Myopericytoma tumor of the glans penis

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Myopericytoma is a low grade spindle cell neoplasm largely occurring in skin. We describe the first reported case of a penile myopericytoma. Histologically, the penile tumor was composed of a perivascular proliferation of tumor cells with ovoid shaped nuclei and abundant eosinophilic cytoplasm. Immunohistochemically, the tumor was reactive for markers of smooth muscle differentiation and vascular differentiation. The tumor was noted to be negative for BRAF by immunohistochemistry and wild-type upon gene sequencing using SnaPshot. Our finding serves to expand the anatomical distribution of myopericytoma and broadens the spectrum of primary mesenchymal neoplasms that may be encountered in the penis.

Key Words: cancer, penile, myopericytoma, pathology, immunohistology

Introduction

Myopericytoma (MPC) is a low grade neoplasm thought to be of perivascular myoid differentiation. Although this histological entity was first proposed by Requena et al, and later refined by Granter et al.[1] to include the concept of perivascular myoid differentiation, it was not until 2002 when the World Health Organization suggested the use of the term "myopericytoma" as a separate morphologically and clinically distinct neoplasm.[2] The tumor is morphologically heterogeneous and can show a broad histologic spectrum from myoid-appearing ovoid, plump, spindled and/or round myoid tumor cells with a concentric perivascular pattern of growth that arises from perivascular myoid cells.[3] It is closely related to a spectrum of tumors that demonstrate pericytic differentiation, including myofibroma, angioleiomyoma, and glomus tumor.[4] Immunohistochemical staining is a useful diagnostic adjunct, as myopericytomas characteristically stain positively for smooth muscle actin, muscle-specific actin and h-caldesmon and are negative for desmin.[3]

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MPC classically occurs in the dermis and subcutaneous regions of the distal extremities or the head and neck region, but they can also present in unusual sites like the oral and nasal cavity, lung, heart, gastrointestinal tract, thoracic spine, intracranial locations, intravascular sites kidney, bladder, and most recently reported, in the thyroid. However, to the best of our knowledge, there has never been a case reported in the literature of a genital myopericytoma. The aim of this case report is to present the first reported case of a myopericytoma tumor of the glans penis. We describe the clinical, histopathological, radiological and immunohistochemical features as well as treatment experience and review the relevant literature.

Case report

The patient is a 57-year-old Caucasian man with a past medical history of diabetes, obesity, and multiple urinary tract infections, who presented to his urologist with increasing urinary frequency and urgency for the previous month in the setting of having a painless penile glans subcutaneous mass which had been growing for over 3 years. His family history was only significant for prostate cancer in his father (unknown age of diagnosis). The mass was biopsied and the pathology was suggestive of a glomus tumor. The patient was then referred to Massachusetts General

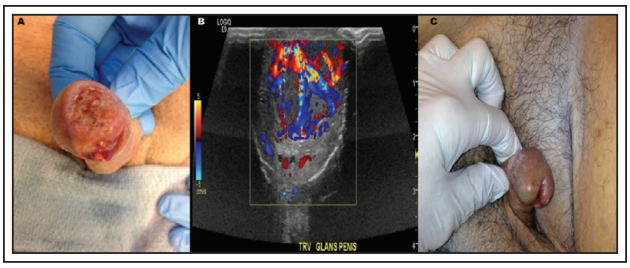

Figure 1. Penile mass. **A)** Physical examination: small inflammatory lesion coming from the ventral aspect of the meatus with an associated non-tender, distal 3 cm penile glans mass deep to the surface epithelium with an overlying ulcer from the prior biopsy. **B)** Penile ultrasound showing a 2.4 cm x 2 cm x 2.3 cm vascular mass in the glans penis. **C)** At 6 weeks postoperatively the patient had a well healed cosmetic result.

