PATHOLOGICA 2024;116:46-54**;**
DOI: 10.32074/1591-951X-953

Original Article

Soft tissue tumours of the penis. The 30-year Istituto Nazionale Tumori di Milano experience

Maurizio Colecchia[1,2], Giacomo Maria Pini[2], Giancarlo Pruneri[3,4], Nicola Nicolai[5], Sascia Servillo[6]

[1] IRCCS San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan, Italy; [2] Department of Pathology, IRCCS San Raffaele Scientific Institute, Milan, Italy; [3] Department of Pathology and Laboratory Medicine, Foundation IRCCS National Cancer Institute, Milan, Italy; [4] Department of Oncology and Hematoncology, University of Milan, Milan, Italy; [5] Urology Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [6] Pathology Unit, Azienda Ospedaliera di Bergamo, Bergamo, Italy

Summary

Objective. Small series and individual cases of penile soft tissue tumours are reported in the literature: these are rare tumours that represent less than 5% of all penile tumours.

Methods. Penile soft tissue tumours were collected from the archive of the Department of Pathology at the Istituto Nazionale dei Tumori of Milan between January 1990 and October 2021. All available medical records were retrieved and reviewed to obtain clinical information.

Results. Our series refers to the 30-year experience of highlighting the heterogeneity in the presentation and microscopic features of these rare sarcomas. 18 penile soft tissue tumours are described, 4 benign and 14 malignant. The mean age at diagnosis was 58.2 years (range 24-96 years) and 53.6 years among malignancies (range 24-89). The most frequent histotype was Kaposi's sarcoma (nr = 4) and very unusual histotypes were observed, namely low-grade fibromyxoid sarcoma, synovial sarcoma, proximal type epithelioid sarcoma and the first reported case of dedifferentiated liposarcoma of the penis.

Conclusions. Among sarcomas of the genitourinary tract, tumours of the soft tissues of the penis are the rarest. Penile sarcomas can present at a young age. Kaposi's sarcoma in HIV-negative patients has a favorable outcome, while deep sarcomas have an aggressive behavior and poor prognosis.

Key words: penis, soft tissue tumours, histopathology

Received: November 19, 2023
Accepted: November 27, 2023

Correspondence
Maurizio Colecchia
E-mail: colecchia.maurizio@hsr.it

How to cite this article: Colecchia M, Pini GM, Pruneri G, et al. Soft tissue tumours of the penis. The 30-year Istituto Nazionale Tumori di Milano experience. Pathologica 2024;116:46-54. https://doi.org/10.32074/1591-951X-953

Introduction

Neoplasms of the penis constitute approximately 0.5% of all malignant neoplasms in the United States and Europe. Mesenchymal malignancies are rare, comprising less than 5% of all penile tumours [1]. Few case reports and small case series over a long time span addressed this issue. Changing classification criteria and evolving therapies are reasons of even greater difficulties in interpretation of data., The 4th Edition of WHO Classification reported the Armed Forces Institute of Pathology (AFIP) data collected between 1970 and 1999 [2], on 116 soft tissue tumours of the penis, with Kaposi sarcoma (KS) being the most common [3]. In this study we report 18 soft tissue tumours of the penis (4 benign, 14 malignant) collected between 1990 and 2021 at Istituto Nazionale Tumori of Milan (INT) in adult males, focusing on their clinicopathologic features and outcomes.

Materials and methods

Penile soft tissue tumours were collected from the archive of the department of Pathology at INT between January 1990 and October 2021, which included hospitalized cases from the Urology Unit at INT, and and outpatient men sent for second opinion. Histological reports and tissue slides were reviewed by a senior author (MC). Ethical approval for the study was obtained and informed consensus was gathered in all cases for patients admitted to INT. All available medical records (discharge letters, outpatient visits and radiological reports) were retrieved and reviewed to obtain age at diagnosis, clinical presentation, prior history of neoplastic diseases, serological HIV status in KS, treatment, local relapses, presence of lymph nodal or distant metastases at time of diagnosis or during follow-up, overall and disease-free survival. Follow-up was censored in December 2022. Penile localisation of metastatic sarcomas with extra-penile primary sites was excluded. Particular attention was paid to re-evaluate the original diagnoses, in order to check that they were all uptodated according to the latest WHO classification [4]. Clinical and pathological reports and available slides were reviewed in order to collect the following informations: type of surgery, gross description, tumour size, tumour location (root/shaft/foreskin/glans), results of immunohistochemical and molecular studies (when available), and resection margin status of surgical specimens. Neoplasms were classified as either superficial or deep infiltrating. Deep infiltration was defined as neoplastic infiltration of either the corpora spongiosum and/or cavernosum. Statistical analysis was performed with IBM SPSS Statistics Data Editor v. 23 to calculate a Kaplan-Meier curve that compares the survival between patients with either superficial or deep neoplastic infiltration, respectively.

Results

Among 1,150 penile neoplasms diagnosed and recorded between January 1990 and October 2021 at the Pathology Department of the INT, we selected 18 (1.5%) primary penile soft tissue tumours, after the exclusion of two metastatic sarcomas (one GIST and one spindle cell sarcoma, NOS). Clinical available data are summarised in Table I. Mean age at diagnosis was 58.2 years (range 24-96 years), and 53.6 years among malignant tumours (range 24-89), while for the 4 benign tumours (hemangiomas) age range at diagnosis was 60- 96 years (mean 74.5). Follow-up was highly variable in the 10 malignant cases followed at the INT: from 7 to 217 months (mean 83.4 months). Four patients had a history of a previous malignancy. Serological HIV status was available in two KS and it was negative. The mean size of the lesions was 3.95 cm (range 0.8 cm-10 cm). The location of the penile sarcomas was known in 16 cases: glans was affected in 8 cases (in 2 with involvement of the foreskin and in one with the shaft), root of penis in 5, shaft only in 2 cases, foreskin in one case, while two cases had unknown primitive site. The therapeutic procedure varied greatly and depended on the location, histotypes, and age of the patient. In those who underwent surgery with radical intent, the resection margins were free of neoplasms in all cases except one. The latter was initially treated with local excision, and subsequently radicalised with partial penectomy. Only two cases were treated with total penectomy (one including nodal dissection), one with partial penectomy, 12 with biopsies, either incisional (3) or excisional (9). As many as 4 cases had pathological review only and clinical data were lacking. After a median follow-up of 9 months, 7 patients relapsed after 2 to 68 months.

