



Trichoblastic Carcinoma: A Case Report and Literature Review of an Extremely Rare and Diagnostically Challenging Cutaneous Malignancy of the Hair Follicle

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Abstract

Trichoblastic carcinoma (TBC) is an extremely rare cutaneous malignancy of the hair follicle, first described in the literature in 1962 as a "primary neoplasm of the hair matrix" (1). Besides its rarity, TBC shares many clinical and histologic characteristics with basal cell carcinoma (BCC), making the diagnosis of TBC difficult to make. Many authors have described TBC as a malignant transformation of a benign trichoblastoma (TB), but a universal understanding of the pathophysiological origin of TBC has not been established (2, 3). We present a case of this uncommon tumor with the hope that this report will add to the small repertoire of available research, and aid clinicians in diagnosis and management of this rare tumor.

Keywords: Trichoblastic, Carcinoma, Cutaneous, Basal cell carcinoma, Stroma, Hair follicle neoplasm. Mitosis

Abbreviations

TBC: Trichoblastic Carcinoma. **BCC:** Basal Cell Carcinoma.
TB: Trichoblastoma. **TBCS:** Trichoblastic Carcinosarcoma

Introduction

Trichoblastic carcinoma (TBC) is a rare malignant skin adnexal tumor. The diagnosis is challenging as TBC shares many similarities with basal cell carcinoma (BCC) and other benign and malignant adnexal tumors. Cases of TBC have also been reported in a myriad of different settings including: Brooke-Spiegler Syndrome/Multiple Familial Trichoepithelioma, underlying nevus sebaceous, and past history of radiation therapy [4-6]. Rare cases of trichoblastic carcinosarcoma (TBCS) have also been reported as a biphasic, dermal based tumor with intertwined epithelial and sarcomatous components [7]. This lack of understanding has resulted in inconsistent terminology used to describe trichoblastic tumors with invasive growth patterns. A review of current literature has found terms such as "unusually aggressive TB," "malignant TB," "trichoblastic BCC," and "plaque variant of trichoblastic fibroma" used to describe TBC [8-10]. While no standard of care currently exists for the treatment of

TBC, it is important to distinguish TBC from other skin tumors with similar clinical presentations such as TB and BCC as TBC is typically aggressive and has a high propensity to metastasize and recur [11].

This case represents an extremely rare entity with very few published cases and reports available. Many other cases and literature reviews of this topic have cited less than 20 documented cases of TBC in the United States. Clinically, these tumors are often large and ulcerated, and present as a solitary nodule usually on the head/scalp, neck, or trunk, more commonly in elderly males [7]. At the present time, there is no clear recommendations on therapeutic management of TBC, though complete surgical resection with wide margins has typically been used as the primary treatment option, there are no recommendations for surgical safety margins or complimentary therapies [11]. We present a case of 63-year-old male patient who developed a recurrent lesion, initially thought to be a sebaceous cyst, but ultimately histologically diagnosed as a TBC. It is our hope that this report raises awareness of clinicians and pathologists to this uncommon tumor and that continued investigation drives further development of efficacious and safe treatments for improving patient outcomes.

Case Report

A 63-year-old male presented to his physician with a 5mm cystic mass on his right forearm. Approximately three years prior to this encounter, the patient had a similar cystic mass at the same location, which was removed and diagnosed as a benign sebaceous cyst. No initial biopsy of current mass was performed, and the mass was surgically removed and submitted for pathologic examination with clinical impression of rule out a recurrent benign sebaceous cyst. The specimen contained a skin fragment measuring 1.3cm x 0.8cm with 0.9cm of underlying subcutis tissue with no evidence of connection to the epidermis but with dermal and hypodermal infiltration. Grossly, the cut

Submitted: 26 September, 2020 | **Accepted:** 14 October, 2020 |
Published: 17 October, 2020

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Citation: Azevedo C, Varney J, Leyva K, White M, NDiTommaso M, et al. (2020) Trichoblastic Carcinoma: A Case Report and Literature Review of an Extremely Rare and Diagnostically Challenging Cutaneous Malignancy of the Hair Follicle. SM J Clin Pathol 4: 4.



surface revealed a 0.4cm oval cystic mass, which was submitted for histological evaluation (**Figure 1A**).

Cytohistologic examination showed epithelial lobules composed of basaloid-like epithelial cells with peripheral basophilic and central eosinophilic cytoplasm, prominent central keratinization with squamous pearls formation and a cellular stroma (**Figure 1B-C**). Scattered foci of necrosis and calcification were also noted. Tumor cells showed large oval nuclei with prominent nucleoli. Mitotic activity was easily identified with up to 6 mitosis/10 HPF (**Figure 1D**). The histomorphologic features were consistent with TBC of the skin and subcutis. The lesion was further described as an infundibulo-cystic variant. The surgical margins were free of tumor. A note was made by the pathologist that although the possibility of a carcinoma arising in a pre-existing benign cyst could not be excluded, the current excision showed no evidence of any benign cyst. There were no histological signs of underlying or associated TB.

