

Oncology

First reported case of penile epithelial-myoeplithelial carcinoma

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ABSTRACT

Epithelial-myoeplithelial carcinoma (EMC) of the penis is a rare malignant tumor which has not previously been described in the literature. Genetic associations exist in EMC that could potentially help guide early diagnosis and treatment of this type of penile cancer. This serves as the first reported case of such cancer of the penis, and highlights the indolent course it takes to presentation, and the need for an appropriate histopathologic evaluation for the correct diagnosis.

Introduction

Epithelial-myoeplithelial carcinoma is an uncommon, malignant neoplasm that was first described in 1972.¹ EMC is histologically biphasic; comprised of an epithelial cell component surrounded by myoeplithelial cells. EMC follows an indolent course, typically warranting a pathological diagnosis. Data suggest that EMC diagnosis usually happens in the sixth decade of life, with female predominance.² EMC most frequently occurs in the salivary glands (sEMC), and accounts for about 1–2% of salivary gland tumors with extraordinary occurrences in other organs such as the lungs, gastrointestinal tract, breasts, and endometrium.² Herein, we report a case of a malignant penile neoplasm that is histopathologically consistent with EMC. To our knowledge, there is no reported case of penile EMC (pEMC), highlighting the need for adding this report to the evolving literature regarding this rare condition.

Case presentation

A 41-year-old male was evaluated by our Urology service in the emergency room regarding a bleeding penile lesion. Comorbid conditions included obesity, obstructive sleep apnea, prior 45 pack-year smoking history, and prior illicit drug use. The patient reported no personal history of malignancy, although his mother died of lung cancer.

Notably, the patient had a stable nodule measuring approximately 1 cm on the left side of his penile shaft since birth. Roughly 12 months prior to presentation it began growing rapidly. During that period, there

was sporadic growth with associated erythema and pain with intermittent relief. Several days before presentation, the lesion ruptured with continuous serosanguineous drainage, necessitating dressing changes every few hours. The patient denied any associated purulence, constitutional, or urinary symptoms.

On examination, the penis was circumcised with an orthotopic meatus; there was a complex cystic-appearing eccentrically-ulcerated mass on the left mid-shaft (Fig. 1). On its inferior aspect, the lesion had an ulceration with serosanguineous drainage; there was no appreciable purulence, induration, fluctuance or lymphadenopathy. A penile ultrasound demonstrated a predominantly solid, hyperemic, heterogenous mass measuring 3.8 × 2.7 × 2.8 cm; the prepuce had cystic components. Upon follow-up, the lesion was noncompressible, with some mobility. Due to suspected malignancy, an uncomplicated local wide excision was performed with subsequent pathological analysis. Grossly, sectioning unearthed granular soft tissue with a hemorrhagic ulcerative cavity. Histological examination revealed a well-circumscribed, non-encapsulated tumor with negative margins, focal areas of necrosis and high-grade cytology, with subcutaneous soft tissue invasion.

The tumor was biphasic with neoplastic cells composed of scattered small duct lumina (Fig. 2A). The inner layer comprised of cuboidal epithelium with eosinophilic cytoplasm and central oval nuclei, and the outer layer of larger polygonal cells with clear cytoplasm and uniform nuclei (Fig. 2B). The duality of the cell populations comprising the tumor were underscored by immunohistochemical staining. Particularly, CD117 positivity indicates epithelial elements, while p63 and smooth muscle actin positivity adduce myoeplithelial contributions to

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Fig. 1. Penile lesion.

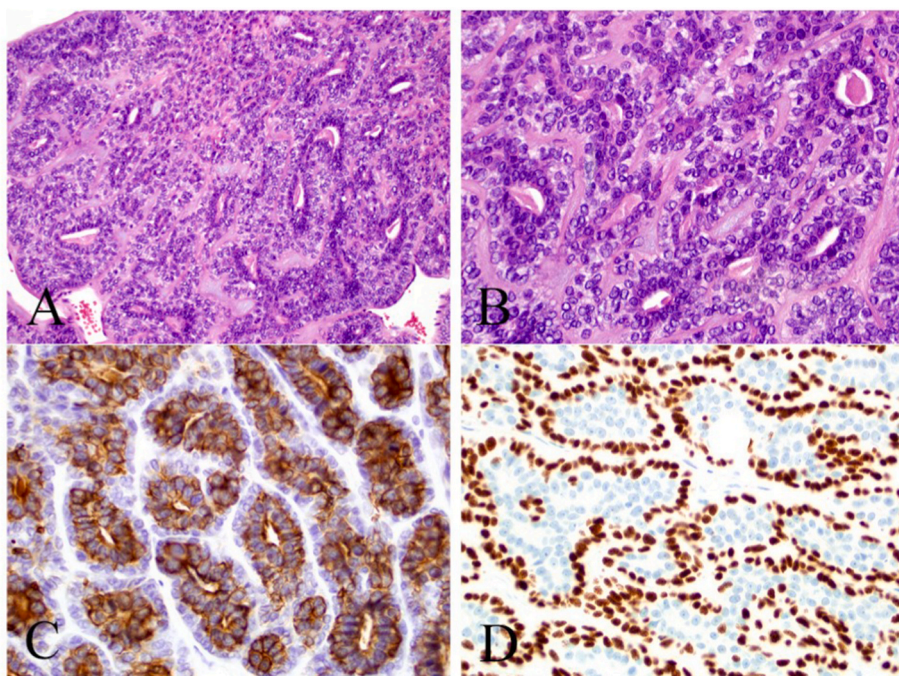


Fig. 2. A. H&E stain, low magnification, prominent basement membrane material surrounds tumor nests. B. H&E stain, high magnification, oval to irregular nests of tumor composed of intercalated duct-like structures surrounded by clear myoepithelial cells. C. Cytokeratin 7 immunohistochemical stain. Note staining of intercalated duct-like areas; myoepithelial cells are not staining. D. P63 immunohistochemical stain. Note staining of only myoepithelial cells; the intercalated duct-like areas are negative with this stain.

the tumor. Ultimately, the staining patterns (Fig. 2A–D) strongly support a diagnosis of EMC.

