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Case Report

Urology Section

Sarcomatoid Carcinoma of the Penis: Report of Two Cases

R VIJAYAKUMAR[1], SACHIN DHARWADKAR[2], J VIVEKANANDAN[3], SAJAN SEHGAL[4], AMRUTHRAJ GOWDA[5]

ABSTRACT

Penile sarcomatoid squamous cell carcinomas are biphasic tumours that combine both sarcomatoid and carcinomatous elements. These tumours are incredibly uncommon, high-grade and aggressive forms of penile cancer. Hereby, the authors described an exceptionally rare urogenital neoplasm in 70 and 65-year-old males, presenting as a proliferative growth on the glans penis, Physical examination revealed induration of the underlying tissues with clinical node-negative disease at the time of presentation. Metastatic evaluation was unremarkable; these patients underwent partial penectomy with clear surgical margins. Histology revealed a sarcomatoid variant of squamous cell carcinoma of the penis and Immunohistochemistry (IHC) confirmed the positivity for cytokeratin, p63 with co-expression of vimentin. These patients are currently under surveillance and one among them developed ipsilateral inguinal node metastasis, for which inguinal lymphadenectomy followed by cisplatin-based chemotherapy was administered. The rarity of these cases emphasises the need of IHC, morphological and histological analysis, thorough and in-depth inquiry in diagnosis, staging, therapy and follow-up.

Keywords: Biphasic, Immunohistochemistry, Partial penectomy, Squamous cell variant

Case 1

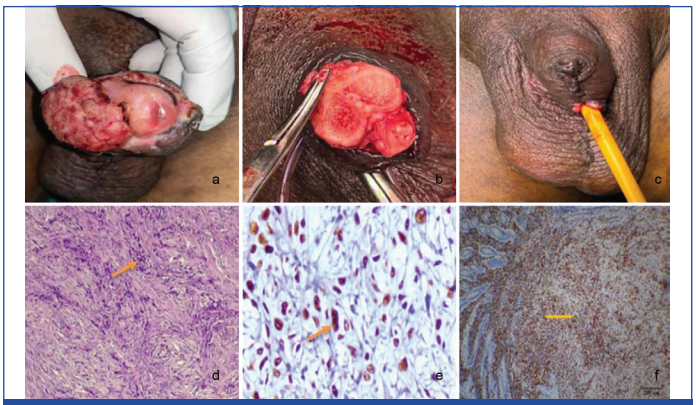
A 70-year-old male, labourer by occupation, presented with neglected, slowly progressive growth on his glans penis for three months. No history of pain, bleeding or purulent discharge from the lesion. No complaints of difficulty in micturition and weight loss. He has no history of tobacco use/circumcision/contact with multiple sexual partners nor any co-morbid illness. Family history was non contributory.

On clinical examination, 4×3.5 cm solitary, ulceroproliferative growth noticed over the lateral aspect of glans penis [Table/Fig-1a] with no extension to penile shaft and urethral meatus. There were no significant palpable lymph nodes.

As metastatic work-up, chest radiograph and an ultrasound of the whole abdomen were within normal limits. With clinical stage T1N0M0 (where T;Tumour: N;Node: M;Metastasis), incisional biopsy from the lesion on dorsolateral aspect of glans penis was done, spindle cells were observed. Although preliminary biopsy negative for atypical cells due to limited sampling of sarcomatoid components and characteristic appearance of penile growth is highly suggestive of malignancy, hence the patient underwent partial penectomy, as part of surgical management.

Under spinal anaesthesia, penile tourniquet applied at base of penis, a circumferential incision was made proximal to the tumour margin. The corpora cavernosa was transected and the corporal vessels ligated. The urethra was divided distal to the corporal transection [Table/Fig-1b] and ventrally spatulated. A wide neomeatus was fashioned by everting the urethral mucosa and suturing it to the penile skin. The penile stump was reconstructed, ensuring adequate length for voiding in standing position and foleys catheter placed [Table/Fig-1c]. The specimen was sent for histopathological examination.

Upon further inspection of the resected specimen, a fleshy proliferative growth measuring 4×3×3.5 cm was observed emerging from the Glans penis. In the subepithelial layer, a cut portion showed a grey-white lesion with gelatinous patches along with areas of ulceration and bleeding. Haematoxylin and Eosin) (H&E) sections were used for microscopic examination, which revealed features of a high-grade Pleomorphic spindle cell tumour [Table/Fig-1d] with high mitotic activity {10-15 mitosis/high power field (hpf)}. Section from distal skin margins of the specimen is free of tumour. The cells tested positive for p63 [Table/Fig-1f], Pan-cytokeratin (Pan-CK) [Table/Fig-1e] and p40 markers via IHC. Cells tested negative for Cluster of Differentiation 31 (CD31), CD34 and E26 Transformation-Specific (ETS)-related Gene (ERG). All these results were aligned with sarcomatoid cancer of the penis.