Given that the surgical margins were free of tumor, the patient did not undergo any further surgical or adjuvant therapy. He underwent active surveillance in the outpatient setting for six years following the initial diagnosis and did not exhibit any signs of recurrence or metastasis. He was unfortunately lost to follow up after six years of surveillance.

Discussion

Given the rarity of TBC, much is still unknown about this malignant follicular neoplasm. A review of current literature does

not yield a universal understanding of the pathophysiology of this rare entity. Many authors describe TBC arising in the setting of malignant transformation of a benign TB, hence the synonymous name “malignant TB” reported by many authors; this was not the case in our patient [13]. Cases of TBC have also been reported in Brooke-Spiegler Syndrome/Multiple Familial Trichoepithelioma, in patients with underlying nevus sebaceous, and in patients with a past history of radiation therapy to the area [4-6]. TB have been described in the literature as an umbrella term for all benign adnexal tumors of follicular germ cells, including TB, trichofolliculoma, trichoadenoma, trichogerminoma, and many more [14, 15, 16]. *Patel et al.* describes TB as lesions with grossly benign features such as smooth symmetric growth patterns, sharp demarcation, and smooth borders. Additionally, *Patel et al.* documents the rare transformation of these benign tumors into malignant adnexal neoplasms such as TBC, trichilemmal carcinoma, and pilomatrix carcinoma [16]. No information regarding the rate of malignant transformation or risk factors for malignant transformation was detailed in the literature, identifying the need for further research to investigate potential preventative measures in patients with underlying benign adnexal tumors.

Malignant changes in TB may be related to its epithelial component (TBC), stromal component (trichoblastic sarcoma), or both (TBCS) [5]. While this discussion will focus mainly on TBC, it should be noted that *Colston et al.* described the first case of TBCS in the United States only recently in 2016, truly demonstrating the exceptional rarity of these adnexal malignancies [17]. As not

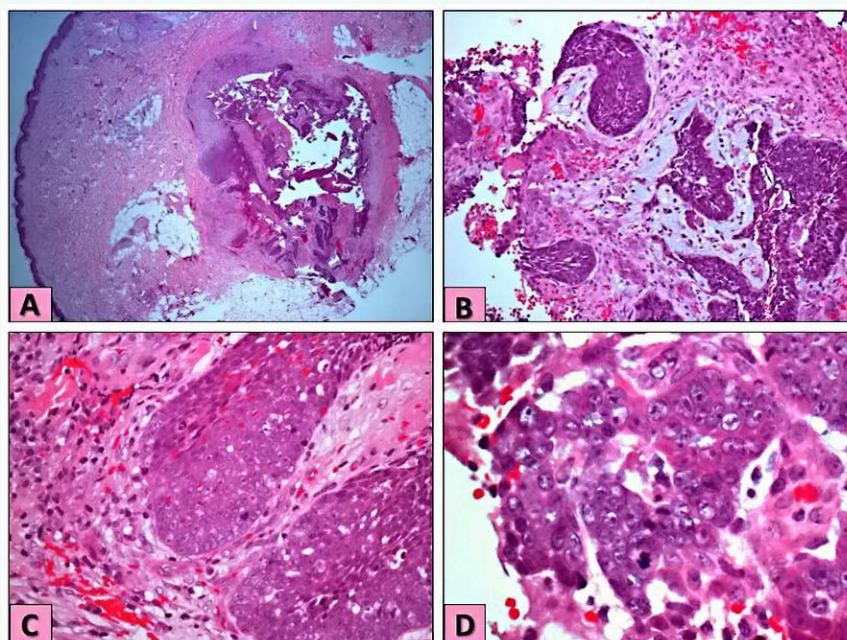


Figure 1 Microscopic examination of the excised mass.

(A): The cut surface revealed a 0.4cm oval solid cystic mass. (H&E stain X20)

(B-C): Epithelial lobules composed of basaloid-like epithelial cells with peripheral basophilic, central eosinophilic cytoplasm, and a cellular stroma (H&E stain X40b and X60)

D: Tumor cells showing large oval nuclei with prominent nucleoli. Mitotic activity easily identified. (H&E stain X60)



all cases of TBC have been associated with underlying TB (such as in our case), it may be more comprehensive to understand TBC as a follicular neoplasm with biphasic differentiation (epithelial and stromal elements) resembling a TB and simultaneously revealing features of malignancy such as invasive growth and cytologic atypia [3,19]. Regardless of the underlying origin, both TB and TBC pose a diagnostic challenge as they share many clinical and histological similarities with BCC. Some authors even consider TBC a synonym for BCC [15]. Clinically, both TBC and BCC can present as a solitary, poorly circumscribed, large (median diameter of 23mm), asymmetric dermal or subcutaneous mass, sometimes infiltrating into underlying muscle [8,20]. *Hua et al.* reviewed 36 cases of patients with biopsy proven TBC and summarized the general clinical characteristics of TBC. TBC mainly occurs in older (median age at time of diagnosis=64 years old), white, males and is typically associated with the face (60% of cases), trunk (20% of cases), and limbs (17.1%) [8]. *Underwood et al.* reviewed the first 8 cases reported of TBC and also noted that 50% of the reviewed cases demonstrated rapid tumor growth in the year prior to diagnosis and three out of the eight cases were associated with a 10+ year history of a stable precursor lesion in the same location [7].