Postoperatively, a CT scan showed pelvic lymphadenopathy prompting pelvic lymph node dissection, revealing nothing concerning. Lower-extremity edema developed bilaterally, and PET scans revealed hypermetabolic lymphadenopathy that spontaneously resolved. He followed with our Oncology service, who advised ongoing surveillance for 1 year.

Discussion

Histologic diagnosis of EMC remains a nuanced process as these tumors can assume a myriad of phenotypic variants.³ Despite being characterized earlier,¹ the World Health Organization (WHO) only recognized it as a distinct tumor type starting in 1991.³ The glandular architecture of the tissue with co-existing epithelial and myoepithelial cells warrants EMC as a differential diagnosis. Unlike other biphasic glandular neoplasms, the key feature of EMC is transformed, often clear, myoepithelial cells with abundant cytoplasm, which must be immunohistochemically stained in order to make necessary distinctions.⁴

In our specimen, most luminal cells were positive for EMA, CEA and cytokeratin 7 (Fig. 2C), but were negative for S100 protein, p63, calponin, vimentin, and muscle-specific actin. Conversely, the outer pale cells and solid areas were positive for neoplastic and myoepithelial markers including S100 protein and p63 (Fig. 2D), respectively. The juxtaposition of these staining patterns elucidates the biphasic nature of the tumor. CD7 and GATA3 were patchy positive. Ki-67 was focally greater than 50%. Taken with the focal mitotic figures (Fig. 2B) and areas of S100 positivity (Fig. 2D) – these findings represent proliferative activity – which is consistent with the salient eruptive growth reported by the patient. Other findings cementing the diagnostic impression of an EMC are gleaned from the focally infiltrative growth pattern of the superficial dermis.

The patient had the lesion since birth, which propounds the notion of an EMC ex pleomorphic adenoma (EMCxPA), but there was no conclusive histologic evidence surrounding this phenomenon. Regardless, the WHO classification criteria state that carcinoma ex pleomorphic adenoma (CxPA) should not be considered a standalone diagnosis.⁴ Although CxPA does not typically exhibit EMC histomorphology, upon

malignant transformation, it is possible.^{4,5}

Furthermore, the patient's mother died from lung cancer at a young age. Canonical EMC has been shown to be strongly associated with *HRAS* gene mutations³; whereas EMCxPA is associated with *PLG1* or *HMG2* mutations.⁵ One wonders if this linkage can be extrapolated to other organs: the genetic concordance of this phenomenon in salivary glands, coupled with the patient's family history, allude to a potential etiology for this novel case of pEMC. Although confirming this conjecture would not alter management, a thorough history and mutational analyses could guide the diagnosis of similar cases wherein histopathology might be less fruitful. Additionally, confirming a genetic basis might enable clinicians to enact a sentinel approach for malignant potential in progeny born with seemingly benign penile lesions.

Conclusions

Although sEMC is typically a low-grade tumor with favorable survival rates, high-grade variants in putative loci have significantly worse outcomes.² However, in this almost idiosyncratic case, it remains uncertain whether focal densities of high-grade pEMC translate to a different clinical course. Here we described the first reported case of pEMC, which serves as a reminder to remain circumspect in pathological evaluation of benign lesions that suddenly erupt into clinical awareness.

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Declaration of competing interest

None.

References

1. Donath K, Seifert G, Schmitz R. [Diagnosis and ultrastructure of the tubular carcinoma of salivary gland ducts. Epithelial-myoepithelial carcinoma of the intercalated ducts]. *Virchows Arch A Pathol/Pathol Anat.* 1972;356(1):16–31.

2. Gore MR. Epithelial-myoeplithelial carcinoma: a population-based survival analysis. *BMC Ear Nose Throat Disord.* 2018;18:15. <https://doi.org/10.1186/s12901-018-0063-2>.
3. Urano M, Nakaguro M, Yamamoto Y, et al. Diagnostic significance of HRAS mutations in epithelial-myoeplithelial carcinomas exhibiting a broad histopathologic spectrum. *Am J Surg Pathol.* 2019;43(7):984–994. <https://doi.org/10.1097/PAS.0000000000001258>.
4. Seethala RR, Stenman G. Update from the 4th edition of the World Health organization classification of head and neck tumours: tumors of the salivary gland. *Head Neck Pathol.* 2017;11(1):55–67. <https://doi.org/10.1007/s12105-017-0795-0>.
5. El Hallani S, Udager AM, Bell D, et al. Epithelial-myoeplithelial carcinoma: frequent morphologic and molecular evidence of preexisting pleomorphic adenoma, common HRAS mutations in PLAG1-intact and HMGA2-intact cases, and occasional TP53, FBXW7, and SMARCB1 alterations in high-grade cases. *Am J Surg Pathol.* 2017;1. <https://doi.org/10.1097/PAS.0000000000000933>. Published online November.