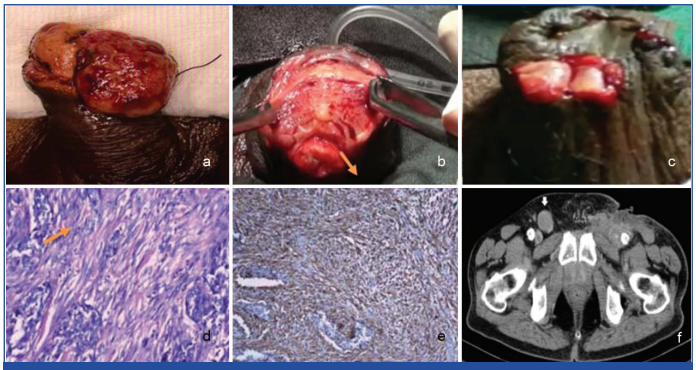
[Table/Fig-1]: a) Ulceroproliferative lesion involving lateral aspect of glans; b) Transected corporal bodies with exposed urethra; c) Urethral slit at 6'0 clock position after spatulation with foleys catheter; d) Atypical squamous cells (arrow) admixed with spindle cells (H&E,10X) e) IHC for p63 show strong nuclear positivity (arrow) by malignant squamous epithelial cells; f) IHC for Pan-CK shows diffuse positivity (arrow).

Cross-sectional imaging of the patient's chest, abdomen and pelvis during the first follow-up showed no abnormalities. Adjuvant therapy is not indicated as surgical margins are free of tumour and no evidence of lymphatic or distant metastasis. The patient is doing well at the six-month postoperative follow-up phase.

Case 2

A 65-year-old male, a farmer by occupation, noticed a growth on his glans penis, but neglected it. Since the mass rapidly increased in size at two months, he visited present hospital. There was no history of tobacco use, sexually transmitted disease, prior genital lesions, or lichen sclerosus. The patient denies constitutional symptoms like fever, malaise and weight loss, family history was unremarkable.

On clinical examination, a solitary proliferative growth measuring 3.5×3.5 cm on the dorsolateral part of the glans [Table/Fig-2a] was noted. No palpable inguinal lymph nodes at presentation.



[Table/Fig-2]: a) Proliferative growth involving dorsolateral aspect of glans; b) Transected corporal bodies with exposed urethra; c) Neourethra after stump flap reconstruction; d) Nests and islands of malignant squamous cells (arrow) with sarcomatous components; e) Sarcomatous components showing immunoreactivity to Vimentin (arrow); f) Axial section of CECT pelvis showing right Inguinal lymphadenopathy on 3-month follow-up.

Clinical stage of this lesion is T1N0M0. Initial wedge biopsy from the dorsolateral side of the lesion demonstrated spindle cell neoplasm, interpreted as undifferentiated pleomorphic sarcoma. However, limited sampling likely captured only the sarcomatoid component of this heterogenous tumour. As a result, the patient was subjected to partial penectomy, as surgical management.

Under spinal anaesthesia, the extent of lesion was reassessed and surgical margin of 10 mm was marked circumferentially proximal to the tumour. After applying soft tourniquet at penile base, circumferential incision placed and dissection carried down to buck's fascia. Corpora cavernosa exposed [Table/Fig-2b], transected after ligation of corporal vessels. Proximal corporal ends closed using polyglactin suture, urethra was divided and ventrally spatulated. The urethral mucosa was everted to create a wide, tension-free neomeatus [Table/Fig-2c], Skin flaps approximated to reconstruct adequate penile stump, foleys catheter placed. The specimen sent for histopathological analysis.

On histological analysis, a grey-white nodular growth measuring 4x4.2x3.6 cm was originated from the glans penis. There is no involvement of the urethra or corpora cavernosa/spongiosa. On microscopic examination, tumour composed of cell sheets with individual cells showing pleomorphic spindle to epithelioid characteristics, evident by vesicular nuclei, large nucleoli and moderate eosinophilic cytoplasm. Low mitotic activity and some squamous pearls are also seen [Table/Fig-2d]. The section from the distal skin margins of the specimen is free of tumour. Lymphovascular and perineural invasion were also noted with lamina propria involvement, suggestive of the Sarcomatoid squamous variant. Vimentin [Table/Fig-2e], p40 and p63 were all detected positive by the IHC. Actin, Human Melanoma Black (HMB)-45 and desmin are all negative in the tumour cells.

