Metastatic trichoblastic carcinoma in the setting of trichoblastomatosis and multiple facial trichoepitheliomas

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Keywords: adnexal tumors; surgery.

INTRODUCTION

Trichoblastic carcinoma (TBC) is an exceedingly rare and aggressive neoplasm that carries metastatic potential. Several recent reports have noted an increased risk of TBC with mutations in the CYLD gene that may arise in patients with multiple familial trichoepitheliomas (MFT).[1-4] Wide local excision or Mohs micrographic surgery is the mainstay of treatment. We report a case of a locally advanced and nodal metastatic TBC arising in the setting of trichoblastomatosis and MFT.

Abbreviations used:

MFT: multiple familial trichoepitheliomas
TBC: trichoblastic carcinoma

CASE REPORT

A 58-year-old Caucasian man presented with several skin-colored subcutaneous facial nodules and an expanding lesion of the right gluteal cleft. Biopsies of 2 representative facial nodules were consistent with trichoepitheliomas. Biopsy of the gluteal cleft lesion was initially concerning for cutaneous basaloid carcinoma and was treated with wide local excision with 1-cm margins. The patient's father had multiple similar facial nodules, suggestive of MFT associated with CYLD mutation. Unfortunately, genetic testing was not performed for definitive confirmation. Margins of the excised gluteal tumor were positive, with histologic features of TBC arising in association with foci of benign trichoblastoma (Figs 1 and 2). The patient was subsequently taken to the operating room, where several re-excisions were performed. Intraoperative frozen sections demonstrated repeated multifocal involvement of lateral and deep margins by trichoblastoma over a broad area (trichoblastomatosis). The final margins were negative for TBC but were involved by trichoblastomatosis. Negative pressure wound healing was used on the defect, measuring 24 × 11 cm. Positron emission tomography scan revealed a hypermetabolic foci of a left inguinal lymph node. Subsequent fine needle aspiration was positive for metastatic carcinoma with basaloid features, and lymph node dissection revealed 1 of 9 lymph nodes with basaloid tumor islands with prominent cytologic atypia, brisk mitotic activity, and foci of necrosis. The nodal histopathologic features resembled those seen in the cutaneous TBC and supported a diagnosis of lymph node metastasis. Given advanced disease, radiotherapy and chemotherapy options were explored. The patient decided not to receive additional therapy and then presented 9 months later with lower extremity edema and advancement of his nodal disease on positron emission tomography/computed tomography. He was initiated on vismodegib 1 year after the initial diagnosis, but he was subsequently lost to follow-up.

DISCUSSION

TBC is a rare adnexal tumor with significant clinical and histologic overlap with basal cell carcinoma. Although some experts regard it as a variant of basal cell carcinoma with follicular differentiation, there is growing evidence to suggest that TBC may

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Funding sources: None.
IRB approval status: Not applicable.
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JAAD Case Reports 2021;16:127-9.
2352-5126

https://doi.org/10.1016/j.jdcr.2021.08.024

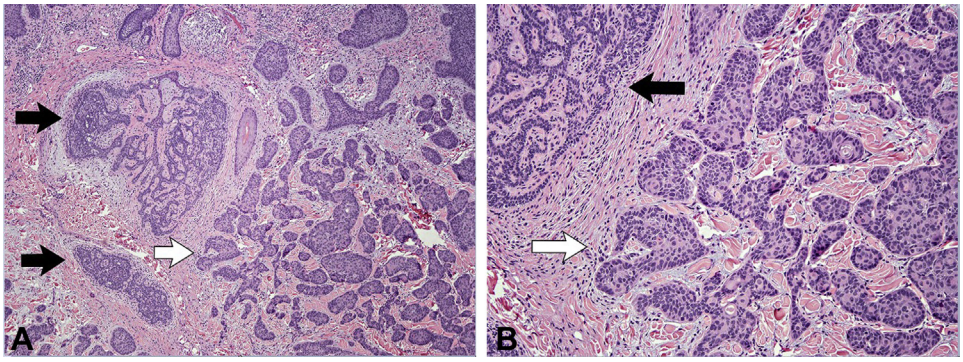

Fig 1. Infiltrative islands of trichoblastic carcinoma (*white arrow*) adjacent to nests of benign trichoblastoma (*black arrows*). (**A** and **B**, Hematoxylin-eosin stain; original magnifications: **A**, ×40; **B**, ×100.)

