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Genitourinary

A report of two deep-seated noncutaneous penile tumors: more than meets the eye

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ABSTRACT

Penile cancer is an uncommon primary genitourinary malignancy, the vast majority representing superficial squamous cell carcinomas. However, less common skin cancers, secondary malignancies, mesenchymal neoplasms, and hematopoietic tumors do affect the penis. Medical history, atypical presentation, and deep epicenter of a penile mass may raise question of a nonepithelial neoplasm. We describe and discuss 2 examples of rare deep-seated penile malignancies, leiomyosarcoma and B-cell lymphoma.

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Introduction

Penile cancer is rare in the United States, accounting for less than 1% of male cancer in the US [1]. Nearly all penile cancers are skin cancers, and most (95%) represent squamous cell carcinoma. Other less common skin cancers of the penis include basal cell carcinoma, melanoma, and adenocar-

cinoma. Much rarer malignancies of the penis include penile metastases, soft tissue sarcomas, and lymphoma. Herein, we present 2 companion examples of rare, deep-seated, less commonly considered penile neoplasms, leiomyosarcoma with myxoid features and relapse of diffuse large B-cell lymphoma with concurrent gene rearrangements, with an emphasis on pertinent magnetic resonance imaging (MRI) findings.

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Case reports

Case 1

A 68-year-old male with a history of chronic kidney disease presented to his primary care physician for evaluation of a small, palpable nodule on his penis. The patient was clinically diagnosed with Peyronie disease, but the lesion grew over the next weeks to months, and he was subsequently referred to our institution for further evaluation. Unenhanced and gadolinium-enhanced MRI of the penis and pelvis was performed, demonstrating a heterogeneous penile mass involving both the corpora cavernosa and spongiosum abutting and slightly displacing the right and left spermatic cords laterally (Fig. 1). The mass exhibited moderately hyperintense T2-weighted signal, avid intravenous contrast enhancement, an area of internal necrosis, and an associated rightward curved deformity of the penile shaft (Fig. 2A-B). The curved deformity likely explains an initial diagnosis of Peyronie disease. After incisional biopsy, penectomy with perineal urostomy was performed successfully without postoperative complication. The final histopathologic diagnosis was leiomyosarcoma with myxoid features, grade III. Surgical margins were negative. At surgery, the spermatic cords were not involved by tumor and, therefore, spared during the operation. The patient declined both adjuvant radiation and chemotherapy, opting for close postoperative surveillance. In a short time, however, he developed a local perineal recurrence (Fig. 3) but without distant metastatic disease. He was then treated with radical scrotectomy, bilateral orchiectomy, perineal resection, and urinary diversion. Adjuvant radiation therapy was planned to improve local control of disease.

Case 2

A 66-year-old male presented to his oncologist with a new palpable penile mass. His medical history included previously

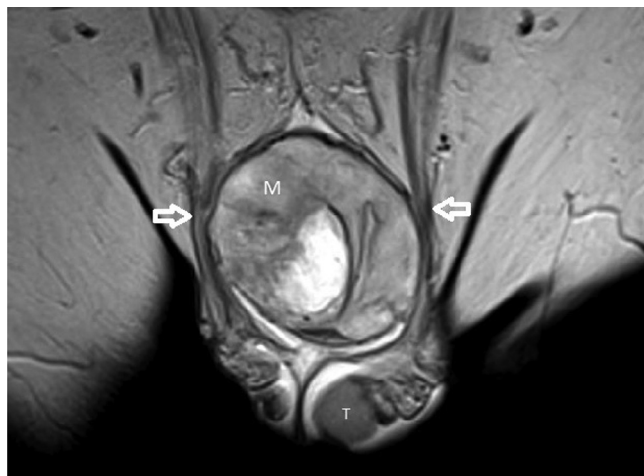


Fig. 1 – Coronal T2-weighted TSE magnetic resonance imaging demonstrates a large mass (M) with an internal area of hyperintense necrosis of the penile shaft involving the corpora and abutting the spermatic cords (arrows). T = testis, left; TSE = turbo spin echo.

