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Surgical and Experimental Pathology

CASE REPORT

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# Penile osteosarcoma

Daniel Abensur Athanazio[1,2*], Maurício Bessa[3], José do Egypto Pereira Filho[4] and Paulo Roberto Fontes Athanazio[1,2]

## Abstract

**Introduction** Extraskeletal osteosarcoma arising in the penis is exceedingly rare and its major differential diagnosis is sarcomatoid carcinoma.

**Case presentation** A 19-year-old patient noticed a deep nodule in the dorsal side of the penis 2 years before this presentation. No skin lesions were noted until recent ulceration. In both biopsy and penectomy specimen, atypical mononuclear cells were diffusely positive for SATB2 (a marker of osteoblastic differentiation), CD99 and vimentin. These cells were negative for pan-keratin, SOX10, S100, EMA, GATA3 and CD68 was expressed only in multinucleated giant (osteoclast-like) cells. Few areas suggestive of osteoid production were noted.

**Conclusion** In high-grade sarcomas, including in the penis, SATB2 staining may be useful to identify extraskeletal osteosarcoma.

**Keywords** Penis, Sarcoma, Osteosarcoma, SATB2, Neoplasms, Connective and Soft Tissue

## Introduction

Extraskeletal osteosarcoma arising in the penis is exceedingly rare. Sarcomatous growth in the penis must be always rule out of diagnosis of the much more common sarcomatous differentiation (including heterologous / ostosarcomatous differentiation) of urothelial (urethra primary) or squamous cell (penile primary) carcinomas.

## Case presentation

A 19-year-old patient noticed a deep nodule in the dorsal side of the penis 2 years before this presentation. The nodule was surveilled clinically in other service. In this period, no skin lesions were noted. In the last months, the lesion rapidly grew causing ulceration in dorsal skin and invaded corpora cavernosa and corpus spongiosum (as evaluated by imaging studies). An incisional biopsy was performed showing a high-grade neoplasm with numerous non neoplastic osteoclast-type multinucleated giant cells. An immunohistochemical panel including SATB2 positivity in mononuclear cells favored sarcoma over sarcomatoid carcinoma. A partial penectomy without lymphadenectomy was performed (see Fig. 1) showing a large tumor with pushing borders and 5-cm maximum diameter.

The microscopic findings of the penectomy specimen mirrored those of the incisional biopsy. The entire tumor was submitted to microscopic evaluation. The tumor showed highly pleomorphic sarcoma with epitheloid and fusiform cells intermixed with numerous non neoplastic osteoclast-type multinucleated giant cells (see Fig. 2). Necrosis was observed within < 10% of the whole tumor volume. There was brisk mitotic activity with 30 mitoses per 2 $mm^2$. Angiolymphatic invasion was also detected. There was no clearcut foci of osteoid matrix, however, some foci of tumor cells showed lace-like or trabecular deposition of matrix which was difficult to discern from collagenous stroma (see Fig. 3).

*Correspondence:
Daniel Abensur Athanazio
dathanazio@gmail.com
[1] Hospital Universitário Professor Edgard Santos / Federal University of Bahia, Salvador, Bahia, Brazil
[2] Imagepat, Laboratory of Pathology, Edf. Eventus Empresarial, 3° Andar Rua Lucaia, 209 Rio Vermelho, Salvador, BA CEP 41940-660, Brazil
[3] AMO Clinic, Salvador, Brazil
[4] Centro Médico do Hospital da Bahia, Salvador, Brazil


**Fig. 1** Gross appearance of penile osteosarcoma. Clinical appearance before surgery (**A**) and after resection and formalin fixation (**B**). Cut surface of the specimen. Fleshy tumor involving corpora cavernosa and corpus spongiosum. Upper left section shows uninvolved margin and bottom right shows the uninvolved distal glans (**C**)

In both biopsy and penectomy specimen, atypical mononuclear cells were diffusely positive for SATB2 (a marker of osteoblastic differentiation), CD99 and vimentin. These cells were negative for pan-keratin, GATA3, EMA, SOX10, S100 and ERG. Desmin was focally expressed. CD68 was expressed only in multinucleated giant (osteoclast-like) cells. Tumors cells showed preserved INI1/SMARCB1 expression. See immunohistochemical photomicrographs in Fig. 4.

