BRIEF ARTICLES

Basal Cell Carcinoma with Adnexal Differentiation, a Rare Entity and Challenging Histopathology Presentation: A Case Report

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ABSTRACT

We report an 88 year-old male with a history of multiple non-melanoma skin cancers who presented for Mohs micrographic surgery with a biopsy proven infiltrative and nodular basal cell carcinoma located on the right posterior ear. During Mohs surgery, frozen sections revealed a typical nodular BCC on stage 1. However, on stage 2, frozen section showed nodular aggregates of regular cuboidal cells with pale cytoplasm with areas mimicking multi-nucleated giant cells. Deeper permanent sections were consistent with BCC with adnexal differentiation. This histopathological presentation of basal cell carcinoma is uncommon and we sought to report the clinical and pathological features of this case.

INTRODUCTION

Basal cell carcinoma (BCC) is the most common malignant neoplasm in humans.[1] It usually occurs in the fourth decade of life in sun exposed areas, though it can present earlier in immunosuppressed patients. This cancer is a slow growing malignancy with low potential risk for metastasis. [1] Basal cell carcinoma has multiple subtypes such as nodular, superficial, morpheaform, micronodular, and others, and can also be divided into indolent and aggressive categories.[2]

Recent evidence suggests that BCC originate from follicular germinative cells instead of surface epidermal cells as was originally described.[2-4] Studies have noted that BCC seems to be derived from the basal stem cells in the follicular bulges, anagen hair bulb, follicular matrix cells, and the interfollicular epidermis.[1,3,4] On occasion, BCC can display unusual variants that show adnexal differentiation. The presence of such adnexal structures makes differentiating between a BCC and a cutaneous adnexal tumor a challenge. Although adnexal differentiation does not seem to affect tumor behavior, this diagnostic difficulty can have implications during Mohs surgery in terms of calling a frozen section clear of malignancy, as well as overall treatment implications if an aggressive adnexal neoplasm is missed. Adnexal BCC is an uncommon histological finding on frozen section pathology during Mohs surgery, therefore it is important to

recognize this entity to provide the best possible treatment for patients.

CASE REPORT

An 88 year-old male with a history of multiple non-melanoma skin cancers and prostate adenocarcinoma presented for routine dermatological evaluation. On exam, there was a 0.4 cm by 0.3 cm crusted erythematous papule on the back of the right ear. A biopsy was performed showing infiltrative and nodular basal cell carcinoma with erosion and serum crust involving deep borders. For this reason, Mohs surgery was recommended.

During Mohs surgery, the pre-operative size was 1 cm x 0.6 cm. Three stages were performed. Stage 1 showed focal nodular BCC. (Figure 1) Stage 2 showed a focus of nodular aggregates of pale cuboidal cells, with some nuclei arranged in a circular fashion, in the reticular dermis. (Figure 2a-b) Toluidine blue stain revealed a band of lavender colored stroma surrounding the aggregates. (Figure 3) A dermatopathologist was consulted since the histology of stage 2 did not resemble the BCC that was noted on stage 1, and there were areas suggestive of multi-nucleated giant cells. The dermatopathologist's differential diagnosis included histiocyte proliferation, possibly with giant cells, and more specifically an atypical mycobacterial or xanthomatous proliferation. The recommendation was to proceed with Mohs surgery to clear the ear, and send the blocks for permanent sections. Stage 3 was noted to be clear of both BCC and the pale cells noted on stage 2. Permanent section obtained deeper into the block of stage 2 showed nodular aggregates of basaloid cells, some with markedly pale cytoplasm, and a background of prominent eosinophilic stroma consistent with BCC with adnexal differentiation. (Figure 4) The post-operative size of the resected lesion was 1.5 x 1.7 cm. The lesion was left to heal via granulation.