Hospital for further management of this mass. On physical examination the patient was found to have a small indurated, erythematous lesion involving the ventral aspect of the penile urethral meatus with an associated non-tender, palpable, 3 cm subcutaneous glans mass and an overlying ulcerated wound from prior biopsy, Figure 1a. The remainder of his genitourinary examination and clinical and laboratory findings were unremarkable. Penile ultrasound showed a 2.4 cm x 2 cm x 2.3 cm vascular mass within the glans penis, Figure 1b. The patient elected for resection of the mass in a penile sparing fashion. The mass involved the urethral meatus and distal aspect of the fossa navicularis and therefore this involved portion was resected en bloc with the mass. Flexible cystoscopy demonstrated no involvement of the urethra more proximally. Resection of the subcutaneous lesion, involved urethral meatus/fossa navicularis and overlying ulcerated wound (from the prior biopsy) was performed with primary closure and distal urethroplasty, which set the ventral aspect of the meatus slightly more proximal on the glans. A urethral catheter was left in place for 1 week. At 6 weeks postoperatively the patient had a well-healed, excellent cosmetic result with no urinary or sexual functional loss, Figure 1c.

Pathologic evaluation

The surgically resected specimen showed a well-circumscribed, homogenous, tan-yellow, nodular mass with punctate areas of hemorrhage measuring 1.9 cm x 1.8 cm x 1.7 cm with central, 1.3 cm x 1.2 cm ulceration, Figure 2a. Histological examination revealed a somewhat hyperplastic squamous mucosal surface

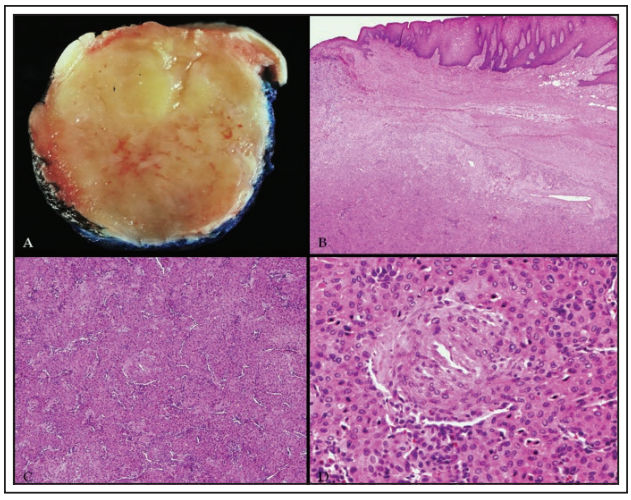

Figure 2. Penile myopericytoma. **A)** Macroscopic image showing a non-encapsulated, well-circumscribed, tan-yellow, nodular mass on cut surface. Microscopic examination revealed **B-C)** ill-defined nodules and whorls of tumor cells underlying a hyperplastic squamous mucosa concentrically arranged around thin-walled vascular lumina (H&E stain, 40x and 100x, respectively). **D)** Scattered medium-sized thick-walled blood vessels cuffed by a perivascular proliferation of eosinophilic tumor cells with round to ovoid nuclei and indistinct cell borders forming an "onion-skin" morphology are also identified (H&E stain, 400x).

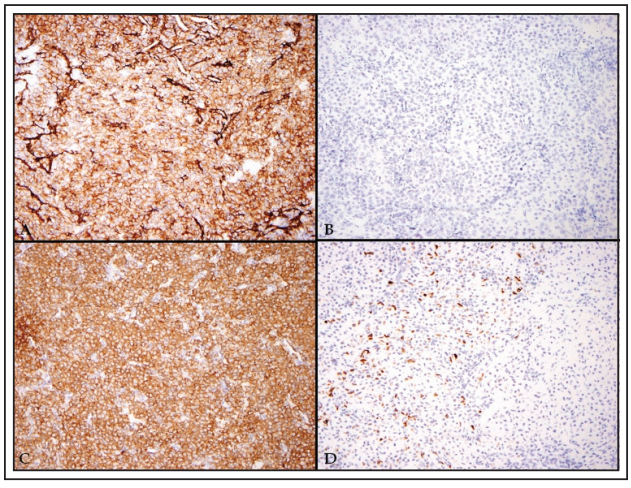

Figure 3. The tumor cells show strong and diffuse cytoplasmic positivity for **A)** SMA (SMA immunostain, 200x), and **C)** CD34 (CD34 immunostain, 200x). A pancytokeratin stain **B)** was negative (CKAE1/AE3/Cam5.2 immunostain, 200x). A desmin immunostain **D)** revealed focal immunoreactivity in scattered in tumor cells (desmin immunostain, 200x).