Imaging studies ruled out any bone primary tumor. The patient developed lung metastases after ten months of follow up.

## Discussion

Special AT-rich sequence-binding protein 2 (SATB2) is a product of gene implicated in cleft palate defects (Berg & Schaeffer, 2017). It is used in Diagnostic Pathology as a immunohistochemical marker that, among carcinomas, is sensitive and specific for colorectal and appendiceal primary sites. It is also expressed in benign and malignant neoplasm with bone differentiation and, among neuroendocrine carcinoma, it is expressed in most Merkel cell carcinomas. It is usually expressed by epithelium of the lower gastrointestinal tract, brain,

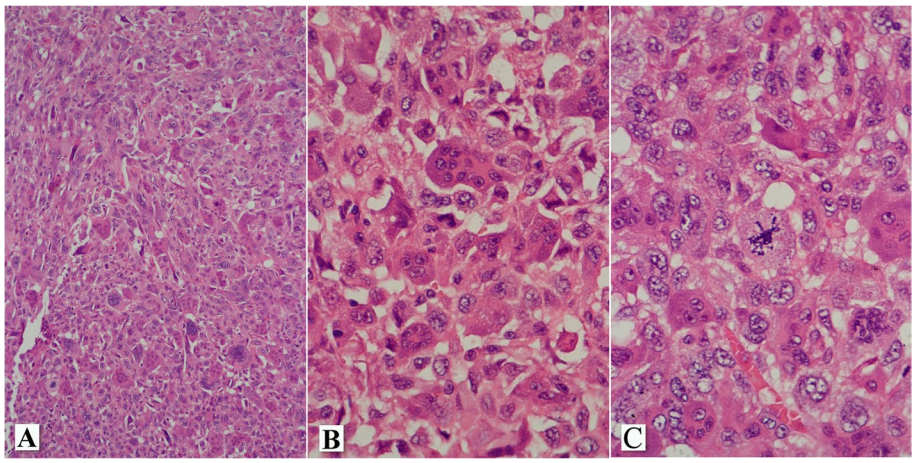


**Fig. 2** High-grade sarcoma with numerous non neoplastic osteoclast-type multinucleated giant cells (**A**: HE, 10x). It shows brisk mitotic activity (**B**: HE, 100x) and frequent atypical mitoses (**C**: HE, 400x). The whole tumor was submitted for histological analysis and few areas of equivocal osteoid matrix production were observed (**C**: 400x, HE stain). Atypical mononuclear cells show diffuse nuclear staining for SATB2 (**E**: 100x and **F**:400x) while only osteoclast-type multinucleated giant cells stained for marker of histiocytic differentiation, CD68 (**G**: 400x)