According to histology, the most frequent were Kaposi sarcoma. The immunohistochemical results of these cases and of the other neoplasms are summarised in Table II. KS was diagnosed in 4 cases (aged 40 to 77), of whom 2 were treated in our institution. The first showed multiple localisations on the prepuce and shaft, all of which were treated only with local exeresis. The second, after suffering from Hodgkin's lymphoma and prostate adenocarcinoma, had a first KS on the knee; the following years were characterised by multiple and widespread recurrences with penile involvement.

The second most frequent entity in the present series was proximal-type epithelioid sarcoma [5]. Three cases were diagnosed at ages of 24, 35 and 59 years. The first two were located at the root of the penis with infiltration of the corpora cavernosa, with a maximum diameter of 6 cm and 4.5 cm respectively, whereas the third case was located on the foreskin (dimensions not available). All the lesions showed loss of nuclear INI1/SMARCB1 expression. The tumour involved the visceral structures of the penile root (predominantly the corpora cavernosa) with an intact overlying skin. Deaths occurred at 7 and 88 months in the first and second cases with disseminated disease, while the third case was lost to follow-up. The case of angiosarcoma occurred in a 69-year-old man with a nodule of the balanopreputial sulcus with diagnosis of epithelioid angiosarcoma on biopsy. He presented in INT with two nodules of the shaft, 7 mm and 8 mm, adjacent to the corpora cavernosa, and underwent chemotherapy and a radical penectomy with bilater-

al inguinal lymphadenectomy. A 9 mm nodule with a hard consistency was observed on the dorsal side of the shaft, showing the features of epithelioid angiosarcoma (Fig. 1). At the last FU he was alive with no evidence of disease (NED). Two cases were classified as sarcomas with myogenic differentiation: a 47 years old male with a history of fibroblastic osteosarcoma of the left tibia, and a 63-years-old man with recurrent glans carcinoma in situ. The histological examination was characterized by solid proliferation of cells with high-grade atypia, spindle and pleomorphic, mitotically active (mitoses between 10 and 20/10HPF), in sclero-hyaline stroma with focal necrosis. None of the cases showed a pattern of recognisable leiomuscular growth and the diagnosis was sarcoma with myogenic differentiation, grade 3 and grade 2, respectively, according to FNCLCC [6]. The patient with G3 sarcoma died 52 months later after surgery, and the other patient is alive without disease (36 months follow-up). A case of dedifferentiated liposarcoma occurred in an 89-year-old man with a 4-cm lesion at the root of the penis that extended along the shaft with infiltrating characteristics on CT scan (Fig. 2) and hyper-capturing on PET-FDG. On biopsy the lesion showed atypi-

Table I. Summary of clinicopathologic features.

	Age	Neoplastic localization	Superficial/ deep neoplastic localization	Neoplastic diameter (cm)	Diagnosis	Distant metastatic disease	Surgical therapy	Follow-up (months)	Outcome	Other neoplastic diseases and other therapies
1	35	Root	Deep	4.5	Proximal-type epithelioid sarcoma	None	Incisional biopsy	7	DOD	CHT (famorubicine +ifosfamide) + RT
2	24	Root	Deep	6	Proximal-type epithelioid sarcoma	None	Incisional biopsy	88	DOD	CHT (cyclophosphamide +etoposide)
3	59	Foreskin	Superficial	NA	Proximal-type epithelioid sarcoma	Lung metastases	Excisional biopsy	8	DOD	Hodgkin lymphoma (CHT + RT)
4	47	Glans and foreskin	Deep	10	Myogenic sarcoma G3	Lung metastases	Total penectomy	52	DOD	Fibroblastic osteosarcoma of the left leg (surgery) + CHT (etoposide + ifosfamide)
5	63	Glans	Deep	4	Myogenic sarcoma G2	None	Laser biopsy + partial penectomy	54	NED	CIS of the gland
6	39	Root	Superficial	2	Epithelioid haemangioendothelioma	None	Excisional biopsy	217	NED	None
7	71	Glans	Superficial	0.8	Kaposi sarcoma	None	Excisional biopsy	96	AWD	None
8	77	Glans and foreskin	Superficial	NA	Kaposi sarcoma	None	Excisional biopsy	161	DWD	Hodgkin lymphoma, prostatic adenocarcinoma + CHT (unspecified) + RT
9	67	NA†	NA†	NA†	Kaposi sarcoma	NA†	NA†	NA†	NA†	NA†
10	39	Shaft	Superficial	NA†	Kaposi sarcoma	NA†	NA†	NA†	NA†	NA†
11	69	Glans and shaft	Superficial	0.9§	Epithelioid angiosarcoma	None	Emasculation + bilateral inguinal lymphoadenectomy	125	NED	nCHT (epirubicin +ifosfamide)
12	89	Root	Deep	4	Dedifferentiated liposarcoma	Lung	Incisional biopsy	26	AWD	RT
13	44	Root	Deep	NA†	Fibromyxoid sarcoma	None	NA†	NA†	LFU	NA
14	27	Shaft	NA†	2,6	Synovial sarcoma	None	Excisional biopsy	NA†	LFU	None
15	74	Glans	Superficial	NA	Haemangioma	NA	Excisional biopsy	NA	NA	None
16	60	NA	NA	NA	Capillary haemangioma	NA	Excisional biopsy	NA	NA	None
17	68	Glans	Superficial	1.5	Epithelioid haemangioma	None	Excisional biopsy	NA	NA	None
18	96	Glans	NA	1.5	Haemangioma	NA	Excisional biopsy	NA	NA	None

†Case sent as consultation with limited clinical and pathological data available; § After nCHT. CHT chemotherapy; DOD died of disease; DWD died with disease; LFU lost to follow-up; NA not available; NED no evidence of disease; nCHT neoadjuvant chemotherapy; RT radiotherapy

Table II. Immunohistochemistry in 13 cases†.