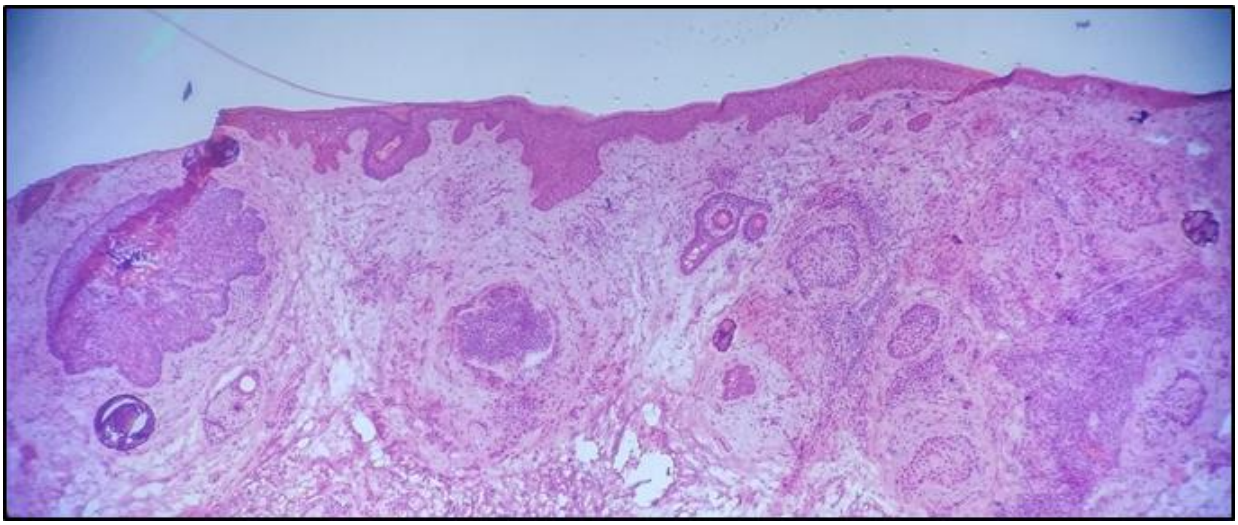

Figure 1: Stage 1 of Mohs procedure showed focal nodular basal cell carcinoma

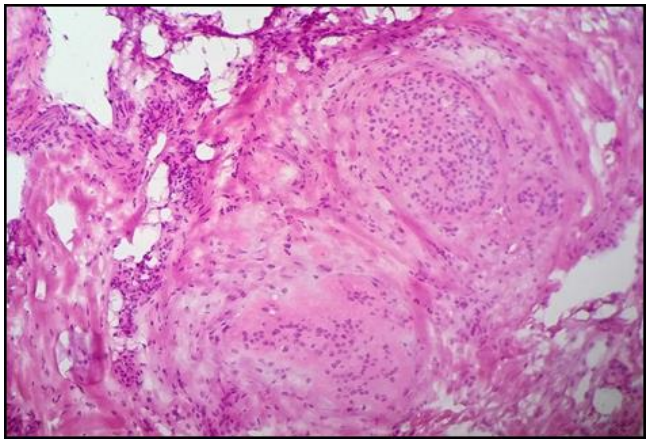

Figure 2: Stage 2 of Mohs surgery showing a focus of nodular aggregates of pale cuboidal cells, with some nuclei arranged in a circular fashion in the reticular dermis

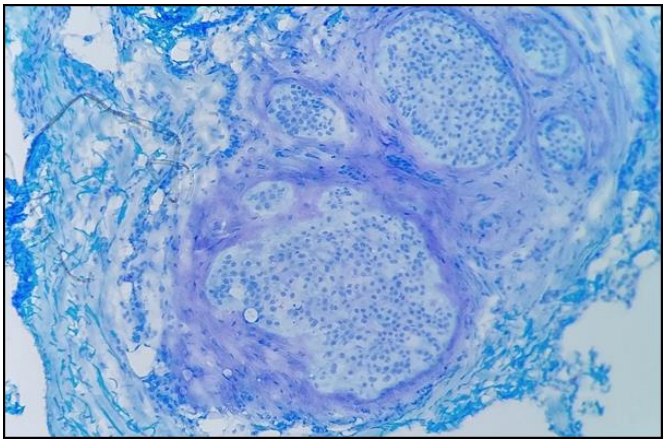

Figure 3: Toluidine blue stain slide revealing a band of lavender colored stroma surrounding the basal cell carcinoma

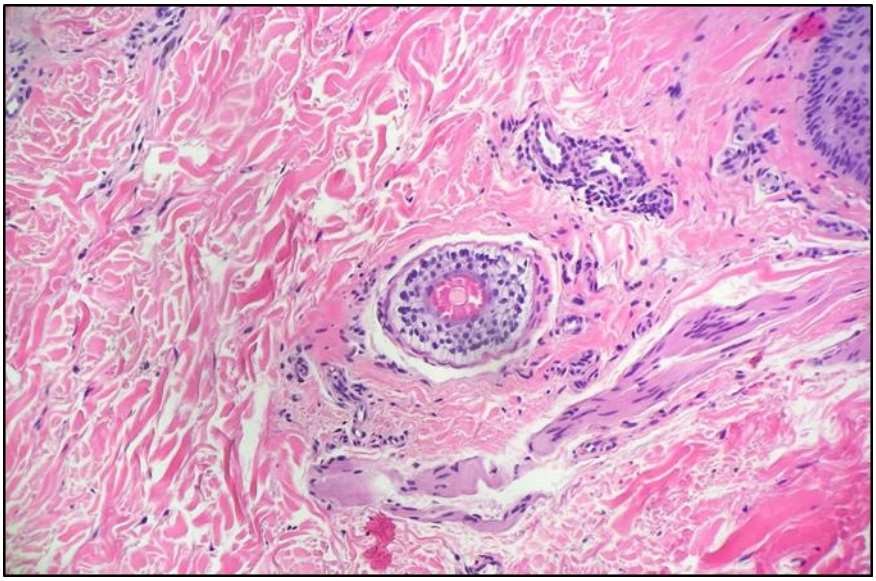

Figure 3: Clear cells with palisading and prominent basement membranes Illustrating basal cell carcinoma with adnexal differentiation from stage 2