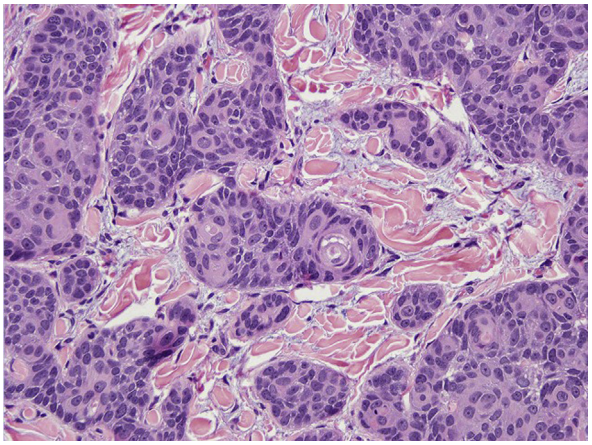

Fig 2. Trichoblastic carcinoma. Invasive dermal nests of tumor cells with enlarged, atypical nuclei and squamoid features. (Hematoxylin-eosin stain; original magnification: ×200.)

be a distinct entity.[5] As described in this case report, as well as 5 previously documented cases, the pre-existing histologic features of benign trichoblastoma with foci of cytologic atypia and infiltrative growth pattern suggest a malignant transformation of trichoblastoma to TBC.[4,6-8] The term trichoblastomatosis is used to describe multifocal trichoblastomas.[9] TBC also lacks key histologic features of basal cell carcinoma, including epidermal connection, retraction artifact, peripheral palisading and presence of myxoid stroma.[10] Although no definitive diagnostic histologic criteria have been described for the diagnosis of TBC, histologic features often include basaloid cells arranged in a trabecular or cerebriform architecture or within nests, fibroblast-rich non-myxoid stroma with high mitotic index, few epidermal connections, and potential foci of necrosis or calcifications.[10] Immunohistochemistry staining with PHLDA1 may help differentiate TBC from basal cell carcinoma.[7]

A recent comprehensive review of 93 cases of TBC revealed that most cases occur in men (66%) with a mean age of 65 years (range, 25-94 years). The face is the most common anatomic site (48.4%), followed by the trunk (18.3%) and scalp (14%). The average reported size is 4.3 cm at diagnosis (range, 0.7-20.0 cm). In addition, 24.7% of cases were misdiagnosed as basal cell carcinoma on initial biopsy. However, all tumors were subsequently classified as TBC upon review of excisional tissue. The majority of tumors occur de-novo (87.1%), while 12 tumors occurred from pre-existing trichoblastoma, trichoepithelioma, or nevus sebaceous.[7] TBC has been associated with mutations in CYLD and noted to arise in patients with MFT and Brooke-Spiegler Syndrome.[1-4]

It is important to distinguish TBC from basal cell carcinoma as the former has higher rates of nodal and visceral metastases, ranging from 8.6 to 11%,[7,11] compared to 0.0028% to 0.55%.[12] This case represents the sixth report of documented nodal metastasis and the largest tumor to date, measuring at least 24 × 11 cm.[7,8,13,14] Three previous cases of distant metastases have been reported.[7] Early-wide local excision or Mohs micrographic surgery are the mainstays of treatment. Most TBCs (82.8%) only require surgical treatment. Excisional margins range from 0.5 to 3.0 cm with a mean of 1.0 cm. The reported local recurrence rate is 10%.[7] Interestingly, only 2% of TBCs in the literature have been treated with Mohs micrographic surgery, which may account for a higher local recurrence rate compared to basal cell carcinoma.[7] Radiation and chemotherapy may have a role in advanced cases, including the use of vismodegib, sunitinib, carboplatin, or cisplatin in combination with 5-fluorouracil.[7,13,14] Due to the rarity of this neoplasm, the prognosis of TBC

compared to metastatic basal cell carcinoma is unknown. Patients with mutations in CYLD manifested by MFT and Brooke-Spiegler Syndrome should be carefully monitored for rapidly enlarging lesions, given the increased risk of TBC. Likewise, evaluation for metastatic spread should be considered in locally advanced tumors.

Conflicts of interest

None disclosed.

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