	Diagnosis	Immunohistochemistry
1	Proximal-type epithelioid sarcoma	Vimentin+, CKAE1/AE3+, CK8/18+, EMA+, CD34+F, CD99+, INI1+, Bcl2+F, Smooth Muscle Actin (1A4)-, Desmin-, S100-, CD117-
2	Proximal-type epithelioid sarcoma	CD99+, CD34+F, CK Cam5.2+, FLI1-, EMA-, INI1-
3	Proximal-type epithelioid sarcoma	EMA+, CK Cam5.2+F, Vimentin+, CD34-, INI1+
4	Myogenic sarcoma G3	Smooth Muscle Actin (1A4)+, Calponin+, Caldesmon+F, HHF35+, Vimentin+, CKAE1/AE3-, CK8/18-, p63-, MDM2- (no nuclear positivity), Myogenin-, Desmin-, high proliferative index (Ki67)
5	Myogenic sarcoma G2	Smooth Muscle Actin (1A4)+, Calponin+F, Caldesmon-, HHF35+, Vimentin+, CKAE1/AE3-, CK8/18-, p63-, Desmin+F, S100+ (focale), CD68+, high proliferative index (ki67)
6	Epithelioid hemangioendothelioma	CAMTA1+
9	Kaposi sarcoma	HHV8+
10	Kaposi sarcoma	CD31+, CD34-, S100-
11	Epithelioid angiosarcoma	CD31+, CD34+, FLI1+, moderate proliferative index (ki67)
12	Dedifferentiated liposarcoma	Vimentin+, Smooth Muscle Actin (1A4)+, Calponin+, p63-, Caldesmon-, Desmin-, HHV8-, Podoplanin-, high proliferative index (ki67)
13	Fibromyxoid sarcoma	MUC4+, Estrogen receptor+F, Vimentin+, CD34-, low proliferative index (ki67)
14	Synovial sarcoma	CD99+, CD31-, CD34-, Calretinin-, Desmin, Thrombomodulin-
17	Epithelioid hemangioma	FLI+, p53-, HHV8-, high proliferative index (ki67)

†The case number reported in the 13 cases with immunostains are the same as Table I. +F = focal immunohistochemical positivity, with < 10% of positive cells. Proliferative index (Ki67): high equals > 50%, moderate equals 5-50%, low equals < 5%

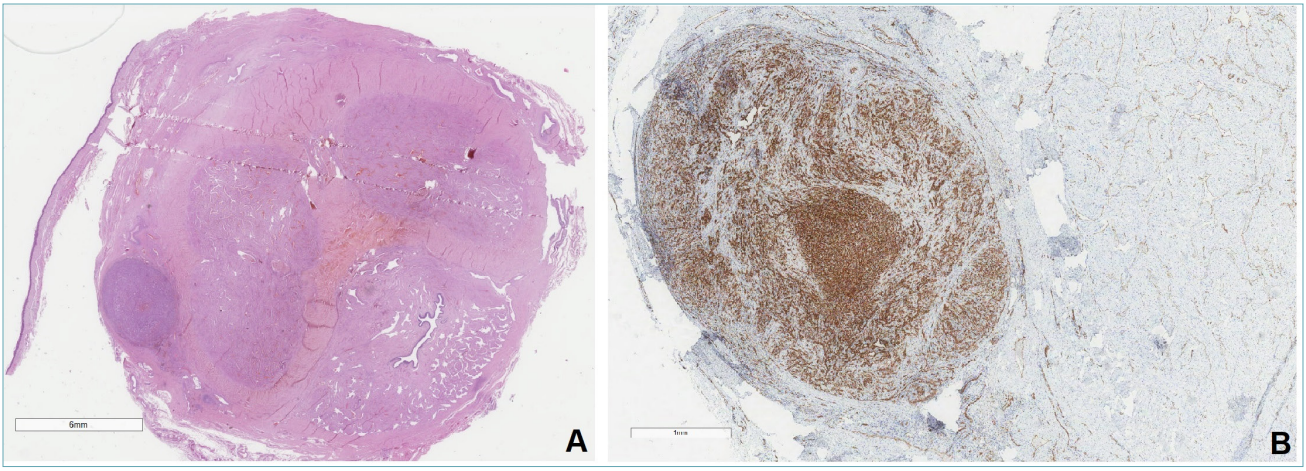

Figure 1. Epithelioid angiosarcoma: (A) nodule observed on the dorsal side of the shaft in the lamina propria (H&E stain); (B) Vascular proliferation stained by CD31.

