occipital lymph node. A wide excision, including a partial thickness craniectomy, was performed, with the tumor measuring 12×13 cm. Surgical margins of the excised tumor were negative for carcinoma. Although an attempt was made to excise the suspicious occipital lymph node during the procedure, the specimen submitted to pathology contained no lymph tissue.

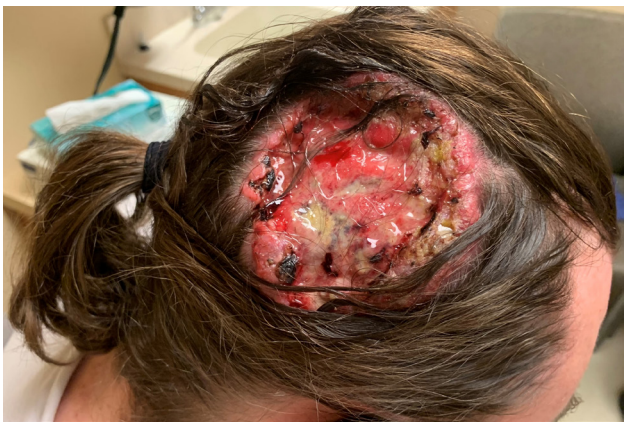

Figure 1. Trichoblastic carcinoma. Preoperative gross image. Large ulcerative mass measuring 12×13 cm.

Histopathologic examination of the excised tumor revealed a deeply infiltrative Clark Level V neoplasm arising as a predominantly dermal/subcutaneous nodule from non-sun-damaged scalp skin (Figure 2). No evidence of a precursor lesion was found, and extensive sectioning was negative for basal cell carcinoma. The neoplasm extended into the subcutaneous panniculus down to the fascia and was composed of irregular aggregates of basaloid cells with areas of central necrosis and peripheral spindle cell stroma. It was continuous with a surface proliferation of cells forming sinus tracts and keratin. Primitive hair follicle-like structures also were observed at the periphery of the surface proliferation. Immunohistochemical staining showed neprilysin (CD10) positivity in the stroma and CD10 negativity in the carcinomatous epithelium. Full immunohistochemistry (IHC) results are detailed in Table 1.

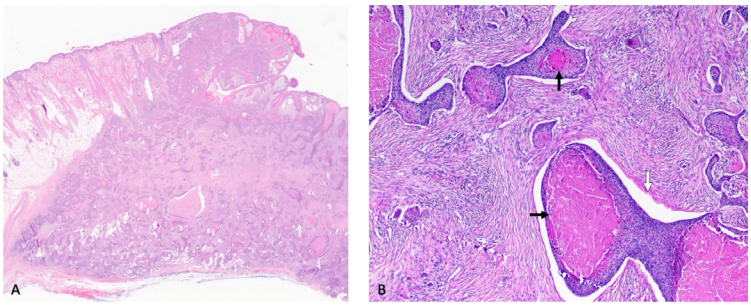

Figure 2. Low-power image showing infiltrative trichoblastic carcinoma invading the subcutaneous panniculus to the level of the fascia (A) High-power image demonstrates infiltrative tumor islands (black arrows) composed of basaloid cells demonstrating comedonecrosis and clefting (white arrow) with the morphologically bland hair follicle-specific stroma (B) (A and B, hematoxylin and eosin stain; original magnifications: A, ×6; B, ×40).

Based on post-operative histopathologic and IHC findings, the initial diagnosis of squamous cell carcinoma was ruled out, and a diagnosis of de novo trichoblastic carcinoma was confirmed. The tumor was successfully excised without complications, and the patient underwent a six-week course of radiation therapy. At follow-up, treatment was well-tolerated, and a five-month post-operative CT scan with contrast of the head and neck showed no evidence of malignancy.

Table 1. Immunohistochemical staining of excised trichoblastic carcinoma.

Antibody	(+/-)
Cluster designation 10	(+) in peritumoral stroma; (-) in tumor epithelial cells
Antihuman epithelial antigen	(+), 4+
Cytokeratin 19	(+), 3+
Carcinoembryonic antigen	(-)
Epithelial membrane antigen	(-)
Androgen receptor	Mostly (-), 1+
p16 tumor suppressor protein	(+), 4+
Cytokeratin 7	(+), 3+
Adipophilin	(-)
GATA-binding protein 3	(+), 4+
Beta-Catenin	Membrane (+), Nuclear (-)
Calretinin	(-)

DISCUSSION

Trichoblastic carcinoma is a rare adnexal tumor that is often misdiagnosed as basal cell carcinoma. Distinguishing between these two conditions is crucial, as trichoblastic carcinoma can be significantly more aggressive, with a metastasis rate of up to 11%, compared to basal cell carcinoma, which has a metastasis rate of only 0.55%.[3,4] Despite their differences, trichoblastic carcinoma and basal cell carcinoma share similarities, including an average age of diagnosis of 65 years and a male predominance (66.7% vs. 54.8%).[2,5] While basal cell carcinoma predominantly occurs in White individuals (92.1%), racial and ethnic trends in trichoblastic carcinoma remain unclear due to limited data.[5] Trichoblastic carcinoma most commonly appears on the face, though it also can develop on the trunk, scalp, and extremities,[1] while basal cell carcinoma primarily is associated with sun exposure and typically manifests on the face, head, and neck.