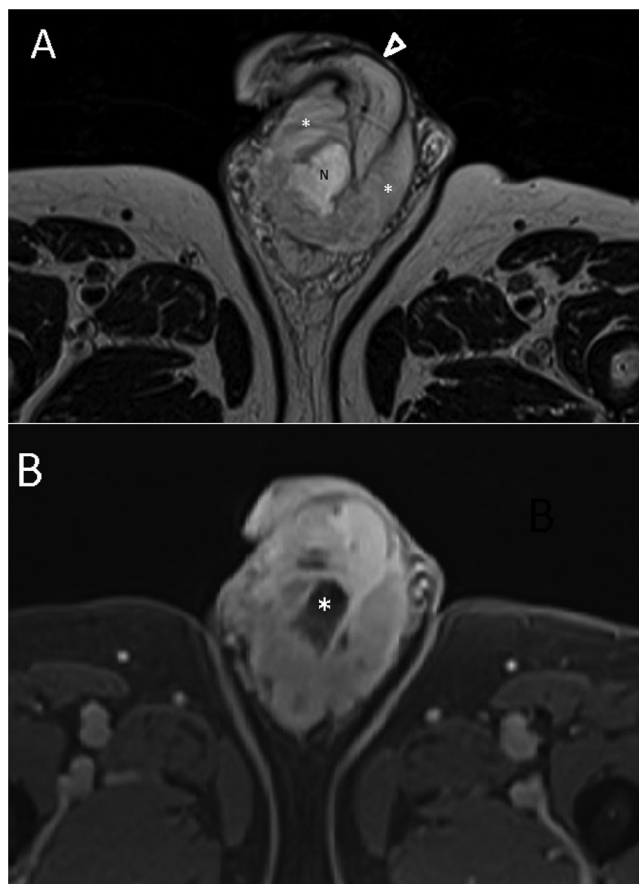


Fig. 2 – (A) Axial T2-weighted TSE and (B) gadolinium-enhanced T1-weighted fat-suppressed 3D-GRE imaging demonstrates a T2-hyperintense, avidly enhancing mass (* in A) with internal necrosis (N in A; * in B) and a rightward curved deformity of the penis (arrowhead in A). GRE = gradient echo.

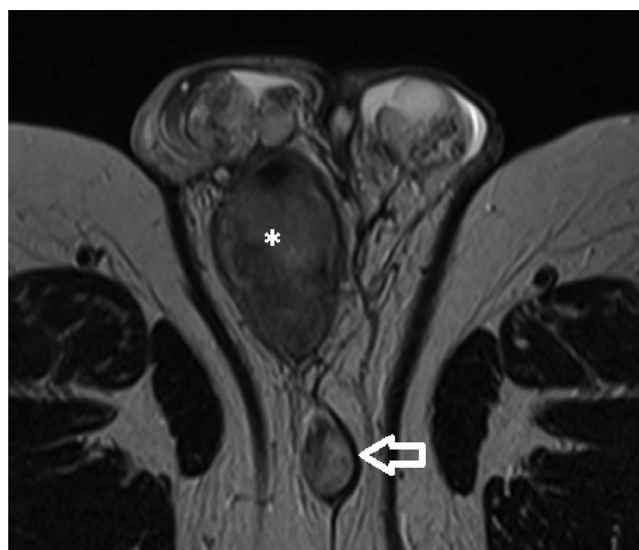


Fig. 3 – Axial T2-weighted TSE imaging three months following penectomy with perineal urostomy (arrow) demonstrates a new perineal mass (*) posterior to the scrotum proven to represent local tumor recurrence.