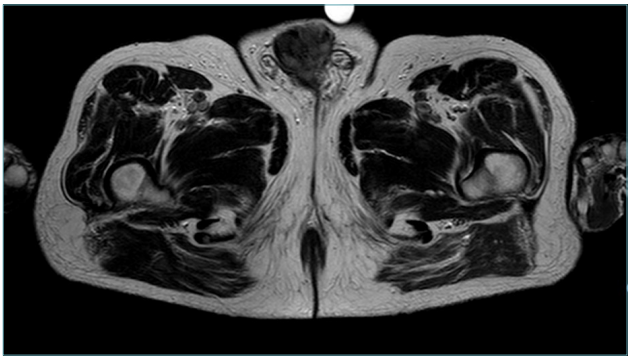

Figure 2. Dedifferentiated liposarcoma: CT scan showing a 4-cm lesion at the root of the penis infiltrating the surrounding tissues.

cal, pleomorphic and spindle cells, with diffuse growth, rare mitoses, absence of necrosis, with expression of vimentin, actin 1A4, desmin, calponin, and MDM2 amplification confirmed by FISH. A diagnosis of dedifferentiated liposarcoma with myogenic differentiation was made (Fig. 3 a-b). At the last follow-up the patient had metastases to the lung. A patient with a previous epithelioid haemangioendothelioma of the penis was referred to INT for the presence of nodular formations, one on the dorsal surface of the penis (2 cm) and another on the ventral surface (0.5 cm) in close proximity to the corpora cavernosa: CAMTA1 positivity

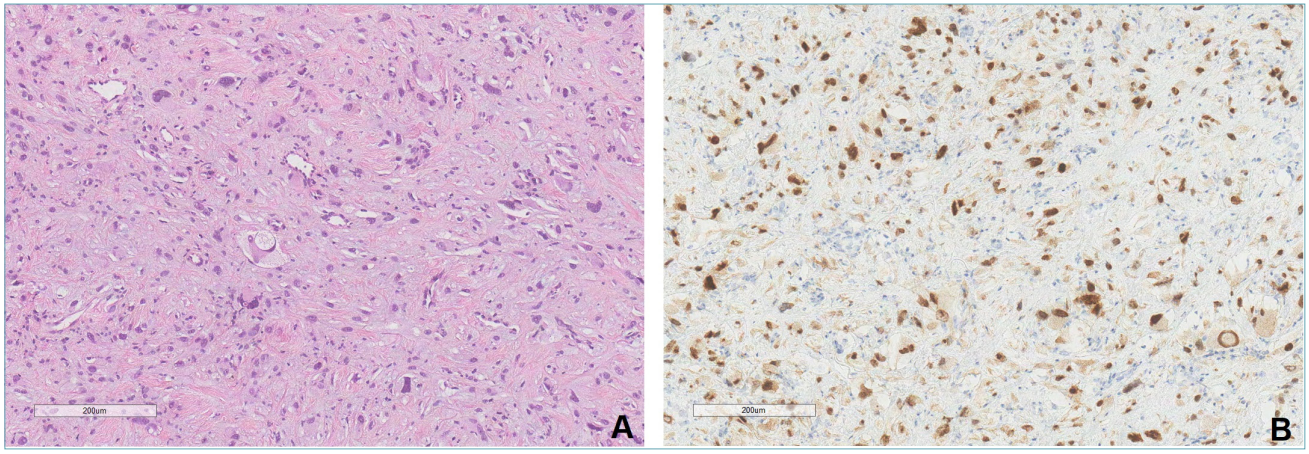

Figure 3. Dedifferentiated liposarcoma: (A) atypical, pleomorphic and spindle cells in bioptical sample (H&E stain); (B) the cells show MDM2 nuclear immunostaining.

confirmed the diagnosis of epithelioid haemangioendothelioma in the bioptical samples. During follow-up further local recurrences of the disease occurred.
In two consultation cases, a case of synovial sarcoma (SS) and a case of fibromyxoid sarcoma, we had limited access to the clinical history and histological materials consisting in H&E and some immunostains. SS occurred as a painful penile mass in a 27-year-old man on the right side of the penis. Magnetic resonance imaging (MRI) showed a dishomogeneous oval lesion close to the right corpus cavernosous, measuring 2.6 cm in diameter. Complete enucleation of the tumour was performed, and the diagnosis was synovial sarcoma, as reported in the case published in 2002 [7]. This patient was lost to follow-up. The second case, provided by an external hospital from North-East Italy, occurred in a 44 years-old man in the root of the penis in a periurethral site. Based on a morphological and molecular study that showed the translocation of the FUS gene in 16p11 by FISH, a diagnosis of low-grade fibromyxoid sarcoma was made. Among the 14 malignant neoplasms, eight cases (57.1%) involved the sub-cutaneous tissue of the prepuce and superficial tissue of the shaft below the Dartos fascia, while six cases (42.9%) involved deep tissues of the glans with involvement of the corpus spongiosum or the shaft. Deep neoplastic infiltration was more frequently observed among patients who died of disease, with a trend towards statistical significance of the Kaplan-Meier curve ($p = 0.073$; Kaplan-Meier curve is shown as supplementary material n. 1).

Discussion

Our series refers to all cases of penile sarcoma evaluated over 31-years, and to our knowledge this is one of the largest single institutional series on penile soft tissue tumours. The frequency of the histotypes of penile sarcomas differs from those occurring in other sites [1,4,8]. Benign neoplasms usually present with painless nodules, while penile sarcomas are frequently deep lesions occurring with urinary obstruction and priapism [4]. They represent approximately 1/3 of the AFIP registry, which collects cases from 1970 to 1999, where KS is reported as the most frequent penile sarcoma [4]. In the California Cancer Registry [9], the prevalence of KS compared with all penile cancers was reported to be 7.4% in the period 1988-1995 decreasing to 1.7% in the period 1995-2004. HHV8-associated penile primary sarcoma had a peak incidence in the years of maximum HIV diffusion, a trend conditioned both by the degree of immunosuppression and by the patient's other possible comorbidities, with a 32.8% 5-year survival rate. This contrasts with the series of Dehner and Smith and the present study, where no deaths were documented. Apart from the association between KS and HHV-8 infection, and a post-radiotherapy penile angiosarcoma [10], knowledge of possible associated external factors is scarce. Differential diagnosis between benign and malignant tumours is sometimes difficult particularly in vascular neoplasms. Epithelioid hemangioendothelioma of the penis was reported in 22 cases, of which 19 were case reports and 3 were reported by Dehner [3,11-26]. The affected sites were the glans, corpora cavernosa, root of the penis, and subcutaneous tissues: three patients developed metastases and two of them died of the disease, while local recurrence was more frequent; in most cases the course was favourable with a documented disease-free interval of up to 5 years. Most authors agree on treat-

