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Pseudoangiosarcomatous squamous cell carcinoma: first case report on penis.

Liseana de Oliveira Barbosa (liseana21@yahoo.com.br)
University Hospital of the Federal University of Maranhao https://orcid.org/0000-0003-4376-6009

José Osvaldo Barbosa Neto
Experimental laboratory for the study of pain. Federal University of Maranhao

Antônio Augusto Lima Teixera Junior
Federal University of Maranhao

Leudivan Ribeiro Nogueira
Aldenora Belo Cancer Hospital

José de Ribamar Rodrigues Calixto
University Hospital of the Federal University of Maranhao

Antônio Machado Alencar Junior
Aldenora Belo Cancer Hospital

Jaqueline Diniz Pinho
Universidade Federal do Para

Francisco Sérgio Moura Silva do Nascimento
Hospital Sao Domingos

Isabela Werneck Cunha
Rede D'Or Sao Luiz

Gyl Eanes Barros Silva
University Hospital of the Federal University of Maranhao

Case report

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Abstract

Background: Pseudoangiosarcomatous squamous cell carcinoma, also called pseudovascular, pseudoangiomatoid or adenoid pseudovascular carcinoma, is an uncommon and highly aggressive variant of squamous cell carcinoma. Histologically, it is characterized by proliferation of atypical keratinocytes with acantholysis and formation of pseudovascular spaces, forming anastomosed channels lined with neoplastic cells that invade the dermis. These cells are positive for cytokeratin and vimentin and negative for vascular markers such as CD31 and CD34. There are few reports of this tumor variant in the literature. Skin, breast, lung and vulva involvement have been described. But to the best of our knowledge, no cases involving the penis have been described. This article aims to describe the first case of angiosarcomatous squamous cell carcinoma of the penis.

Case Report: The patient presented with a painful lesion in the penis associated with urinary retention. Macroscopic findings exhibited an ulcerative vegetating lesion that involving the entire glans and part of the penile body, as well as infiltration of penile structures and scrotal skin. Microscopy shows atypical proliferation of sarcomatous keratinocyte pattern mimicking vascular spaces. These neoplastic squamous cells were positive for the cytokeratin marker and were negative for the CD31 and CD34 markers. Human papilloma virus biomarkers, p16, E6 protein and PCR, were all negative.

Conclusion: This report presents the first reported case of penile pseudoangiosarcomatous squamous cell carcinoma, as an important differential diagnosis.

Introduction

Penile squamous cell carcinoma is an uncommon neoplasia in developed countries, but has a high incidence in South America, Southeast Asia and Africa. In Brazil its incidence is 6,1 / 100 thousand inhabitants [1]. This type of tumor is strongly associated with socioeconomic factors, genital hygiene, HPV infection and important developmental factors [2].

Penile lesions usually present as a vegetative lesion, and sometimes ulcerated. Histologically, penile squamous cell carcinoma is classified according to its histomorphological characteristics and its relation or not to HPV. Non-HPV-related variants include the usual variant, pseudohyperplastic, pseudoglandular, verrucous, papillary, adenosquamous, sarcomatoid, and mixed. HPV-related variants are basaloid, Warty, Warty-basaloid, clear cells tumor, and lymphoepithelioma-like. Histological grading is an important prognostic and predictive factor for metastasis to inguinal lymph nodes [2]. The poorly differentiated pseudoangiosarcomatous variant of squamous cells carcinoma (SCC) exhibits proliferation of polygonal or flattened atypical keratinocytes that form interanastomosing channels that mimic vascular proliferation these pseudovessels have prominent neoplastic cells and red blood cells inside [3-6]. These atypical cells are positive for cytokeratins and vimentin, and negative for vascular markers such as CD31 and CD34 [3,7,8]. It is also positive for p16 in the presence of HPV [2]. This report presents the first case of

penile pseudoangiosarcomatous squamous cell carcinoma, describing its clinical, histological and immunohistochemical characteristics, as well as HPV status.