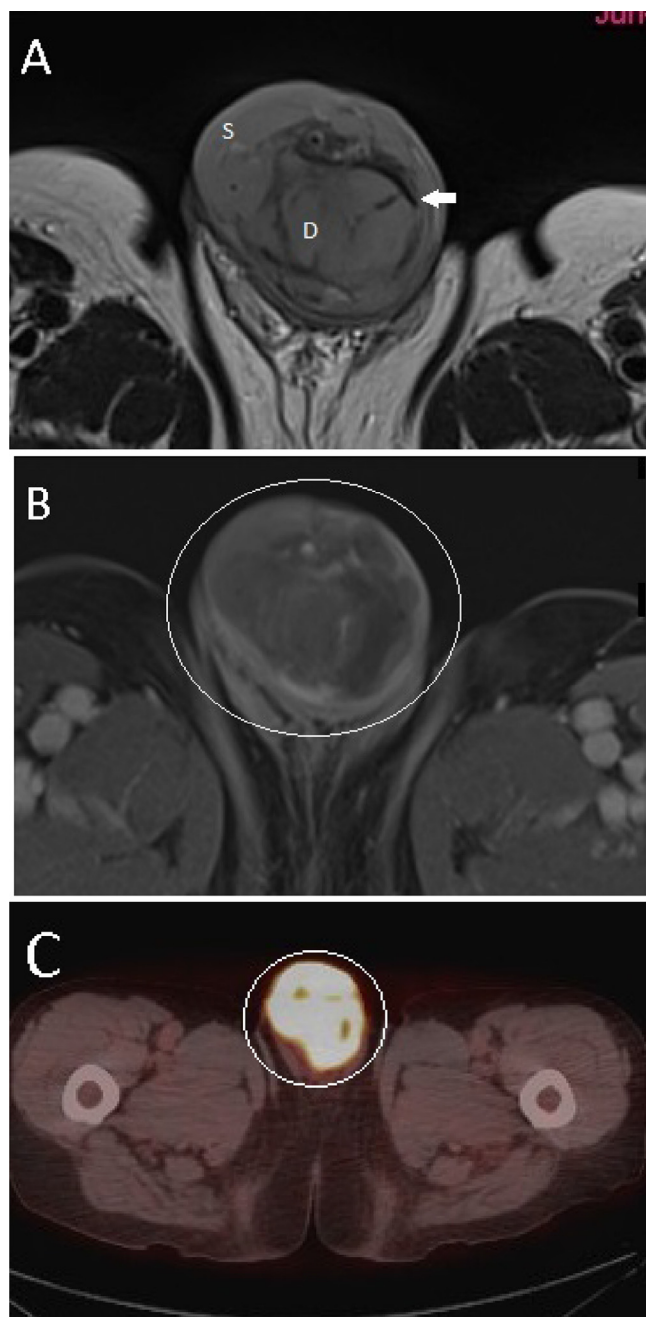


Fig. 4 – (A) Axial T2-weighted TSE imaging demonstrates an infiltrative hypointense deep (D) and superficial (S), defined by hypointense investing fascia (arrow), penile mass replacing the normally T2-hyperintense corpora, violating the fascia, and infiltrating the superficial subcutaneous fat. **(B)** Gadolinium-enhanced T1-weighted 3D-GRE imaging demonstrates mass (circle) with mild diffuse enhancement. **(C)** F-18 FDG PET/CT demonstrates mass (circle) with marked FDG avidity. FDG PET/CT = fluorodeoxyglucose positron emission tomography/computed tomography.

treated stage IV diffuse large B-cell lymphoma in complete remission following 6 cycles of rituximab, cyclophosphamide, doxorubicin, and vincristine, prednisolone before the current presentation. Given his history, this new penile mass raised

