CASE IN POINT

Leiomyosarcoma of the Penis: A Case Report and Re-Appraisal

Zainub Ajmal, MBBS[a]; Abdul Moiz Khan, MBBS[a]; Fatima Tuz Zahra, MBBS[a]; Lezah McCarthy, MD[b]; Rebecca O'Malley, MD[b]; and Syed Mehdi, MD[b]

Background: Penile leiomyosarcoma arises from smooth muscles, which can be from dartos fascia, erector pili in the skin covering the shaft, or from tunica media of the superficial vessels and cavernosa. We describe presentation, treatment options, and recurrence pattern of this rare malignancy.

Case Presentation: We present a case of penile leiomyosarcoma in a 70-year-old patient who presented to the urology clinic with 1-year history of a slowly enlarging penile mass associated with phimosis.

Conclusions: Prognosis of penile LMS is difficult to ascertain because reported cases are rare. Penile leiomyosarcoma can be classified as superficial or deep based on tumor relation to tunica albuginea. Deep tumors (> 3 cm), high-grade lesions, and tumors with involvement of corpora cavernosa, tend to spread locally and metastasize to distant areas and require more radical surgery with or without postoperative radiation therapy. In contrast, superficial lesions can be treated with local excision only.

Author affiliations can be found at the end of this article.
Correspondence: Zainub Ajmal (ajmalz@amc.edu)

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Penile cancer is rare with a worldwide incidence of 0.8 cases per 100,000 men.[1] The most common type is squamous cell carcinoma (SCC) followed by soft tissue sarcoma (STS) and Kaposi sarcoma.[2] Leiomyosarcoma (LMS) is the second most common STS subtype at this location.[3] Approximately 50 cases of penile LMS have been reported in the English literature, most as isolated case reports while Fetsch and colleagues reported 14 cases from a single institute.[4] We present a case of penile LMS with a review of 31 cases. We also describe presentation, treatment options, and recurrence pattern of this rare malignancy.

CASE PRESENTATION

A patient aged 70 years presented to the urology clinic with 1-year history of a slowly enlarging penile mass associated with phimosis. He reported no pain, dysuria, or hesitancy. On examination a 2 × 2-cm smooth, mobile, nonulcerating mass was seen on the tip of his left glans without inguinal lymphadenopathy. He underwent circumcision and excision biopsy that revealed an encapsulated tan-white mass measuring 3 × 2.2 × 1.5 cm under the surface of the foreskin. Histology showed a spindle cell tumor with areas of increased cellularity, prominent atypia, and pleomorphism, focal necrosis, and scattered mitoses, including atypical forms. The tumor stained positive for smooth muscle actin and desmin. Ki-67 staining showed foci with a very high proliferation index (Figure). Resection margins were negative. Final Fédération Nationale des Centres de Lutte Contre Le Cancer score was grade 2 (differentiation, 1; mitotic, 3; necrosis, 1). Computed tomography of the chest, abdomen, and pelvis did not show evidence of metastasis. The tumor was classified as superficial, stage IIA (pT1cN0cM0). Local excision with negative margins was deemed adequate treatment.

DISCUSSION

Penile LMS is rare and arises from smooth muscles, which in the penis can be from dartos fascia, erector pili in the skin covering the shaft, or from tunica media of the superficial vessels and cavernosa.[5] It commonly presents as a nodule or ulcer that might be accompanied by paraphimosis, phimosis, erectile dysfunction, and lower urinary tract symptoms depending on the extent of local tissue involvement. In our review of 31 cases, the age at presentation ranged from 38 to 85 years, with 1 case report of LMS in a 6-year-old. The highest incidence was in the 6th decade. Tumor behavior can be indolent or aggressive. Most patients in our review had asymptomatic, slow-growing lesions for 6 to 24 months before presentation—including our patient—while others had an aggressive tumor with symptoms for a few weeks followed by rapid metastatic spread.[6,7]

Histology and Staging

Diagnosis requires biopsy followed by histologic examination and immunohistochemistry of the lesion. Typically, LMS shows fascicles of spindle cells with varying degrees of nuclear atypia, pleomorphisms, and necrotic regions. Mitotic rate is variable and usually > 5 per high power field. Cells stain positive for smooth muscle

actin, desmin, and h-caldesmon.[8] TNM (tumor, nodes, metastasis) stage is determined by the American Joint Committee on Cancer guidelines for STS.

Pratt and colleagues were the first to categorize penile LMS as superficial or deep.[9] The former includes all lesions superficial to tunica albuginea while the latter run deep to this layer. Anatomical distinction is an important factor in tumor behavior, treatment selection, and prognosis. In our review, we found 14 cases of superficial and 17 cases of deep LMS.

Treatment

There are no established guidelines on optimum treatment of penile LMS. However, we can extrapolate principles from current guidelines on penile cancer, cutaneous leiomyosarcoma, and limb sarcomas. At present, the first-line treatment for superficial penile LMS is wide local excision to achieve negative margins. Circumcision alone might be sufficient for tumors of the distal prepuce, as in our case.[10] Radical resection generally is not required for these early-stage tumors. In our review, no patient in this category developed recurrence or metastasis regardless of initial surgery type (Table 1).[6,11,12]

For deep lesions, partial—if functional penile stump and negative margins can be achieved—or total penectomy is required.[10] In our review, more conservative approaches to deep tumors were associated with local recurrences.[7,13,14] Lymphatic spread is rare for LMS. Additionally, involvement of local lymph nodes usually coincides with distant spread. Inguinal lymph node dissection is not indicated if initial negative surgical margins are achieved.

