

## Case Report

# Carcinoma penis manifesting as upfront supraclavicular lymph node metastases detected by <sup>18</sup>F-fluorodeoxyglucose positron emission tomography scan: Report of an extremely rare and aggressive case

## ABSTRACT

Carcinoma penis is a rare malignancy accounting 0.5%–1% of cases in the developed countries with a slightly higher incidence in the developing nations. Slow locoregional progression is characteristic of penile carcinoma (PC) and distant metastases are very uncommon. We hereby report a case of highly aggressive squamous cell PC in a 46-year-old male with fulminant upfront distant dissemination to left supraclavicular lymph nodes (LNs) without involving the inguinal and pelvic nodes detected by whole-body <sup>18</sup>F-fluorodeoxyglucose positron-emission tomography scan. The scan also detected lytic destructive lesion involving the pelvic and adjacent bones with infiltration of skeletal muscles. He was treated with palliative radiotherapy to the weight-bearing sites followed by systemic chemotherapy. A thorough review of literature reveals that our case may be one of the rarest cases ever reported in world literature where an asymptomatic PC presents with upfront supraclavicular LN metastasis bypassing the inguinal, pelvic, and retroperitoneal LN chains.

**Keywords:** <sup>18</sup>F-fluorodeoxyglucose positron emission tomography scan, carcinoma penis, metastases, supra-clavicular lymph nodes

## INTRODUCTION

Distant dissemination from penile carcinoma (PC) is very rare accounting for <3% cases.<sup>[1]</sup> PC metastasizes most commonly to superficial and deep inguinal, external and internal iliac, and para-aortic lymph-nodes (LN). Lung, liver, brain, bones,<sup>[1]</sup> and skin<sup>[2]</sup> are the distant organs affected. However, direct supraclavicular LN (SCLN) involvement from PC without affecting the regional lymphatics is rarely heard of.<sup>[3]</sup> Breast, lung, and ovary are the other known nonregional primaries reported to metastasize to supraclavicular LNs.<sup>[4]</sup> apart from the thyroid and larynx. Biopsy remains the gold standard of diagnosis while <sup>18</sup>F-fluorodeoxy-glucose positron-emission computed-tomography (<sup>18</sup>F-FDG-PET/CT) scan has proven to be the most precise tool in detecting LN and occult distant metastases.<sup>[5]</sup>

## CASE REPORT

A 58-year-old male with comorbidity of HTN and tobacco

smoker/chewer for over 40 years presented with painless swelling left the supraclavicular area for about 7 months duration which gradually increased in size. He gave no history of dysphagia, hoarseness of voice, fever, weight loss,

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breathing difficulty, abdominal discomfort, high-risk sexual behavior, and erectile issues. However, he complained of mild urinary retention. Local examination revealed 4 cm × 3 cm hard, non-tender swelling left supraclavicular area fixed to overlying skin and underlying tissue. No lesions were identified in the head-and-neck examination. No abdominal distension, generalized lymphadenopathy, or penile ulcer was found. Swelling of the right thigh was noted and tenderness over the right iliac bone was elicited.