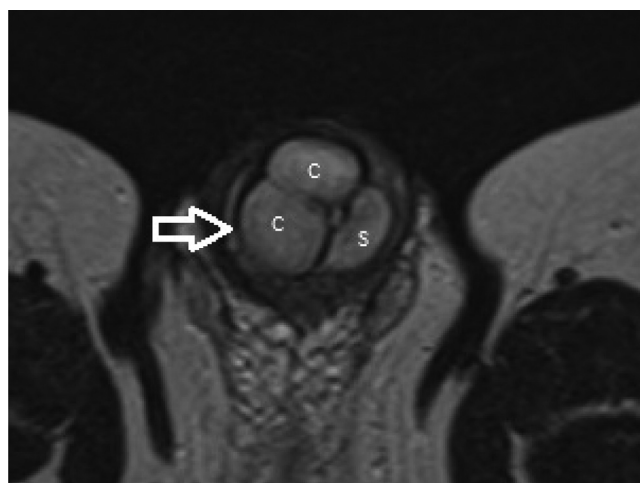


Fig. 5 – Axial T2-weighted TSE MR imaging on treatment 6 months later demonstrates marked interval response to therapy with near complete resolution of the penile mass and return of expected signal intensity of the corpora cavernosa (C) and spongiosum (S). Note hypointense investing fascia surrounding the corpora, which defined superficial vs deep-seated tumors.

clinical concern for relapse, despite rare location and remote history of the treated disease. Unenhanced and gadolinium-enhanced MRI and F-18 fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) were performed. T2-weighted TSE MRI demonstrated a hypointense deep and superficial penile mass infiltrating the corpora cavernosa and spongiosum, disrupting the investing fascia, and extending throughout the superficial subcutaneous fat (Fig. 4A). Gadolinium-enhanced imaging revealed minimal contrast enhancement and no pelvic lymphadenopathy (Fig. 4B). PET revealed avid FDG uptake within the mass (Fig. 4C) as well as FDG-avid sites of disease in the chest and spine (not shown). Penile biopsy confirmed relapse of aggressive B-cell lymphoma; the specimen stained diffusely positive for CD20, CD10, and bcl-6 with Ki-67 labeling index >90%, immunohistochemical markers confirming B-cell lymphoma, whereas fluorescence in situ hybridization (FISH) demonstrated 68% positivity for the BCL2 and 54% positivity for the C-MYC gene rearrangements—the presence of both of these gene translocations is consistent with “double-expresser” or “double-hit” lymphoma, a small subset of high-grade B-cell lymphomas with mixed response to standard therapies and poorer prognosis. In this case, the patient was treated with chemotherapy and immunotherapy, which resulted in symptomatic improvement and a marked decrease in the size of the penile mass (Fig. 5).

Discussion

Penile cancer is rare in the United States, accounting for less than 1% of all male malignancies [1,2]. Most patients present in the sixth to seventh decade of life with a palpable mass or skin lesion. There are several histologic subtypes of primary penile cancers, most of which are skin tumors, of which the

overwhelming majority are squamous cell carcinoma. Other subtypes of skin cancers include basal cell carcinoma, melanoma, and adenocarcinoma (extramammary Paget disease) [2]. Mesenchymal tumors including soft tissue sarcomas and hematopoietic cancers including lymphomas much less often involve the penis. Reported histologic subtypes of sarcoma involving the penis include epithelioid sarcoma, Kaposi sarcoma, angiosarcoma, leiomyosarcoma, and rhabdomyosarcoma [2]. Reported subtypes of lymphoma include diffuse large B-cell lymphoma, Burkitt lymphoma, extra-nodal marginal zone lymphoma, chronic lymphocytic leukemia or small lymphocytic leukemia, mantle cell lymphoma, plasmacytoma, post-transplant lymphoproliferative disorder, and peripheral T-cell lymphoma [3]. Secondary tumors of the penis also occur, most of which represent metastases from primary genitourinary tract cancers (70%); however, other reported primary sites of disease include the gastrointestinal tract, lung or bronchus, and thyroid gland [2,4]. Lymphomatous involvement of the penis can also represent a secondary site of disease in patients with systemic lymphoma.