Case Report

A 38-year-old patient was admitted to the urology outpatient clinic with a history of painful penile injury and urinary retention. Physical examination revealed extensive, vegetative and large lesion that compromised the urethral meatus, associated with bilateral lymphadenopathy. The patient underwent emasculation and bilateral orchiectomy surgery, and the material was sent for the pathology division. Macroscopy revealed two ulcerative vegetating lesions, the largest measuring 5.5 x 4.5 cm, circumferential, infiltrating the penis 13 cm deep and destroying the glans and part of the penile body, and extended to the scrotum skin. Microscopy showed poorly differentiated atypical squamous cells infiltrating the underlying stroma forming channels that simulated vessels containing neoplastic, inflammatory, and red blood cells (Figure 1a). Some neoplastic cells also contained large intracytoplasmic vacuoles, simulating a capillary (Figure 1b). The lesion infiltrated the corpus spongiosum, corpus cavernosum, urethra and scrotum, with free surgical margins. No angiolymphatic invasion was found, but perineural invasion was observed. These neoplastic squamous cells were positive for the cytokeratin marker and were negative for the CD31 and CD34 markers (Figures 1c– 1e). HPV biomarkers, p16, E6 protein and polymerase chain reaction (PCR), were all negative (Figure 1f). The histological diagnosis was undifferentiated squamous cell carcinoma (G4), angiosarcomatous type, occupying the entire glans and infiltrating the penile body. Testicles and epididymis showed no histological changes. The pathological staging was pT4 pNx pMx.

At follow-up, the patient underwent right iliac chain lymphadenectomy with histopathological report of metastasis to 7 lymph nodes, with confluence and extra-capsular extension. Then, a left iliac chain lymphadenectomy was performed, with histopathological report of metastasis to 2 lymph nodes, with extra-capsular extension in one of them. The patient was then re-staged for pT4 pN3 pMx and referred for radiotherapy, and treatment with 28 sessions of 5.040 cGy cobalt in the pelvis was indicated in the month following the last surgery. After 20 sessions, the patient was discharged with outpatient follow-up.

Discussion

The case described above is a rare variant of SCC in the penis, which mimics an angiosarcoma, requiring careful histological evaluation and immunohistochemical study for correct diagnosis. The microscopic findings of this case are similar to those described in a study in which complex anastomosed labyrinthine channels lined with polygonal or flattened cells were observed, and the pseudo lumen containing occasional tumor cells and red blood cells [9]. Cells covering these channels were positive for AE1 / AE3 and negative for CD31, CD 34. In this case report it was observed that the degree of morbidity and mortality of angiosarcomatous SCC is higher than in other variants of SCC, probably due to its anaplastic nature, demonstrating high rates of early recurrence and metastases. These findings were also observed in a report of two cases of pseudoangiosarcomatous squamous cell carcinoma that affected the vulva [9].

According to a literature review in which 12 studies were included, with a total of 19 patients, eight of these had regional lymph node metastasis, and 10 died of lung metastasis [8]. The case presented in this report showed invasion of the corpus spongiosum, corpus cavernosum, urethra and scrotum, with lymph node metastasis, demonstrating the aggressive behavior of this tumor and the need for early diagnosis and radical treatment.

Although this is the first case described of penile angiosarcomatous squamous cell carcinoma, which limits the comparison of prognosis with other cases, it could be observed that this was an aggressive case, with scrotal sac skin invasion and lymph node metastases.

Conclusion

The above report is an atypical presentation of an HPV-negative advanced penile squamous cell carcinoma with aggressive lymph node metastasis. Further studies to assess the association of this finding with a worse prognosis are needed.

Abbreviations

HPV - Human papilloma virus

PCR - polymerase chain reaction

SCC - squamous cells carcinoma

Declarations

Ethics approval and consent to participate:

This case report was approved by Research Ethics Committee of the University Hospital of the Federal University of Maranhão (Approval number: 1.093.435). The informed consent form was provided by the study patient.

Consent for publication:

Consent for publication was provided by the study patient.

Availability of data and materials:

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests:

The authors declare that they have no competing interests.

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Authors' contributions:

LOB idealized the case report, assembled the data presented in the article, provided artwork, and co-wrote the manuscript.

JOBN co-wrote, formatted and revised the manuscript.

AALTJ

LRN was part of the surgical team that attended to the patient and reviewed the manuscript.

JRRC was part of the surgical team that attended to the patient and reviewed the manuscript.

AMAJ was part of the oncology team that attended to the patient and reviewed the manuscript.

JDP

FSMSN was part of the surgical team that attended to the patient and reviewed the manuscript.

IWC analyzed and interpreted study data and reviewed the manuscript.

GEBS co-wrote, formatted, analyzed and interpreted study data, reviewed and gave final approve to the manuscript.

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Figures

Figure 1

Series of images produced under microscopy. (a) Atypical squamous cells infiltrating the underlying stroma forming channels that simulated vessels containing neoplastic, inflammatory, and red blood cells. (b) Some neoplastic cells also contained large intracytoplasmic vacuoles, simulating a capillary. (c) The neoplastic squamous cells were positive for the cytokeratin marker (AE1/AE3). (d) The neoplastic squamous cells were negative for the CD34 marker. (e) The neoplastic squamous cells were negative for the CD31 marker. (f) The p16 marker was negative.