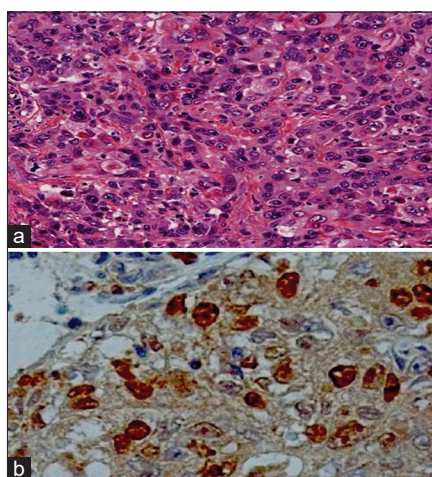
An excision biopsy of left supraclavicular swelling was done which revealed metastatic deposit of poorly differentiated keratinized squamous cell carcinoma (SCC) with p53 expression on immunohistochemistry (IHC) [Figure 1]. For assessment of the primary lesion <sup>18</sup>F-FDG-PET/CT scan was done which showed a metabolically active FDG avid soft tissue density lesion at the root of the penis measuring 3.2 cm × 2.7 cm × 2.5 cm with maximum standard uptake value (SUV<sub>max</sub>) of 7.8 likely the site of primary. FDG uptake was also seen in left SCLN measuring 2.5 cm in MSAD (SUV<sub>max</sub> 12.6) along with FDG avid destructive expansile lytic lesion of right hemipelvis (SUV<sub>max</sub> 13.4) with soft-tissue invasion. No metabolic activity was noted in inguinal, pelvic, or para-aortic LNs [Figure 2]. To confirm the findings of the PET scan, image-guided biopsy from penile root-lesion was done which showed SCC. IHC was positive for p53, cyclin-D1 and epidermal growth factor receptor [Figure 3], while negative for human papillomavirus (HPV). Based on immune-histopathological findings, the diagnosis of PC with SCLN and bone metastasis was established within 2 weeks of presentation. He was treated with palliative radiation-therapy 20 Gy/5 fractions to the pelvis followed by palliative chemotherapy consisting

of paclitaxel, ifosfamide, and cisplatin. However, the patient succumbed to his extensive disease within 5 months of starting chemotherapy.

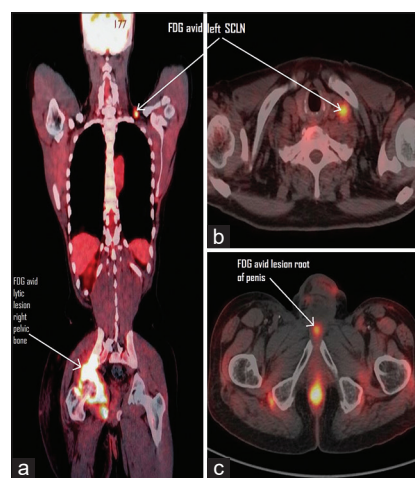
## DISCUSSION

PC is very rare malignancies with an incidence of 0.5%–1% in developed nations and about 1%–10% in poor socioeconomic nations being associated with HPV through viral oncogenes E6 targeting p53 and E7 attacking RB1 tumor-suppressor genes, which are actively transcribed by HPV-DNA.<sup>[6]</sup> culminating into widespread dissemination and grave prognosis.<sup>[7]</sup> SCC is the most common malignant histology affecting 50–70 years old men, apart from sarcoma, basal cell carcinoma, and malignant melanomas.<sup>[1]</sup> SCC penis generally metastasizes distantly to the lung, liver, brain, bones, heart, adrenals, eye,<sup>[1]</sup> and skin,<sup>[2]</sup> and locoregionally to inguinal and pelvic LNs. However, bibliographical search in online database sites such as PubMed, PubMed-Central, Medline, and Google Scholar did not show any report on exclusive upfront SCLN metastasis from PC. Secondary spread to left SCLN occurs mainly from lymphoma, thoracic or retroperitoneal cancers and to right SCLN from lung or gastrointestinal cancers,<sup>[8,9]</sup> while noncancerous affection occurs from tuberculosis, sarcoidosis, and toxoplasmosis.<sup>[10]</sup>

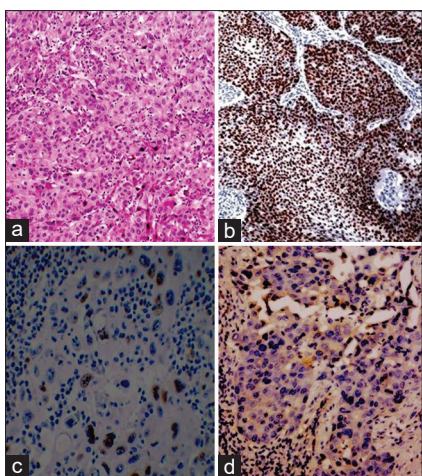
PC is a slow-growing malignancy in its early stages with 66% incidence of localized and locoregional spread.<sup>[6]</sup> Patients tend to present late reportedly for about a year,<sup>[6]</sup> partly due to psychological factors, social stigmata and also because PC rarely interferes with erectile functions, as was seen in