DISCUSSION

This case illustrates a presentation of a basal cell carcinoma with adnexal differentiation. BCC is characteristically described as discrete nests of basaloid cells in the dermis with retraction clefts and peripheral palisading of the cells.[1] The tumor stroma is often pale and mucinous.[1,5] The basaloid tumor cells are generally pleomorphic and can contain mitotic figures and necrotic areas. [5] Certain architectural growth patterns (micronodular, infiltrative) are known to indicate more aggressive biologic behavior, and thus warrant more aggressive treatment.[1] In this case, the BCC had histopathological features that are

typically associated with adnexal neoplasms such as clear/pale cells and prominent basement membrane-like stroma surrounding some areas, and a background of prominent eosinophilic stroma. In this case, a possible origin for the tumor would the outer root sheath. BCC with adnexal differentiation can also have structures mimicking follicular structures, apocrine, and sebaceous glands.[2]

In 1987, Tozawa and Akerman described the first basal cell carcinoma with follicular differentiation which they called infundibulocystic basal cell carcinoma.[6] This neoplasm was showed symmetrical, circumscribed aggregates of basaloid cells containing numerous structures resembling infundibular cysts.[6] In addition, other BCC with adnexal differentiations have been described and can be broadly divided into sebaceous, apocrine glands, and follicular lineages.[2] Features reminiscent of follicular epithelium include shadow cells and clear cells, while keratinization, sebocytes, tubular structures such as ducts and glands, thickened basement membrane, fibrocyte-rich collagenous stroma, and signet ring cells can also be seen.[2] Names reported in the literature include keratotic BCC, follicular BCC, pleomorphic BCC, BCC with sweat duct differentiation, BCC with sebaceous differentiation, and BCC with clear cells.[1]

It is important to distinguish BCC with adnexal differentiation from true adnexal neoplasms, as the biological behavior and treatment may differ. There are multiple adnexal tumors reported. Some are benign and others are malignant. Benign adnexal tumors include trichoepithelioma, pilomatricoma, sebaceoma, cylindroma, and spiradenoma. Some malignant adnexal neoplasms are microcystic adnexal carcinoma, sebaceous carcinoma, and sweat gland carcinoma.[7]

There are a variety of different techniques and stains that are useful in distinguishing BCC with adnexal differentiation from true adnexal neoplasms. The classic histopathological features used to distinguish BCC from an adnexal tumor are the peripheral palisading of cells, slit like retraction spaces, and increased mitosis. [7] Immunohistochemical stains can be used for any additional types of cells. BCC will stain positive for epithelial cell adhesion molecule (Ber-EP4), as will BCC with matricial differentiation, and BCC with sebaceous differentiation.[2] CD 117 (c-kit) expression can be used to identify an adenoid cystic carcinoma instead of a BCC.[8] Epithelial membrane antigen (EMA) and carcinoembryonic antigen (CEA) stains are positive for most adnexal neoplasms except BCC with sweat duct and sebaceous differentiation.[1, 2, 9] Tichoepithelioma and BCC can mimic each other, and immunohistochemical stains can be helpful here as well. BCC stroma will be positive for stromelysin 3 and CD 34 negative, with Bcl-2 positive and CK 15/CK20 negative cells. In contrast, trichoepithelioma would be stromelysin 3 negative, CD 34 positive in the stroma, and with Bcl-2, CK 15 and CK20 positive cells.[2,7,8]

When it comes to frozen sections during Mohs surgery, immunohistochemical stains are not easily available. Thus, it is important to be able to recognize and differentiate a variety of BCC with adnexal differentiation and true adnexal tumors. In most cases, cutting deeper into a Mohs block may reveal more classic BCC alongside more indeterminate areas, allowing one to make a definitive diagnosis if necessary. A closer examination of Stage 1 in this case showed some areas with pale cuboidal cells that were slightly more similar to the cells noted on Stage 2 than classic BCC. (Figure 3) Cutting deeper into the block for Stage 2 for

frozen sections would also have likely revealed the areas of more classic BCC adjacent to paler, more indeterminate areas. This case is unique, however, in its arrangement of pale cells such that the nuclei were ringed in a fashion resembling multi-nucleated giant cells.

Basal cell carcinoma with adnexal differentiation is an uncommon histopathological presentation. It is important to remember that BCC can have different histopathological features and variants so that appropriate treatment can be performed. The overall morphological appearance, the histology and a variety of different stains and immunohistochemistry are crucial in discerning BCC from adnexal tumors. When only frozen sections without immunohistochemistry are available, obtaining deeper sections and searching from more classically differentiated areas can aid in making the final diagnosis and planning treatment.

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