Given the aggressive histology, the patient was placed on intensified surveillance with a low threshold for nodal assessment. Immediate lymph node dissection was deferred as the patient was clinically node-negative (cN0). Current National Comprehensive Cancer Network (NCCN) guidelines recommend surveillance or minimally invasive nodal staging in such cases to avoid overtreatment and morbidity associated with prophylactic lymphadenectomy [1].

On follow-up after three months, clinical examination revealed firm, matted, 3x3 cm right inguinal lymph nodes. Ultrasound of the abdomen revealed a few sub-centimetric lymph nodes in the bilateral inguinal region, the largest measuring 3.4x1.7cm on the right side, with loss of the fatty hilum, likely necrotic. Contrast-enhanced Computed Tomography (CECT) abdomen and pelvis showed a well-defined heterogenous lesion measuring 16.5x35x22 mm in the right inguinal region with significant fat strandings, likely neoplastic aetiology [Table/Fig-2f].

No evidence of visceral metastasis. Hence, ultrasound-guided fine needle aspiration from right inguinal node showed features of metastatic squamous cell carcinoma. Early inguinal metastasis likely reflects progression of occult micro-metastasis at diagnosis, compounded by the aggressive nature of sarcomatoid carcinoma. This underscores the importance of surveillance and early nodal evaluation in aggressive histologic subtypes.

The patient underwent superficial inguinal lymph node dissection, whose histopathology was conclusive of metastatic squamous cell carcinoma. Patient received cisplatin based combination chemotherapy using the TIP regime (Paclitaxel, Ifosfamide and Cisplatin) for four cycles. The patient has been followed for six months after completion of chemotherapy and currently shows no evidence of disease.

DISCUSSION

The frequency of penile carcinoma is fewer than one per 100,000 males, making it a rare malignancy [2]. Nonetheless, there is a considerable geographical variance, with a higher frequency in regions where unhygienic practices are prevalent and human papillomavirus infection is common, particularly in poorer nations. Squamous cell carcinomas make up around 95% of penile cancers, but its variant: Sarcomatoid carcinoma accounts for about 1% to 2% incidence, with poorer prognosis [3].

An admixture of sarcomatous and carcinomatous components (biphasic tumours) is known as Sarcomatoid carcinomas [4]. They can spread by both hematogenous and lymphatic route, resulting in both local and distant metastases, because they contain both epithelial and mesenchymal components [5].

Most sarcomatoid penile carcinomas are Human Papilloma Virus (HPV) negative. They usually arise via chronic inflammation, lichen sclerosus and poor sanitary measures. When HPV is present (rare), it is usually HPV-16 (<10-15%). Hence, HPV testing has a limited and mostly prognostic role in sarcomatoid carcinoma of penis, as it doesn't change the management [6].

Penile carcinoma typically presents as a painless ulcerative or exophytic lesion involving glans or prepuce commonly, often accompanied by inguinal lymphadenopathy. Diagnosis is established by biopsy of the primary lesion, which provides histological subtype and grade. Physical examination remains central to initial assessment, while imaging is reserved for suspected nodal or advanced disease [7].

Management of penile cancer is guided by tumour stage, histologic grade and nodal status, with primary objectives of achieving oncologic control while preserving penile function whenever feasible. Early-stage disease is amenable to organ-preserving approaches, whereas invasive or high-grade tumours require more radical surgery to minimise local recurrences [7].

Regional lymph node involvement represents the most significant prognostic factor and early lymphadenectomy offers the only potential for cure in node-positive disease. Not all palpable nodes are malignant, as 30-50% enlarged nodes are reactive, hence there is no role for prophylactic lymphadenectomy. Sentinel lymph node biopsy is reserved for low-risk clinically palpable node patients, not amenable to surgery and planned for observation only. Multimodal therapy, including chemotherapy, is reserved for advanced or metastatic disease [8].

In two of present case reports, organ preserving surgery (Partial penectomy) was performed as they were T1 tumours confined to glans penis. In both specimens, histopathological examination showed the tumour composed of squamous cell carcinoma elements and sarcomatous elements (spindle cells). Immunohistochemical stains revealed that both carcinomatous and sarcomatous elements were positive for Vimentin, p40 and p63 markers. Based on these findings, a diagnosis of sarcomatoid carcinoma of the penis was made. IHC signifies diagnosis and prognosis in-terms of risk stratification, rarely dictates treatment directly [9].