From a histopathological standpoint, TB/TBC and BCC can share many similarities including islands of peripherally palisading basaloid epithelial cells, follicular papillae, and germinative cells [19]. TBC are typically poorly differentiated and associated with high mitotic activity, infiltrating growth, and necrosis. Clues to histologically distinguish TBC from BCC include an abundance of atypical basaloid keratinocytes with crowded, hyperchromatic nuclei, and increased mitotic activity in TBC [20]. The presence of blue-grey ovoid nests and blue-grey globules have also been cited as distinguishing features of TBC when compared to BCC [10]. Additionally, the presence of hypercellular stroma is a criterion for distinguishing TBC from BCC [20,21]. PHLDA1, a follicular stem cell marker, has also been used to help differentiate TBC from BCC, as some reports have shown that up to 94% of TBC express PHLDA1 [8]. The differential diagnosis of TBC includes TB, trichoepithelioma, trichoblastic sarcoma, and TBCS. Per the aforementioned review by *Underwood et al.*, all lesions clinically present similarly, with histopathology providing differentiation. A benign TB or trichoepithelioma demonstrates both a benign epithelial and mesenchymal component. Alternatively, a TBC demonstrates a biphasic tumor with malignant epithelial basaloid cells and benign fibroblastic/collagenous mesenchyme. A trichoblastic sarcoma reveals a biphasic tumor with benign epithelial basaloid cells and malignant fibroblastic mesenchyme. Lastly, a TBCS shows a biphasic tumor with both a malignant epithelial component and a malignant spindled mesenchymal component [7]. The presence of perineural infiltration on biopsy is a negative prognostic factor for local control [12].

Once the diagnosis of TBC has been made, the degree of clinical malignancy helps to triage these tumors into low- and high-grade lesions. Low-grade TBC are often described as morphologically similar to benign TB but with infiltrative growth patterns, often exhibiting BCC-like indolent growth and low chance of metastasis [5,9]. High-grade TBC are characterized by rapid

growth, associated inflammation, large size (>3cm), and necrosis. High-grade lesions are far more aggressive and associated with higher mortality and a poor prognosis due to the potential for systemic spread, especially to the lungs [5,12]. No standard treatment protocol has been established, although surgical excision appears to be the treatment of choice. Surgical excision can occur in a one-step wide excision, as was done for our patient, or in a multi-step, tissue sparing Mohs micrographic procedure. A standard surgical safety margin for wide excision has not yet been described, but many case reports have recommended a 1cm surgical margin, although some cases have demonstrated successful resection with 5mm surgical margins [5,8]. According to recommendations by *Laffay et al.* a low-grade TBC with a good prognosis (diameter <2cm with no perineural infiltration) should undergo surgery with a 1cm surgical safety margin followed by active surveillance every 6 months. A high-grade TBC with a poor prognosis (diameter >2cm with perineural invasion) may require surgery with a 3cm surgical safety margin and active surveillance every 3 months [12]. Due to the extreme rarity of this tumor, research has not been conducted on appropriate adjuvant therapy. *Laffay et al.* used radiotherapy as an adjuvant therapy, citing the large diameter of the patient's tumor (4.8cm x 4.0cm), the deep infiltration of the tumor, and the young age of the patient (43 years old) as reasons for using radiotherapy. Their patient was disease free at 1 year [12]. In the 36 patients retrospectively reviewed by *Hua et al.* all reported cases of TBC exhibited benign behavior without local or distant recurrence after complete surgical resection [8].

In summary, TBC is an extremely rare malignant follicular neoplasm composed of both epithelial and mesenchymal components. While it frequently originates at the site of a stable, benign, underlying TB, it can also arise *de novo*, as seen in our patient. Complete surgical resection of a TBC is necessary to avoid recurrence and metastasis. Because of its clinical and histopathologic similarities with BCC, TBC often poses a diagnostic challenge for dermatopathologists. We hope that this case report will add to the small repertoire of available research, and aid clinicians in diagnosis and management of this rare tumor.

Acknowledgement

Special thanks to Brittni Copton, Andrea Cevallos, and Rona Bari, MD candidates, American University of the Caribbean for their assistance in reviewing the final manuscript.

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