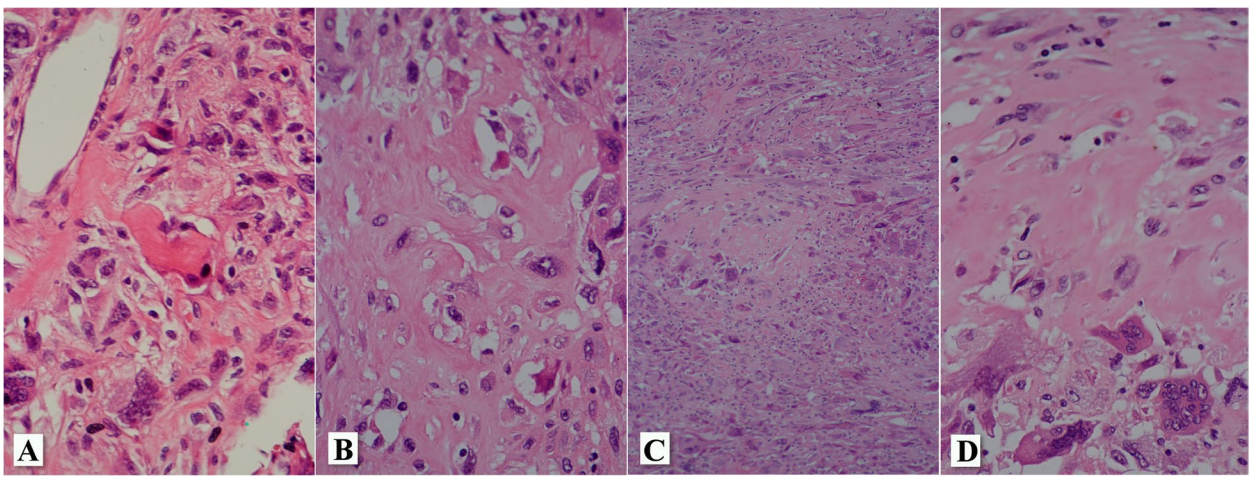


**Fig. 3** Equivocal areas of osteoid formation that may yield differential diagnosis with collagenous stroma (HE – **A**, 400x; **B**, 400x, **C**, 40x; **D**, 400x)

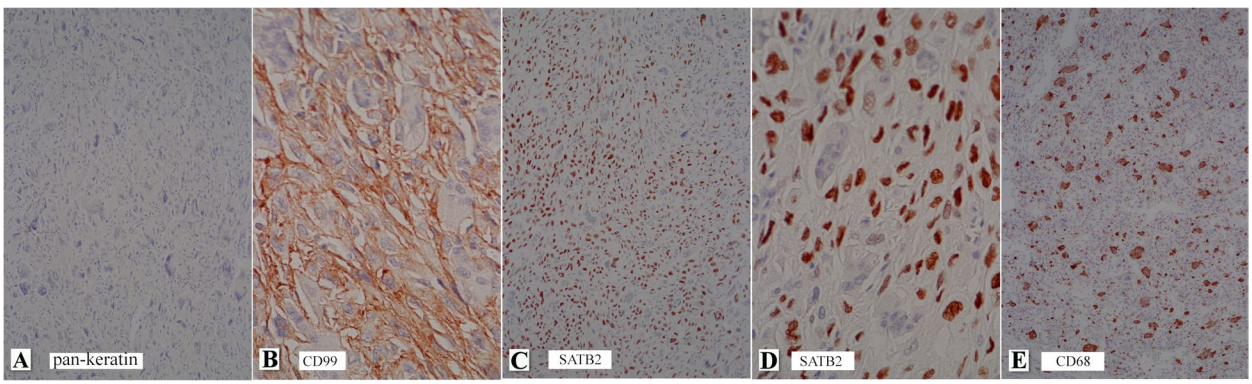


**Fig. 4** Immunophenotype of a giant-cell rich penile osteosarcoma: no pan-keratin expression (**A**, 40x), CD99 expression restricted to neoplastic cells (**B**, 40x), SATB2 expression in tumor cells (**C**, 40x; **D**, 400x), and CD68 positivity in giant osteoclast-type cells (**E**, 40x)

nongerminal center lymphoid cells, ductal epithelium of the testis and epididymis.

Among high-grade soft tissue sarcomas, SATB2 expression can be used as an indicative of extraskeletal osteosarcomas with poor matrix production (Yamashita & Hameed, 2020). Indeed, the recent new WHO Classification states that "SATB2 immunoreactivity could be useful to detect osteoblastic differentiation when immature osteoid is difficult to distinguish from collagenous stroma" (Yamashita & Hameed, 2020).

This tumor also showed focal areas of p63 expression. Staining was always weak. Rather than evidence of squamous differentiation in this case, we interpreted this feature as expected in giant cell tumors (both bone and soft tissue primaries) and osteoclast-rich osteosarcomas (Shooshtarizadeh et al., 2016; Jo & Fletcher, 2011).

Primary penile extraskeletal osteosarcomas are exceedingly rare. A recent report also showed the feature of osteoclast-rich areas (Wu et al., 2012). The same is true for extraskeletal osteosarcomas of other sites (Oh & Chang, 2017).