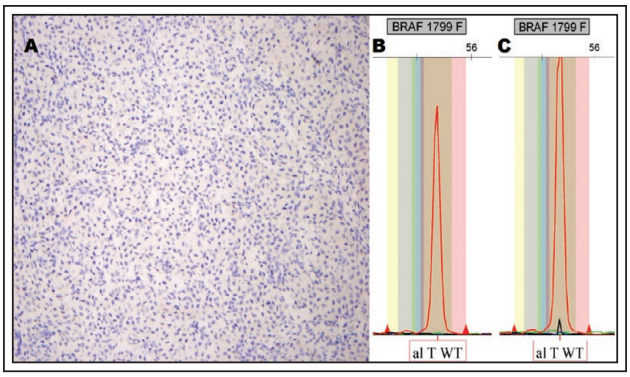

Figure 4. Tumor was negative for BRAF. **A)** BRAF immunostain was negative in the tumor cells (BRAF immunostain, 200x). **B)** Direct sequencing for BRAF mutation from SnaPshot. Wild-type BRAF sequence in **B)** the penile myopericytoma and **C)** genomic control (forward direction, nucleotide 1799).

overlying this nodular, whorled lesion with somewhat ill-defined boundaries. The tumor cells had round to ovoid shaped nuclei, with abundant eosinophilic cytoplasm and ill-defined cell borders. The tumor cells were concentrically arranged around thin-walled, irregular staghorn or hemangiopericytoma-like vascular lumina, Figure 2b and 2c. Scattered medium-sized, thick-walled blood vessels cuffed by a perivascular proliferation of tumor cells in an "onion-skin" pattern was also identified, Figure 2d. The tumor cells lacked nuclear atypia or mitoses.

Immunohistochemical stains revealed that the tumor cells were diffusely and strongly immunoreactive for smooth muscle actin (SMA) and CD34, Figure 3a and 3c respectively. No immunoreactivity was observed for pancytokeratin, Figure 3b. There were a few scattered cells that were positive for desmin, Figure 3d. The tumor was also noted to be negative for BRAF by immunohistochemistry and wild-type upon gene sequencing using SNaPshot, Figure 4. Based upon the histologic features and immuno-profile, the tumor was found to be most consistent with a myopericytoma, rather than a glomus tumor as diagnosed on initial biopsy.

Discussion

Myopericytoma is a rare tumor, with less than 200 cases reported in the literature. However, more recently, it has been increasingly recognized clinicopathologically as a distinct, low grade mesenchymal tumor that is part of a spectrum of tumors showing perivascular myoid differentiation, including myofibroma, angioleiomyoma, glomus tumor, myopericytoma, and lesions with hybrid features (such as glomangiopericytoma). Specifically, it is thought to be derived from myopericytes, which are transitional cells between pericytes and vascular smooth muscle cells. Histologically, MPC is characterized by collagenous fibrous capsulation and the presence of surrounding numerous small to medium-sized vessels with a concentric perivascular arrangement of neoplastic cells.[3] Morphologically tumor cells exhibit ovoid nuclei, evenly distributed chromatin, and distinct nucleoli with abundant eosinophilic cytoplasm.[3]

In this article, we present a case of myopericytoma involving the glans penis. To our knowledge, this is the first report of a genital myopericytoma in the literature. The penile tumor reported here demonstrates many of the typical histologic and immunohistochemical characteristics of reported soft tissue MPC, including a multinodular growth pattern and a concentric, swirling, perivascular arrangement of ovoid/spindle-shaped myoid neoplastic cells with expression of immunohistochemical markers of smooth muscle differentiation.