**Figure 1:** Excision biopsy from the supraclavicular lymph-node swelling showing (a) metastatic deposits of poorly differentiated squamous cell carcinoma (H and E, ×200); (b) immunohistochemistry showing p53 expression



**Figure 2:** Whole body <sup>18</sup>F-fluorodeoxy-glucose positron-emission tomography computed-tomography scan (a) coronal section showing fluorodeoxy-glucose avid left supraclavicular lymph-node and fluorodeoxy-glucose avid destructive expansile lytic lesion of right pelvic bone; (b) axial section showing fluorodeoxy-glucose avid left supraclavicular lymph-node; (c) axial section showing fluorodeoxy-glucose avid lesion root of the penis



**Figure 3:** Image-guided biopsy from penile root lesion showing (a) squamous cell carcinoma penis (H and E,  $\times 100$ ); (b) immunohistochemistry detecting p53; (c) cyclin D1; and (d) epidermal growth factor receptor

our patient. Pain and discharge from the penis are the late symptoms indicative of invasive disease which actually bring patients to a physician. Distant metastasis is usually late with an incidence of  $<3\%$ .<sup>[1]</sup> PC metastasizes to inguinal LNs in about 47%–85% of cases,<sup>[6]</sup> and to pelvic LNs in 19%–48% cases,<sup>[3]</sup> however, a thorough review of literature did not reveal reported incidence of direct SCLN spread. Bilateral or multiple nodal involvement, pelvic LN spread (*vis-a-vis* inguinal), and extra-nodal dissemination are the harbinger of poor disease outcomes.<sup>[3]</sup> Bone metastasis to the axial skeleton was also seen in this case which is also very rare with poor prognosis.<sup>[1]</sup> Tissue diagnosis with fine-needle aspiration cytology, incision/excision biopsy, sentinel node biopsy is the gold standards to diagnose primary and secondary malignancies. IHC showing p53 overexpression is predictive of both local and distant lymphatic dissemination, extra-nodal spread, and fulminant behavior of PC.<sup>[7]</sup>

In addition to the invasive techniques stated above, non-invasive diagnostics such as CT scan and magnetic resonance imaging have improved the detection of primaries,  $^{18}\text{F}$ -FDG-PET/CT has evolved as the primary modality for detecting primary as well as occult secondaries and LN mapping due to the inherent property of FDG elevation/uptake in malignant cells with multiplicative glycolytic rates.<sup>[10]</sup> In PC, high FDG uptake has been reported both in primary lesion and metastatic LNs, though with lesser sensitivity in nonpalpable cN0 inguinal LNs, although higher specificity and increased false-positives in inflammatory reactive LNs.<sup>[5-10]</sup>  $^{18}\text{F}$ -FDG-PET/CT has shown a sensitivity of 91% and specificity of 100% for pelvic LNs and about 85% and 86%, respectively, for distant metastatic sites in PCs.<sup>[5-10]</sup> while such data on SCLN are hardly available, thus depicting the extreme rarity of upfront SCLN dissemination.

In conclusion, a very high clinical suspicion of PC is necessary to initiate an appropriate investigative strategy in clinically asymptomatic patients presenting with upfront SCLN mass to optimize therapeutic efficacy. Although the role of  $^{18}\text{F}$ -FDG-PET/CT remains ambiguous and limited in PC, it definitely plays an important role in clinical decision-making as was seen in our case where only a visible SCLN mass hiding more sinister disease was unearthed only by PET.  $^{18}\text{F}$ -FDG-PET/CT is of immense value for identifying the location and extent of suspected occult metastasis and recurrence, thus enhancing the selection of patients who are most likely to benefit from an aggressive multi-disciplinary approach.

#### Declaration of patient consent

The authors certify that they have obtained appropriate patient consent form. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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#### Conflicts of interest

There are no conflicts of interest.

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