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"Apocrine adenocarcinoma of the scrotum: A quandary in differential diagnosis and review of the literature"

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ABSTRACT

Apocrine adenocarcinoma is a rare aggressive malignancy arising from apocrine glands in the skin with great metastatic potential. Primary cutaneous apocrine carcinoma (PCAC) of the scrotum is extremely rare. This tumor can mimic a metastatic process from the breast, and other similar skin malignancies. A 50-year-old male presented with a painless, slow-growing left scrotal mass with new rapid growth before admission. Clinical examination showed a 7 cm fungating mass on the left scrotum, with associated left inguinal lymphadenopathy, and multiple bone metastases. Clinically, no evidence of bladder, testis, breast, or other skin cancer was present. A partial scrotectomy and laminectomy of vertebral body T7 were performed. Sectioning of the scrotal mass showed a tan-yellow, solid, variegated, vaguely lobulated cut surface. Histopathology in both tumors showed similar features with a solid, trabecular, and papillary-glandular architecture; cells with abundant eosinophilic cytoplasm with focal cytoplasmic decapitation, nuclear pleomorphism, clear chromatin with conspicuous nucleoli. Abundant mitotic figures and focal necrosis were seen. By immunohistochemistry, the tumor cells stained for pancytokeratin (AE1/AE3), CK7, EMA, CAM5.2, CK19, Her2 (score 3 and by FISH), GATA-3, CEA (focal), and Preferentially expressed Antigen in Melanoma (PRAME). The tumor cells showed no staining for p63, p40, p16, HMB45, SOX10, PSA, NKX3.1, CK20, ER, and PR. This immunoprofile was not-specific for tumor origin, but in the context of the clinical history, it was consistent with the diagnosis of PCAC. This rare tumor requires a comprehensive assessment of clinical, radiographic, and pathologic evaluation.

INTRODUCTION

Primary cutaneous apocrine carcinoma (PCAC) of the scrotum is an extremely rare malignant entity derived from apocrine glands. The diagnosis of PCAC is challenging and requires a high index of suspicion. The clinical behavior of PCAC is quite variable depending on stage and histologic grade. Up to 30% of cases present with lymph node and distant metastasis. In terms of treatment, a wide surgical excision with clear margins is the treatment of choice for localized tumors. For locally advanced or metastatic disease, lymphadenectomy, radiotherapy, chemotherapy, endocrine therapy and immunotherapy with limited clinical response.

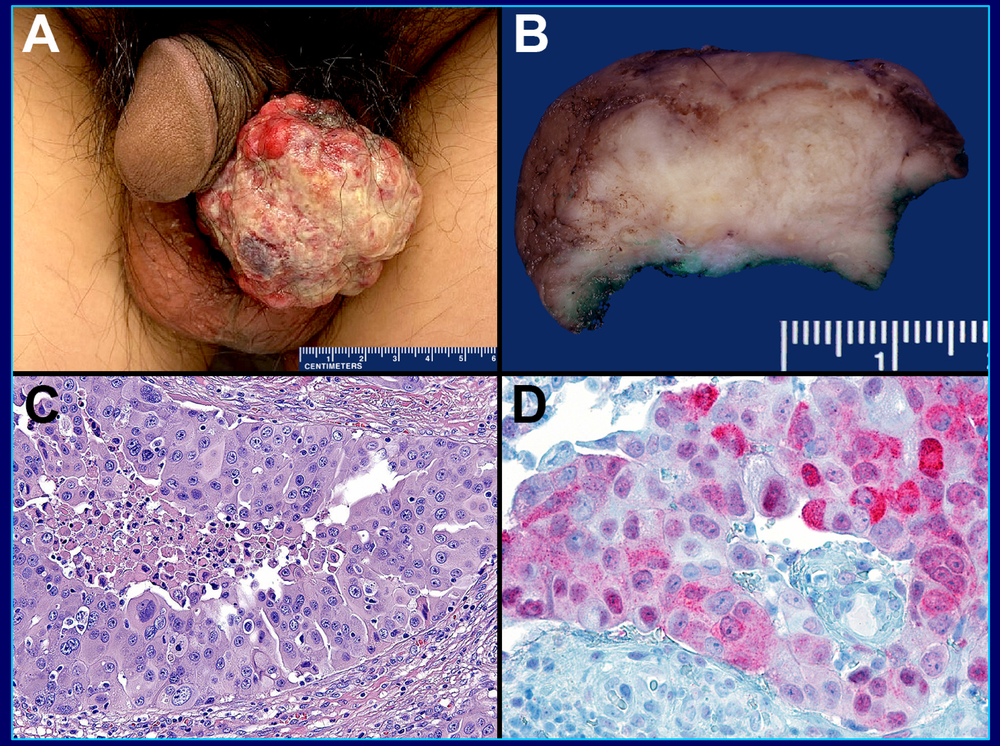

Figure 1. Lesion in left scrotum demonstrates a red multinodular, fungating mass covered by a yellow thin membrane and focal areas of hemorrhage **(A)**. Scrotectomy shows a tan-yellow solid mass with variegated, vaguely lobulated cut surface extending to the inked margins **(B)**. Histopathology showed a solid, trabecular, and papillary-glandular architecture; tumor cells show a predominant apocrine morphology with prominent nucleoli, abundant mitotic figures and focal necrosis **(C, 400x)**. Immunostains showed tumor cells staining for PRAME **(D, 400x)**, pancytokeratin, CK7, EMA, CAM5.2, CK19, Her2, GATA-3, and CEA.