Immunohistochemical profiles of myopericytomas in different anatomic locations have shown consistent reactivity with antibodies to muscle-specific actin, smooth muscle actin, h-caldesmon, CD34 and bcl-2. MPC are mostly negative for epithelial markers (including various cytokeratins, and epithelial membrane antigen), endothelial markers (factor VIII-related antigen and CD31), neuroendocrine markers (chromogranin A, synaptophysin), melanocytic markers (HMB45, melan-A), desmin and S100 protein.[5]

A review of the English literature by Wu et al[6] in 2013 using the PubMed search engine identified 115 cases of myopericytomas from 1998 to 2012. The authors noted a slightly male predominance with a male to female ratio of 1.25:1. Ages ranged from 10 to 87 years, with a median age of 49 years. The majority of patients were over 40 years of age with less than 10 cases reported in children. The majority of MPC are reported to be slow-growing, and usually less than 2 cm at presentation. They are predominantly located in the skin and superficial soft tissue of the distal extremities. The most common locations, in order of decreasing frequency, are the lower extremity, upper extremity, head and neck, trunk (including the spine), oral cavity, lung and pancreas. In the urinary tract, only four examples of renal MPC and one example of urinary bladder MPC have been reported in the English literature to date.[7,8] In most cases, neoplasms were superficial, although there were a few cases in which neoplasms were deep-seated. In rare cases, the lesions were multicentric and multiple anatomic regions were involved.

Most reported cases of myopericytoma have behaved in a benign fashion with a good prognosis.[5] Excellent results have been observed after complete surgical excision.[5] However, even if there is local recurrence, which occurs only in very rare cases, repeat resection can still achieve favorable outcomes.[5] In the largest case series of myopericytoma available in the literature, Mentzel et al examined 54 cases of myopericytoma of skin and soft tissues. Follow up information was available in 46 patients and despite positive margins in 23 of 46 cases, they found that only 2 neoplasms (1 malignant and 1 intravascular myopericytoma) recurred locally (within 1 and 4 years, respectively).[5] However, it is important to note that often it is difficult to distinguish a local recurrence from a residual nodule, especially in multicentric cases.

Atypical or malignant MPCs are extremely rare, however, those reported cases have often presented with local recurrence and distant metastases in other organs.[5] Although the rate of subsequent malignant transformation is not known, only few rare cases have been reported.[3] Local recurrences have been mostly the result of incomplete excision, and metastasis has been associated with the depth of the neoplasm on initial biopsy or resection.[5] Although the precise depth at which this neoplasm has an increased risk of metastasis is not known, in a series of 5 malignant myopericytomas, Mcmenamin et al[3] show that metastatic neoplasms only occurred in the setting of deep-seated lesions. In contrast, one superficial malignant myopericytoma did not show local recurrence or metastasis at 18 months of follow up. This highlights the strong association between the clinical course and the depth of these neoplasms.

Superficial lesions or lesions of the extremities are more easily excised due to accessibility and, depending upon extent of the lesion, wider margins can be taken with a lesser likelihood of recurrence. For those lesions in visceral organs, genitalia, or head and neck, achieving clear surgical margins without causing additional morbidity may be more challenging, and close clinical follow up is needed to monitor for recurrence. Interestingly, it has recently been reported that a subset of the more deep-seated lesions or those with likelihood for recurrence or multifocality may be associated with mutations in BRAF (V600E).[9] Our patient lacks BRAF mutation and likely has a low risk for recurrence with clear margins.

As myopericytoma is generally a benign lesion we recommend that any resection of such a lesion in the male genitalia be performed in an organ-preserving manner when technically possible. Our group has demonstrated the feasibility and safety of these penile sparing techniques in malignant lesions of the penis[10] and they can certainly be applied for benign lesions as well.

Conclusion

In summary, we describe a perivascular myoid cell tumor (myopericytoma) involving the glans penis. To our knowledge, this is the first report of a genital myopericytoma in the literature, which serves to expand the anatomical distribution of myopericytoma and also broadens the spectrum of primary mesenchymal neoplasms that may be encountered in the penis. As the diagnosis of MPC is relatively rare, its diagnostic efficacy depends on histopathological features, especially immunohistochemical confirmation. Histological and immunohistochemical diagnosis can be a challenge, since MPC share common morphologic features with other perivascular myoid neoplasms such as hemangiopericytoma, myofibroma, glomus tumor and angioleiomyoma. MPC is treated surgically with complete resection, in an organ preserving fashion, leading to cure. Local recurrence is rare, though largely is the result of an inability to secure lesion-free surgical margins. With recurrence, malignant transformation should be ruled out. Heightened clinicopathological awareness of myopericytoma is pivotal to the diagnosis, especially in the urinary tract and genital locations where it is rarer. □

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