For STS at other sites in the body, radiation therapy is recommended postoperatively for high-grade lesions, which can be extrapolated to penile LMS as well. The benefit of preoperative radiation therapy is less certain. In limb sarcomas, radiation is associated with better local control for large-sized tumors and is used for patients with initial unresectable tumors.[15] Similar recommendation could be extended to penile LMS with local spread to inguinal lymph nodes, scrotum, or abdominal wall. In our review, postoperative radiation therapy was used in 3 patients with deep tumors.[16-18] Of these, short-term relapse occurred in 1 patient.

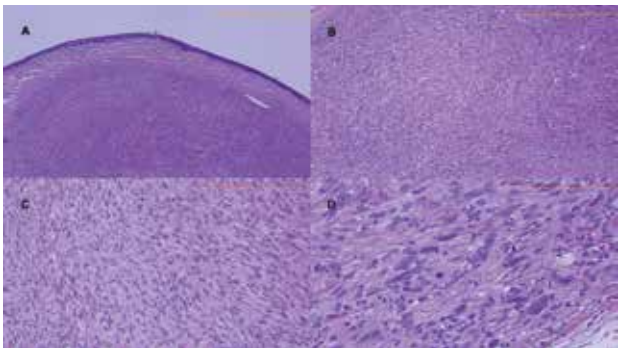
Chemotherapy for LMS remains controversial. The tumor generally is resistant to chemotherapy and systemic therapy, if employed, is for palliative purpose. The most promising results for adjuvant chemotherapy for resectable STS is seen in limb and uterine sarcomas with high-grade, metastatic, or relapsed tumors but improvement in overall survival has been marginal.[19,20]

Single and multidrug regimens based on doxorubicin, ifosfamide, and gemcitabine have been studied with results showing no efficacy or a slight benefit.[8,21] Immunotherapy and targeted therapy for penile STS have not been studied. In our review, postoperative chemotherapy was used for 2 patients with deep tumors and 1 patient with a superficial tumor while preoperative chemotherapy was used for 1 patient.[16,18,22] Short-term relapse was seen in 2 of 4 of these patients (Table 2).

Metastatic Disease

LMS tends to metastasize hematogenously and lymphatic spread is uncommon. In our

FIGURE Hematoxylin and Eosin Stains



A, ×40 magnification shows squamous surface of the foreskin with spindled cell neoplasm underneath; B, ×100 magnification shows areas with spindled cell nuclear atypia including nuclear enlargement and pleomorphism; C, ×200 magnification shows bland spindled cells in fascicular architecture; D, ×400 magnification shows several mitotic figures, nuclear atypia, and pleomorphism.

TABLE 1 Superficial Tumors[6,11,22]

Characteristics	Results
Tumor sites, No.	14
Glans	6
Prepuce	5
Shaft	2
Frenulum	1
Initial treatment, No.	
Local excision	9
Partial penectomy	4
Total penectomy	1
Recurrence/metastasis at follow-up, No.	0
Duration of follow-up, mean, mo	9

TABLE 2 Chemotherapy for Deep Tumors

Authors, y	Timing	Regimen	Relapse/ Metastasis	Follow-up
McDonald et al, 1983[16]	Preoperative	Cyclophosphamide, doxorubicin, dacarbazine	Right perineum and lungs	Died 7 mo postdiagnosis
Lacarrière et al, 2012[22]	Postoperative	Anthracycline based	Lungs	Died 2 mo postdiagnosis
Smart, 1984[18]	Postoperative	Cyclophosphamide, vincristine, actinomycin	None	Disease free at 6 mo

review, 7 patients developed metastasis. These patients had deep tumors at presentation with tumor size > 3 cm. Five of 7 patients had involvement of corpora cavernosa at presentation. The lung was the most common site of metastasis, followed by local extension to lower abdominal wall and scrotum. Of the 7 patients, 3 were treated with initial limited excision or partial penectomy and then experienced local recurrence or distant metastasis.[7,13,14,23] This supports the use of radical surgery in large, deep tumors. In an additional 4 cases, metastasis occurred despite initial treatment with total penectomy and use of adjuvant chemoradiation therapy.

In most cases penile LMS is a de novo tumor, however, on occasion it could be accompanied by another epithelial malignancy. Similarly, penile LMS might be a site of recurrence for a primary LMS at another site, as seen in 3 of the reviewed cases. In the first, a patient presented with a nodule on the glans suspicious for SCC, second with synchronous SCC and LMS, and a third case where a patient presented with penile LMS 9 years after being treated for similar tumor in the epididymis.[17,24,25]

Prognosis

Penile LMS prognosis is difficult to ascertain because reported cases are rare. In our review, the longest documented disease-free survival was 3.5 years for a patient with superficial LMS treated with local excision.[26] In cases of distant metastasis, average survival was 4.6 months, while the longest survival since initial presentation and last documented local recurrence was 16 years.[14] Five-year survival has not been reported.

CONCLUSIONS

LMS of the penis is a rare and potentially aggressive malignancy. It can be classified as superficial or deep based on tumor relation to the tunica albuginea. Deep tumors, those > 3 cm, high-grade lesions, and tumors with involvement of corpora cavernosa, tend to spread locally, metastasize to distant areas, and require more radical surgery with or without postoperative radiation therapy. In comparison, superficial lesions can be treated with local excision only. Both superficial and deep tumors require close follow-up.

Author affiliations

[a]Albany Medical Center, New York
[b]Stratton Veterans Affairs Medical Center, Albany, New York

Author disclosures

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Ethics and consent

Verbal consent was obtained from the patient prior to submitting and publishing; information has been adjusted to avoid patient identification.

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