CASE PRESENTATION

This is a 50-year-old male with 4 years history of a painless, slow-growing scrotal lesion, that showed accelerated growth shortly before admission. Clinical exam revealed a 7 cm fungating mass on the left scrotum, (**Figure 1A**), left inguinal lymphadenopathy and multiple bone metastasis. The patient underwent a partial scrotectomy, lymphadenectomy and vertebral body-T7 laminectomy. He has received post-operatory chemoradiation and recently pembrolizumab.

PATHOLOGY FINDINGS

Grossly, the tumor showed a white solid lobular cut surface extending to the surgical margins (**Figure 1B**). Microscopically, the tumor showed a varied architecture between solid, trabecular and papillary, with focal necrosis. The tumor cells showed abundant eosinophilic cytoplasm with apical cytoplasmic snouts (**Figure 1C**). Tumor cells stained for pan-cytokeratin (AE1/AE3), GATA3, Her2 (3+) and PRAME (nuclear & cytoplasmic) (**Figure 1D**), and no staining for p63, p40, p16, HMB45, SOX10, PSA, NKX3.1, CK20, ER, and PR. This antigenic profile was consistent but not specific for PCAC.

DISCUSSION

The diagnosis of PCAC is challenging and is based on histopathological and antigenic features in correlation with the clinical history, with main localizations in the axilla, anogenital, and scalp regions; rarely present somewhere else. PCAC is a dermal-based tumor with a variety of morphologic patterns including tubular, papillary, and solid growth, with usual perineural and vascular invasion. The tumor cells have an apocrine morphology with abundant eosinophilic cytoplasm, atypical morphology with cytoplasmic snouts, high mitotic rate, and necrosis. A low-grade variant of PCAC is described as a primary cutaneous cribriform apocrine carcinoma, a well-circumscribed dermal tumor comprised of interconnected aggregates of cells with a predominant tubular and cribriform pattern, and usually GATA3 negative. PCAC frequently shows staining for GCDFP-15, CK7, ER, PR, AR and GATA3 with no staining for mammaglobin.

The differential diagnosis of PCAC with other similar skin tumors includes:

- Metastatic apocrine breast carcinoma: Morphological and antigenic pattern almost identical to PCAC. However, staining of tumor cells for mammaglobin, and the clinical finding of a primary breast tumor are key in the differential diagnosis.
- Adenoid cystic carcinoma: Cribriform glandular elements composed of bland basaloid cells with a "Swiss-cheese" or sieve-like patterns with intervening stroma, with deep infiltration and perineural invasion.
- Microcystic adnexal carcinoma: Superficial cords and nests of bland keratinocytes with follicular or tubular morphology resembling syringomas, with solid growth into the deep dermis and with diffuse perineural invasion.
- Hidradenocarcinoma: Cystic nodules of epithelioid tumour cells with hyaline stroma, often with basaloid, poroid, mucinous, or clear cell changes, sometimes with eosinophilic cytoplasm, with focal squamous differentiation and duct formation. Perineural invasion is common.
- Tubular apocrine adenoma: Rare benign tumor, often seen in the scalp, face, axilla, leg, & genitalia, mainly in female (2:1), with well circumscribed intradermal nodules with variably-sized tubules lined by multilayered benign epithelial cells with decapitation secretion and intact peripheral myoepithelial cell layer.
- Extramammary Paget disease (PD): Similar to primary PD, but it originates in regions with rich apocrine secretions outside the breast, mainly vulva & scrotum. Primary EP tumor cells stain for CK7 and not CK20; extramammary PD tumors stain for both.

REFERENCES

1. Hollowell KL, et. al. Cutaneous apocrine adenocarcinoma: defining epidemiology, outcomes, and optimal therapy for a rare neoplasm. *J Surg Oncol.* 2012 Mar PMID: 21913192.
2. Loh SH, Oh YJ, Lew BL, Sim WY. Primary Cutaneous Apocrine Carcinoma. *Ann Dermatol.* 2016 PMID: 27746659
3. Jang SB, et. al. Co-occurrence of apocrine adenocarcinoma and invasive mammary-type ductal carcinoma in extramammary Paget disease of the axilla. *Arch Plast Surg.* 2020 Jan; PMID: 31964128.
4. Fernandez-Flores A. A Modern Approach to Differential Diagnosis Between Cutaneous Apocrine Carcinoma and Metastasis From Breast Carcinoma. *Am J Dermatopathol.* 2016 Feb. PMID: 26825162.
5. Li J, et. al. Clinicopathological and Prognostic Significance of PRAME Overexpression in Human Cancer: A Meta-Analysis. *Biomed Res Int.* 2020 Dec PMID: 33381588.
6. Elsensohn A, et. al. Preferentially expressed antigen in melanoma expression in nonmelanoma skin cancers and melanocytes in surrounding skin. *J Cutan Pathol.* 2021 Sep PMID: 33719089.