Currently, there are no definitive clinical criteria for diagnosing trichoblastic carcinoma. It is described as an aggressive, sometimes painful tumor originating in the dermal or subcutaneous layer, growing as a solitary, poorly circumscribed, asymmetric mass.[2,6] A retrospective case review of 21 reports found that 95% of trichoblastic carcinoma cases were clinically misdiagnosed as basal cell carcinoma, highlighting the challenge of identifying trichoblastic carcinoma based on clinical presentation alone.[3] Therefore, biopsy is the gold standard for trichoblastic carcinoma diagnosis. Trichoblastic carcinoma and basal cell carcinoma can share several histopathologic features, such as basaloid cells with uniform, ovoid nuclei, lobular tumor nests, and peripheral palisading.[6-8] However, trichoblastic carcinoma is distinguished by a biphasic presentation with high mitotic activity, a deeply infiltrative growth pattern, central necrosis, hypercellular stroma, and the presence of primitive hair follicle-like structures.[9] These histopathologic differences can be subtle, contributing to the initial biopsy misclassification rate of 24.7%.[1] When histopathologic findings are inconclusive, cluster designation 10 (CD10) staining has proven highly effective in differentiating trichoblastic carcinoma from basal cell carcinoma.[10] Specifically, trichoblastic carcinoma shows CD10 positivity in the stroma and CD10 negativity in the carcinomatous epithelium, whereas basal cell carcinoma shows the opposite pattern.

In our patient's case, the differential diagnosis included basal cell carcinoma, squamous cell carcinoma, sebaceous carcinoma, and porocarcinoma. Squamous cell carcinoma is the second most common skin cancer in the United States, presenting with scaling, crusting, erythema, and ulceration, often progressing from precursor lesions like actinic keratoses.[11] It stains p63+, epithelial membrane antigen (EMA)+, and antihuman epithelial antigen (BerEP4)-.[12] Sebaceous carcinoma, another aggressive cutaneous adnexal neoplasm, differs from trichoblastic carcinoma in that it shows sebaceous gland rather than hair follicle differentiation and typically occurs in the orbital region, with extra-orbital cases presenting as yellowish nodules with ulceration.[13] Histopathologic features include small basaloid cells, nuclear palisading, central comedonecrosis with pagetoid spread, and spindle cell proliferation areas.[14] It stains EMA+, BerEP4-, and adipophilin+.[15] Porocarcinoma, an eccrine gland malignancy, often develops from a pre-existing eccrine poroma and presents as a nodular, sometimes ulcerated, fungating lesion.[16,17] Histopathology reveals basaloid cells with hyperchromatic nuclei and duct-like structures containing eosinophilic cuticular borders, with EMA+ and carcinoembryonic antigen (CEA)+ staining in the duct-like structures.[17]

Given the clinical ambiguity of trichoblastic carcinoma and its frequent misclassification as basal cell carcinoma, IHC is essential for accurately narrowing the differential diagnosis. Unfortunately, IHC staining is rarely used in trichoblastic carcinoma diagnosis, having been performed in only 31.2% of published cases.[2]

In our patient's case, we were able to lower our suspicion of basal cell carcinoma by staining for CD10, which revealed CD10+ hair follicle stroma and CD10- carcinomatous epithelium (Table 1). Staining for EMA was negative, effectively ruling out squamous cell carcinoma, sebaceous carcinoma, and porocarcinoma. Additionally, BerEP4+ staining further supported the exclusion of squamous cell carcinoma and sebaceous carcinoma, while negative adipophilin and CEA stains excluded sebaceous carcinoma and porocarcinoma, respectively. Although other biphasic neoplasms with follicular differentiation, such as trichoblastoma and trichoepithelioma, were considered in the differential diagnosis, their slow-growing, benign nature made trichoblastic carcinoma the most likely diagnosis.

CONCLUSIONS

In this case report, we discuss a 38-year-old man who presented with a large ulcerative lesion on the right parietal scalp, ultimately diagnosed as trichoblastic carcinoma. Immunohistochemistry proved to be a valuable tool in identifying this rare neoplasm, which was challenging to diagnose based on clinical presentation and initial biopsy alone. Although there are no established staining criteria for trichoblastic carcinoma, we hope the immunohistochemistry findings presented here contribute to the existing literature on trichoblastic carcinoma staining characteristics, encouraging more widespread use of immunohistochemistry in suspected cases, and aiding in the development of definitive diagnostic criteria.

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