The differential diagnosis of penile sarcomatoid carcinoma includes true sarcomas (leiomyosarcomas, fibrosarcoma, undifferentiated pleomorphic sarcoma), spindle cell melanoma, malignant peripheral nerve sheath tumour, epithelioid sarcoma and anaplastic lymphoma. IHC plays a pivotal role, excluding major mimics by the absence of melanocytic, lymphoid and lineage-specific mesenchymal markers [10].

The difference between these patients was noted on surveillance (follow-up) where one had no metastasis and other developed inguinal lymph node metastasis after 3-months of primary tumour management, signifying the aggressiveness of the tumour.

In 2004, Lont AP et al., retrospectively analysed five cases of sarcomatoid penile carcinoma, most presenting at advanced stage with nodal or distant metastasis. Four of five patients died within one year, underscoring the aggressive nature of this variant with poor survival. IHC was essential for diagnosis due to the predominance of spindle cell morphology obscuring epithelial origin [11].

Velazquez EF et al., reported 15 cases of sarcomatoid penile carcinoma in a clinicopathological series among 400 penile cancers, describing high-grade tumours with predominant spindle cell morphology. IHC showed vimentin and p53 positivity in sarcomatoid areas with variable epithelial marker expression. Nearly 90% had inguinal node metastasis and most patients experienced rapid progression and poor survival [12].

Huang Q et al., reported a case of sarcomatoid carcinoma of the penis presenting as a rapidly enlarging glans lesion with bilateral inguinal lymphadenopathy. Histology showed biphasic morphology with spindle cell predominance and IHC confirmed epithelial origin (cytokeratin/p63 positive, vimentin positive, p16 negative). The patient underwent partial penectomy with bilateral inguinal lymph node dissection and no short-term recurrence on follow-up [13].

In a case reported by Shankar K et al., the tumour presented as an aggressive ulceroproliferative glans lesion, histopathology demonstrated classical biphasic morphology with spindle cell predominance, confirmed by IHC showing epithelial origin with cytokeratin and Vimentin expression. Similar histopathological features were observed in our cases. The aggressive biological behavior of this variant, characterised by early node involvement and poor survival, underscores the need for prompt diagnosis and definitive surgical management [14].

The majority of the cases documented in the literature had distant metastases or lymph nodes, indicating significant vascular involvement as a contributing factor to the poor outcome. Inguinal lymph node metastases evident at presentation or during follow-up after primary surgery in most patients with sarcomatoid carcinoma of the penis as documented in the literature, indicates an unfavourable prognosis.

Upon follow-up, these tumours have a very high-risk for systemic metastases. In cases of advanced, ulcerated tumours, palliative surgery may be considered to temporarily reduce discomfort, bleeding and temporarily retreat the tumour. Thus, surveillance strategy for these patients is aimed at detecting early local recurrence, metastasis and minimising morbidity while preserving quality of life [15].

The following can be learned from these cases: Sarcomatoid carcinomas of the penis rapidly grow and are highly aggressive, necessitating the need for early diagnosis. Therefore, efforts should be made to disseminate methods for an early diagnosis. Concerning treatment, this carcinoma should be regarded as an orphan disease and even negative data should be disclosed in the form of case reports to share information among more clinicians and develop more effective treatment.

CONCLUSION(S)

Sarcomatoid carcinoma of the penis is an aggressive variant of squamous cell cancer. It has poor prognosis and is linked to early metastatic dissemination. It is often uncommon malignancy and frequently challenging to identify; IHC and a thorough study of the tumour as a whole aid in the diagnosis.

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PARTICULARS OF CONTRIBUTORS:
1. Professor, Department of Urology, JSS Medical College and Hospital, Mysuru, Karnataka, India.
2. Professor, Department of Urology, JSS Medical College and Hospital, Mysuru, Karnataka, India.
3. Senior Resident, Department of Urology, JSS Medical College and Hospital, Mysuru, Karnataka, India.
4. Senior Resident, Department of Urology, JSS Medical College and Hospital, Mysuru, Karnataka, India.
5. Professor and Head, Department of Urology, JSS Medical College and Hospital, Mysuru, Karnataka, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
J Vivekanandan,
G-001, Ground Floor, JSS Doctors Quarters, Opposite to Sri Mahalakshmi Auto Consultant, Agrahara, Fort Mohalla, Mysuru-570004, Karnataka, India.
E-mail: viveksurgeon@gmail.com

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