ment based on local excision in small cases, followed by follow-up [11]. Some tumours are characterised by the presence of the SERPINE1-FOSB fusion gene, demonstrated by PCR but also by immunohistochemical expression of FOSB [27]. In our case the lesion was localised to the root of the penis, the patient underwent local excision and he is alive without disease. The only angiosarcoma observed as a recurrence in the shaft of the penis can be easily differentiated from an anastomosing haemangioma, which has the genitourinary tract, in particular the kidney [28], the retroperitoneum and the paraspinal region as its preferential sites. The differential diagnosis is based on morphology, but cellular atypia and infiltrative growth are missing, the vessels are well formed and can be thrombosed, in addition to the possible presence of extramedullary hematopoiesis [28-30]. Another mimicker of benign lesions is the epithelioid sarcoma (ES), which clinically overlaps with Peyronie' s disease [31]. This entity was first described in 1970 by Enzinger [32], while one of the cases reported in his series by Dehner [3], a 35-year-old man diagnosed with "fascial sarcoma," was a true ES as quoted by Rossi [31]. Clinical history begins more than 5 years before the diagnosis in the majority of ES. The tumour is characterised by slow growth, and when the lesion is located at the root or shaft of the penis, it causes focal induration and deviation associated with pain during erection. In cases subjected to biopsy, the morphological appearance is characterised by large epithelioid elements with granulomatous-like growth, sometimes necrotizing, often overlooked simulating Peyronie's disease (Fig. 4 a-d) [33]. Unlike the latter, sarcomatous lesions fail to respond or relapses following Peyronie's therapy, increasing in size by infiltrating and replacing the surrounding tissue, and causes urinary symptoms [34]. An alteration described in over 90% of