Penile primary extraskeletal osteosarcoma is exceedingly rare and that would be the eighth described in English literature (Wu et al., 2012; Bastian et al., 2003; Fraser et al., 2000). The first in which recently available SATB2 immunohistochemistry was helpful to identify osteoblastic differentiation. The 2-year evolution is a more protracted course than expected from osteosarcomas of the bone. Interestingly, other case of giant cell rich-extraskeletal osteosarcoma of the penis was diagnosed as a small nodule (1.2 cm) with 1 year period of slow growth (Wu et al., 2012).

The main differential diagnosis in this case would be melanoma with osteosarcomatous differentiation and sarcomatoid carcinoma. Melanoma was ruled out by absent expression of S100 and SOX10. Sarcomatoid carcinoma was considered in the differential diagnosis, but the patient experienced a two-year growth of a deep palpable nodule with no relationship with penile skin or urethra. The dorsal skin was ulcerated after rapid and recent growth. The urethra was uninvolved in the resection specimen, even though the erectile tissue of corpus spongiosum was infiltrated. The uninvolved urethra and lack of GATA3 expression argue against a sarcomatoid urothelial carcinoma. Pan-keratin was negative. P63 expression - as discussed above - cannot be used in the differential between squamous carcinoma and giant cell rich tumors of soft tissue. In addition, sarcomatoid squamous cell carcinoma is typically an HPV-independent neoplasm that are much more common in older patients. Preserved INI1/SMARCB1 expression argues against the diagnosis of epithelioid sarcoma.

We also considered the possibility of metastatic osteosarcoma. Imaging of the skeleton, however, showed no suspicious bone lesions.

Soft tissue neoplasms of the penis are rare, and the incidence is difficult to estimate since these cases are mostly documented as case reports. The most common benign soft tissue tumors of the penis are those with vascular differentiation including hemangioma (including epithelioid hemangioma), angiokeratomas an lymphangiomas. The most common malignant sarcomas of the penis are leiomyosarcoma and vascular neoplasms (such as angiosarcoma, Kaposi sarcoma and epithelioid hemangioendothelioma) (Amin et al., 2014). Some recent examples of soft tissue malignancies reported as primary of the penis include Kaposi sarcoma in the set of HIV infection / transplant patients (Tammam et al., 2022; Anderson et al., 2021), post-radiation sarcomas (Rodriguez-Perez et al., 2021; Hoyos et al., 2022) and primitive neuroectodermal tumor (PNET)/Ewing's sarcoma (Asari et al., 2021; Krakorova et al., 2021; Estaphanous et al., 2022). Distinguishing true penile sarcomas from sarcomatoid carcinoma is crucial for prognosis and treatment, and this including even the proposed surgery since lymphadenectomy may considered for sarcomas but is obligatory for sarcomatoid carcinoma since 75–89%% of sarcomatoid squamous cell carcinomas of the penis show nodal metastasis at the time of diagnosis (Alvarado-Cabrero et al., 2022).

## Conclusion

In high-grade sarcomas, including in the penis, SATB2 staining may be useful to identify extraskeletal osteosarcoma.

#### Abbreviations

| | |
|---|---|
| CD68 | Cluster of differentiation 68 |
| CD99 | Cluster of differentiation 99 |
| EMA | Epithelial membrane antigen |
| GATA3 | GATA Binding Protein 3 |
| SATB2 | Special AT-rich sequence-binding protein 2 |
| SOX10 | SRY-Box Transcription Factor 10 |

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None.

#### Authors' contributions

DAA and MB conceived the idea. DAA was the major contributor to the writing of the manuscript. PRFA and DAA diagnosed the cases. MB and JEPF were major contributors for critically revising the manuscript for important intellectual content. The authors read and approved the final manuscript.

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#### Availability of data and materials

Supplementary data is available upon request.

## Declarations

### Ethics approval and consent to participate

Written informed consent was obtained from the patient for participation in this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

### Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

### Competing interests

The authors declare that they have no competing interests.

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## Publisher's Note