Penile neoplasms have variable clinical presentations including painless palpable nodule, bulky mass, penile pain, swelling or enlargement, hematuria or stricture with urinary obstruction, skin ulceration, and inguinal lymphadenopathy. Deep-seated tumors arising below Buck's fascia are more likely than superficial tumors to present with urinary symptoms related to urethral involvement [5]. The cases illustrated herein both presented with enlarging, palpable masses. Because most penile tumors are superficial and epithelial in origin, staging is typically performed by physical examination. Imaging is typically utilized to assess the local extent of disease and regional lymph node involvement [2]. At MRI, most penile cancers are superficial, hypointense infiltrative soft tissue masses on T1- and T2-weighted imaging with variable degrees of intravenous contrast enhancement. Metastases typically involve the corporal bodies [2] and most often appear as T2-hypointense lesions relative to the surrounding hyperintense corpora [6]. Soft tissue sarcomas have varying imaging appearances based on tumor histology and cell lineage, but generally demonstrate markedly increased T2-weighted signal and avid contrast enhancement, often with internal heterogeneity due to hemorrhage and necrosis. Lymphomatous soft tissue masses typically demonstrate moderately increased T2-weighted signal and mild intravenous contrast enhancement related to histomorphology consisting of sheets of densely packed small round blue cells.

The deep fascia, or Buck's fascia, involving the corpora cavernosa and corpus spongiosum, which includes the urethra, typically appears as a thin continuous T2-hypointense structure on MRI (Fig. 5) and separates the superficial and deep tissues of the penis. These two cases both demonstrate deep neoplastic involvement of the corpora, violation of the tunica albuginea and Buck's fascia, and extension of disease into the superficial subcutaneous tissues of the penile shaft. On T2-weighted MRI, the normally hyperintense corpora have been replaced by abnormal heterogeneous soft tissue signal and the normally hypointense tunica and investing fascia have been disrupted. These findings suggest tumor origin deep within the penis rather than on the skin surface, which should prompt consideration of diagnoses other than squamous cell carcinoma.

Soft tissue sarcomas, including leiomyosarcoma, are mesenchymal spindle cell neoplasms that may arise from smooth or striated muscle in the penis. Sarcomas of the penis are described as superficial or deep, as discussed earlier, which carry differing risks of distant metastatic disease and prognosis. Tumor size, mitotic activity, and depth are the most useful predictors of patient outcomes [7–9]. Superficial leiomyosarcoma arises from the dartos muscle, erector pilorum muscle, or wall of a superficial blood vessel and often presents as small painless nodules without deep invasion or urinary symptoms [5]. Treatment in these cases typically consists of wide local tumor excision vs partial penectomy. Distant metastatic disease is rare with a good prognosis for recurrence-free survival [7,8]. Conversely, deep-seated tumors arise from the smooth muscles of the vessels comprising the corpora and tend to be more aggressive with rapid growth, urinary symptomatology, and poorer prognosis. Treatment typically consists of radical penectomy with consideration of radiation therapy and chemotherapy. Distant pulmonary metastatic disease is not uncommon in patients with penile sarcoma and many patients succumb to the disease. Lymph node dissection is not routinely performed given low risk of lymphatic spread and limited survival benefit following lymphadenectomy. This is different from squamous cell carcinoma, where lymphadenectomy is typically performed [5,7].

Primary penile lymphoma is extremely rare, with fewer than 30 reported cases identified by our literature search [10–13]. Primary penile lymphoma would only be considered in the absence of evidence of systemic disease elsewhere such as lymphadenopathy, other sites of visceral involvement, or a known history of lymphoma. Most cases of penile lymphoma represent direct extension of pelvic disease or hematogenous or lymphatic spread of disease from elsewhere [11]. The presentation of penile lymphoma varies, presenting as a palpable mass, skin ulcer, or diffuse swelling [11–14]; additional symptoms such as dysuria or pyuria may be present, with phimosis or priapism less often seen [12,13]. Most cases are located on the penile shaft or on the glans penis [11–13]. Treatment typically consists of chemotherapy and more recently immunotherapy.

In conclusion, penile cancer is a rare genitourinary malignancy, most of which represent primary neoplasms of the skin with squamous cell carcinoma histology. However, less common malignancies of the penis should be considered in patients presenting with a non-keratin-producing mass or in the setting of a known primary cancer elsewhere with a propensity for penile metastases. Diagnostic imaging is most helpful in evaluating the epicenter of the mass, assessing local extent of disease, and involvement of any regional lymph nodes.

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