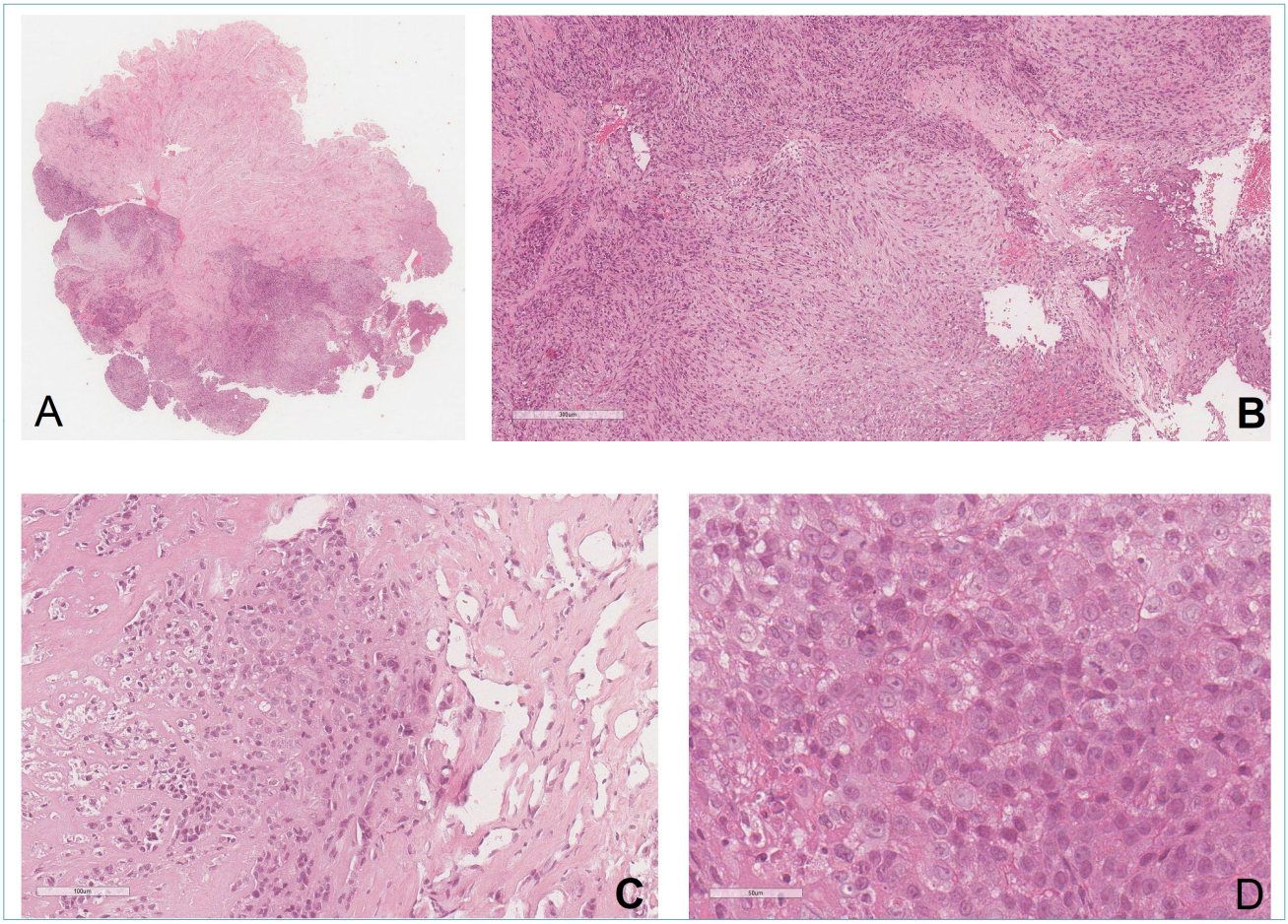

Figure 4. Proximal-type epithelioid sarcoma: (A) low magnification image of incisional biopsy of epitheliod sarcoma of the shaft of the penis showing a multinodular growth pattern of epithelioid cells; (B-C-D) higher magnification of epithelioid elements sometimes necrotising, showing pleomorphic tumour cells with deep eosinophilic cytoplasm and enlarged vesicular nuclei with prominent nucleoli (carcinoma-like). These features are typical of proximal-type epithelioid sarcoma.

cases of ES [35] of both variants is the loss of expression of the protein INI1/SMARCB1. Epithelioid features of this entity could be misdiagnosed as squamous cell carcinoma [36]. Nodular lesions occurring in young males that grow on the root or shaft and affect the corpora cavernosa and/or spongiosa, without involvement of the epithelium, make epithelial origin unlikely. Unfavourable parameters are deeper locations (i.e., corpora cavernosa invasion), larger size, higher tumour stage, and the proximal subtype [6]. We have reported two cases of sarcoma with myogenic differentiation not attributable to any mature tissue, mainly consisting of spindle-shaped and pleomorphic elements expressing one or more muscular markers: according to the WHO, to make a diagnosis of leiomyosarcoma, areas with leiomuscular morphology must be present, at least focally [4]. Leiomyosarcoma represents 5-6% of cases in Dehner's series [3] and the most numerous series is the one already described by Fetsch [37]. The neoplasm affects any age, but most cases are in the fourth and fifth decades of life. Prognosis appears to be related to the lesion size. Then we have reported the first occurrence of penile liposarcoma, which is also the most common malignant mesenchymal neoplasms in the genitourinary system, with frequent occurrence in the paratesticular soft tissues [38-42]. However, no cases have yet been described in the penis, and the presence of adipose tissue in the penile fascia (Buck's fascia) lining the corpora cavernosa and in the tunica albuginea in penectomy samples [43] in correspondence with the glans penis and penile shaft has been documented in a percentage ranging between 19% and 53%. The adipocytic neoplasia in our case led us to consider the presence of adipose tissue in the root of the penis. The differentiated component with myogenic differentiation observed in the biopsy can justify the metastatic onset with localisation to the lung, considering the aggressive biological behaviour of this morphology [44]. The other rare cases reported were synovial sarcoma and low-grade fibromyxoid sarcoma, but we lack information regarding the outcomes, because they were sent for a second opinion. About the predictive factors of relapse, Dotan reported in an analysis of 131 sarcomas of genitourinary tract, significant differences in disease-specific survival both between the group of patients who underwent or who did not undergo surgery, and among those with resection margins affected or not affected by the tumour [38]. By comparing patients' prognosis to the depth of tumoural infiltration, 6 cases (46.1%) involved deep tissues of the glans and shaft, where tumours involving the corpus cavernosus or corpus spongiosum were considered deep and tumour-related death was significantly associated with deep extension. Some bias affects the selection of the cases: the most important being almost total absence of benign tumours, excluding vascular neoplasms, that are not referred to a center for treatment of soft tissue sarcomas. Another problem common to many other rare tumours is the absence of therapies other than surgery. Need for other cases delucidating the behavior and best practice to treat these patients is a compelling issue for the rarest among rare penile tumours.lude a review of the key literature. If there are relevant controversies or disagreements in the field, they should be mentioned so that a non-expert reader can delve into these issues further. The discussion should consider the major conclusions of the work along with some explanation and/or speculation on their significance. How do the conclusions affect the existing assumptions and models in the field? How can future research build on these observations? What are the key experiments that remain? The discussion should be concise with solid arguments.

Conclusions

Among sarcomas of the genitourinary tract, tumours of the soft tissues of the penis are the rarest. Penile sarcomas can present at a young age. This single-institutional case series does not allow useful conclusions to be drawn for their clinical management due to the heterogeneity of the histotypes. Kaposi's sarcoma in HIV-negative patients has a favourable outcome, while deep sarcomas have an aggressive behaviour and poor prognosis.

Conflict of interest statement

The authors declare no conflict of interest.

Funding

None

Authors' contributions

Study concept and design: MC and GMP. Acquisition of pathology data: MC and SS. Supply of clinical data: NN and SS. Analysis and interpretation of data: MC, GMP. Drafting of the manuscript: MC, GMP, SS. Statistical analysis: GMP. Administrative, technical and material support: SS. Critical revision of the manuscript for important intellectual content and supervision: MC, GMP, SS, NN, GP.

Ethical consideration

The research was conducted ethically, with all study procedures being performed in accordance with the requirements of the World Medical Association's Declaration of Helsinki.

References

1 Lucia MS, Miller J, Histopathology of malignant lesions of the penis. Urol Clin North Am. 1992;19,227-46. PMID: 1574814

2 WHO Classification of Tumours of the Urinary System and Male Genital Organs. WHO Classification of Tumours, 4th Edition, Volume 8, 2016.

3 Dehner LP, Smith BH. Soft tissue tumors of the penis. A clinicopathologic study of 46 cases. Cancer. 1970;25(6):1431-47. https://doi.org/10.1002/1097-0142(197006)25:6<1431::aid-cncr2820250624>3.0.co;2-b. PMID: 4316326.

4 Soft Tissue and Bone Tumours WHO Classification of Tumours, 5th Edition, Volume 3, 2020.

5 Guillou L, Wadden C, Coindre JM, et al. "Proximal-type" epithelioid sarcoma, a distinctive aggressive neoplasm showing rhabdoid features. Clinicopathologic, immunohistochemical, and ultrastructural study of a series. Am J Surg Pathol. 1997;21(2):130-46. https://doi.org/10.1097/00000478-199702000-00002. PMID: 9042279.

6 Trojani M, Contesso G, Coindre JM, et al. Soft-tissue sarcomas of adults; study of pathological prognostic variables and definition of a histopathological grading system. Int J Cancer. 1984;33(1):37-42. https://doi.org/10.1002/ijc.2910330108. PMID: 6693192.

7 Sasso F, Delicato G, Gentile G, et al. Primary synovial sarcoma of the penis. J Urol. 2002 Aug;168(2):633. Erratum in: J Urol. 2003;169(2):622. PMID: 12131325.

8 Katona T, Lopez-Beltran A, MacLennan G, et al. Soft tissue tumors of the penis: a review. Anal Quant Cytol Histol.2006;28:193-206. PMID: 16927639

9 Woldrich JM, Silberstein JL, Saltzstein SL, et al. Penile Kaposis sarcoma in the state of California. Can J Urol. 2012;19(2):6178-82. PMID: 22512961.

10 Prescott RJ, Mainwaring AR. Irradiation-induced penile angiosarcoma. Postgrad Med J. 1990;66(777):576-9. PMID: 2217021.

11 Sardaro A, Bardoscia L, Petruzzelli MF, et al. Epithelioid hemangioendothelioma: an overview and update on a rare vascular tumor. Oncol Rev. 2014;8(2):259. PMID: 25992243

12 Williams JJ, Mouradian JA, Hagopian M, et al. Hemangioendothelial sarcoma of penis. Cancer. 1979;44(3):1146-9. PMID: 476592.

13 Barnett CP, Low JR. Hemangio-endothelioma of the corpus cavernosum penis: case report. J Urol. 1960;83:160-2. https://doi.org/10.1016/S0022-5347(17)65676-3. PMID: 13796907.

14 Bensadoun H, Quillard J, Henry P, et al. Hemangio-endotheliosarcome des corps erectiles. A propos d'une ob-servation Hemangioendotheliosarcoma of the erectile bodies. A propos of a case. Ann Urol (Paris). 1987;21(6):435-7. French. PMID: 3435064.

15 Srigley JR, Ayala AG, Ordonez NG, et al. Epithelioid hemangioma of the penis. A rare and distinctive vascular lesion. Arch Pathol Lab Med. 1985;109(1):51-4. PMID: 3838233.

16 Kamat AM, Plager C, Tamboli P, et al. Metastatic epithelioid hemangioendothelioma of the penis managed with surgery and interferon-alpha. J Urol. 2004;171(5):1886-7. https://doi.org/10.1097/01.ju.0000119821.10704.6a. PMID: 15076299.

17 Wedmid A, Masterson TA, Maki RG, Russo P. A case of high-risk penile epithelioid hemangioendothelioma. Nat Rev Urol. 2009;6(4):223-7. https://doi.org/10.1038/nrurol.2009.26. PMID: 19352397.

18 Elhosseiny AA, Ramaswamy G, Healy RO. Epithelioid hemangioendothelioma of penis. Urology. 1986;28(3):243-5. https://doi.org/10.1016/0090-4295(86)90054-3. PMID: 3750609.

19 Gutiérrez García R, Capdevila Hernández JM, Pinto Blázquez J, et al. Hemangioendotelioma epitelioide de pene Epithelioid hemangioendothelioma of penis. Actas Urol Esp. 2004;28(10):771-3. Spanish. https://doi.org/10.1016/s0210-4806(04)73180-0. PMID: 15666521.

20 Artiles Medina A, Fraile Poblador A, Hevia Palacios M, et al. Primary epithelioid hemangioendothelioma of the penis: a case report and literature review. Transl Androl Urol. 2021;10(9):3697-3703. https://doi.org/10.21037/tau-21-277. PMID: 34733664; PMCID: PMC8511538.

21 Zastrow S, Baretton GB, Wirth MP. Multifocal recurring epithelioid hemangioendothelioma of the penis. Urology. 2008;71(2):351.e9-10. https://doi.org/10.1016/j.urology.2007.10.027. PMID: 18308123.

22 Shin DH, Chen M, Niemeier LA. Primary epithelioid hemangioendothelioma of the kidney and penis. Can J Urol. 2010 Dec;17(6):5480-2. PMID: 21172116.

23 Deutsch M, Leen RL, Mercado R Jr. Hemangioendothelioma of the penis with late appearing metastases: report of a case with review of the literature. J Surg Oncol. 1973;5(1):27-34. https://doi.org/10.1002/jso.2930050105. PMID: 4709286.

24 Gharajeh A, Siemens DR, Isotalo PA, et al. Borth CS. Multifocal penile epithelioid hemangioendothelioma masquerading as superficial penile vein thrombosis. Urology. 2006;68(3):673.e1-3. https://doi.org/10.1016/j.urology.2006.03.051. Epub 2006 Sep 18. PMID: 16979710.

25 Wen CC, Munarriz R, Goldstein I. Three-chamber priapism in a patient with primary epithelioid hemangioendothelioma of penis. Urology. 2004;64(1):156-8. https://doi.org/10.1016/j.urology.2004.03.028. PMID: 15245958.

26 Kutas M, Streit B. A penis haemangioendotheliomáról egy eset kapcsán Hemangioendothelioma of the penis, report of a case. Orv Hetil. 1980;121(22):1329-30. Hungarian. PMID: 7443220.

27 Ide YH, Tsukamoto Y, Ito T, et al. Penile pseudomyogenic hemangioendothelioma/epithelioid sarcoma-like hemangioendothelioma with a novel pattern of SERPINE1-FOSB fusion detected by RT-PCR--report of a case. Pathol Res Pract. 2015;211(5):415-20. https://doi.org/10.1016/j.prp.2015.02.003. Epub 2015 Feb 17. PMID: 25749627.

28 Brown JG, Folpe AL, Rao P, et al. Primary vascular tumors and tumor-like lesions of the kidney: a clinicopathologic analysis of 25 cases. Am J Surg Pathol. 2010;34(7):942-9. https://doi.org/10.1097/PAS.0b013e3181e4f32a. PMID: 20534992.

29 Montgomery E, Epstein JI. Anastomosing hemangioma of the genitourinary tract: a lesion mimicking angiosarcoma. Am J Surg Pathol. 2009;33(9):1364-9. https://doi.org/10.1097/PAS.0b013e3181ad30a7. PMID: 19606014.

30 Kryvenko ON, Gupta NS, Meier FA, et al. Anastomosing hemangioma of the genitourinary system: eight cases in the kidney and ovary with immunohistochemical and ultrastructural analysis. Am J Clin Pathol. 2011;136(3):450-7. https://doi.org/10.1309/AJCPJPW34QCQYTMT. PMID: 21846922.

31 Rossi G, Ferrari G, Longo L, et al. Epithelioid sarcoma of the penis: a case report and review of the literature. Pathol Int. 2000;50(7):579-85. https://doi.org/10.1046/j.1440-1827.2000.01078.x. PMID: 10886744.

32 Enzinger FM. Epitheloid sarcoma. A sarcoma simulating a granuloma or a carcinoma. Cancer. 1970;26(5):1029-41. https://doi.org/10.1002/1097-0142(197011)26:5<1029::aid-cncr2820260510 > 3.0.co;2-r. PMID: 5476785.

33 Moore SW, Wheeler JE, Hefter LG. Epitheloid sarcoma masquerading as Peyronie's disease. Cancer. 1975;35(6):1706-10. https://doi.org/10.1002/1097-0142(197506)35:6<1706::aid-cncr2820350633 > 3.0.co;2-a. PMID: 1149001.

34 Hoebeke PB, Rottey S, Van Heddeghem N, et al. One-stage penectomy and phalloplasty for epithelioid sarcoma of the penis in an adolescent: part 2. Eur Urol. 2007;51(6):1744-7. https://doi.org/10.1016/j.eururo.2006.10.032. PMID: 17575585.

[35] Hornick JL, Dal Cin P, Fletcher CD. Loss of INI1 expression is characteristic of both conventional and proximal-type epithelioid sarcoma. Am J Surg Pathol. 2009;33(4):542-50. https://doi.org/10.1097/PAS.0b013e3181882c54. PMID: 19033866.

[36] Rippentrop JM, Joslyn SA, Konety BR. Squamous cell carcinoma of the penis: evaluation of data from the surveillance, epidemiology, and end results program. Cancer. 2004;101(6):1357-63. https://doi.org/10.1002/cncr.20519. PMID: 15316902.

[37] Fetsch JF, Davis CJ Jr, Miettinen M, et al. Leiomyosarcoma of the penis: a clinicopathologic study of 14 cases with review of the literature and discussion of the differential diagnosis. Am J Surg Pathol. 2004;28(1):115-25. https://doi.org/10.1097/00000478-200401000-00014. PMID: 14707873.

[38] Dotan ZA, Tal R, Golijanin D, et al. Adult genitourinary sarcoma: the 25-year Memorial Sloan-Kettering experience. J Urol. 2006;176(5):2033-8; discussion 2038-9. https://doi.org/10.1016/j.juro.2006.07.021. PMID: 17070247.

[39] Russo P, Brady MS, Conlon K, et al. Adult urological sarcoma. J Urol. 1992;147(4):1032-6; discussion 1036-7. https://doi.org/10.1016/s0022-5347(17)37456-6. PMID: 1552580.

[40] Wang X, Tu X, Tan P, et al. Adult genitourinary sarcoma: Clinical characteristics and survival in a series of patients treated at a high-volume institution. Int J Urol. 2017;24(6):425-431. https://doi.org/10.1111/iju.13345. Epub 2017 May 3. PMID: 28470716.

[41] Nazemi A, Daneshmand S. Adult genitourinary sarcoma: A population-based analysis of clinical characteristics and survival. Urol Oncol. 2020;38(5):334-343. https://doi.org/10.1016/j.urolonc.2019.12.004. Epub 2020 Feb 21. PMID: 32094047.

[42] Mondaini N, Palli D, Saieva C, et al. Clinical characteristics and overall survival in genitourinary sarcomas treated with curative intent: a multicenter study. Eur Urol. 2005;47(4):468-73. https://doi.org/10.1016/j.eururo.2004.09.013. Epub 2004 Nov 10. PMID: 15774243.

[43] Rodriguez IM, Cuevas M, Silvero A, et al. Novel Histologic Finding: Adipose Tissue Is Prevalent Within Penile Tunica Albuginea and Corpora Cavernosa: An Anatomic Study of 63 Specimens and Considerations for Cancer Invasion. Am J Surg Pathol. 2017;41(11):1542-1546. https://doi.org/10.1097/PAS.0000000000000953. PMID: 28922187.

[44] Gronchi A, Collini P, Miceli R, et al. Myogenic differentiation and histologic grading are major prognostic determinants in retroperitoneal liposarcoma. Am J Surg Pathol. 2015;39(3):383-93. https://doi.org/10.1097/PAS.0000000000000366. PMID: 25581729.