

Carcinoma Penis Manifesting as Upfront Supraclavicular Lymph Node Metastases Detected by ^{18}F -Fluorodeoxyglucose Positron Emission Tomography Scan: Report of an Extremely Rare and Aggressive Case

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Abstract

Keywords

- ▶ carcinoma penis
- ▶ metastases
- ▶ supraclavicular lymph nodes
- ▶ ^{18}F -fluorodeoxyglucose positron emission tomography scan

Carcinoma penis is a rare malignancy accounting 0.5 to 1% cases in the developed countries with a slightly higher incidence in the developing nations. Slow locoregional progression is characteristic of penile carcinoma and distant metastases are very uncommon. We hereby report a case of highly aggressive squamous cell penile carcinoma in a 46-year-old male with fulminant upfront distant dissemination to left supraclavicular lymph nodes without involving the inguinal and pelvic nodes detected by whole-body ^{18}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 penile carcinoma presents with upfront supraclavicular lymph node metastasis bypassing the inguinal, pelvic, and retroperitoneal lymph node chains.

Introduction

Distant dissemination from penile carcinoma (PC) is very rare accounting for less than 3% cases.¹ PC metastasizes most commonly to superficial and deep inguinal, external, and internal iliac, and para-aortic lymph nodes (LNs). Lung, liver, brain, bones,¹ and skin² are the distant organs affected. However, direct supraclavicular LN (SCLN) in-

volvement from PC without affecting the regional lymphatics is rarely heard of.³ Breast, lung, and ovary are the other known nonregional primaries reported to metastasize to SCLNs⁴ apart from thyroid and larynx. Biopsy remains the gold standard of diagnosis, while ^{18}F -fluorodeoxyglucose positron emission tomography computed tomography (^{18}F FDG-PET/CT) scan has proven to be the

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Fig. 1 Patient with left supraclavicular lymph node excision biopsy.

most precise tool in detecting LN and occult distant metastases.⁵

Case Report

A 58-year-old male with comorbidity of hypertension and tobacco smoker/chewer for over 40 years presented with complaints of painless swelling on left supraclavicular area for the last 7 months that has gradually increased in size. The patient had mild urinary retention issues. He gave no history of dysphagia, hoarseness of voice, fever, weight loss, breathing difficulty, any abdominal discomfort, high-risk sexual behavior, and erectile issues. Local examination revealed 4 × 3 cm hard nontender swelling on left supraclavicular area that was fixed to overlying skin and underlying tissue. No lesions were identified in head and neck examination. No abdominal distension, generalized lymphadenopathy, or penile ulcer was found; however, tenderness over right iliac bone was elicited and swelling of right thigh was noted.

An excision biopsy of the left supraclavicular swelling was done (►Fig. 1) that revealed metastatic deposit of poorly differentiated keratinized squamous cell carcinoma (SCC) with p53 expression on immunohistochemistry (IHC) (►Fig. 2). A ¹⁸F-FDG-PET/CT scan was done that revealed FDG avid lesion root of penis measuring 3.2 × 2.7 × 2.5 cm with standard uptake value (SUV) of 7.8 and FDG uptake left SCLN with a SUV of 12.6. No inguinal, pelvic, or para-aortic LNs were detected. Also seen was FDG avid destructive lytic lesion of right pelvic bone with soft tissue invasion (►Fig. 3). Image-guided biopsy from penile root lesion showed SCC penis with IHC detecting p53, cyclin D1, and epidermal growth factor receptor (►Fig. 4); however, it was negative for human papilloma virus (HPV), thus confirming the diag-

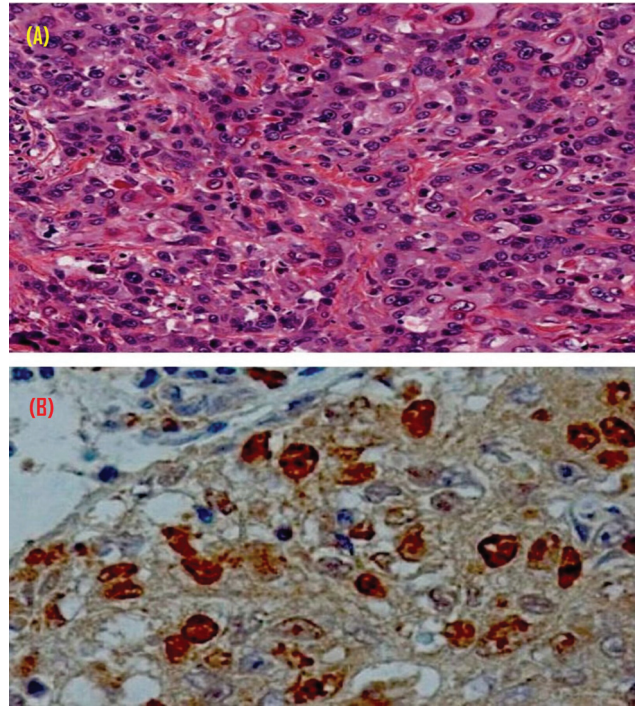


Fig. 2 Excision biopsy from the supraclavicular lymph node swelling showing (A) metastatic deposits of poorly differentiated squamous cell carcinoma (hematoxylin and eosin 200×); (B) immunohistochemistry showing p53 expression.

nosis of PC with SCLN and bone metastasis. He was treated with palliative radiation therapy 20 Gy/5 fractions to pelvis followed by palliative chemotherapy consisting of paclitaxel,

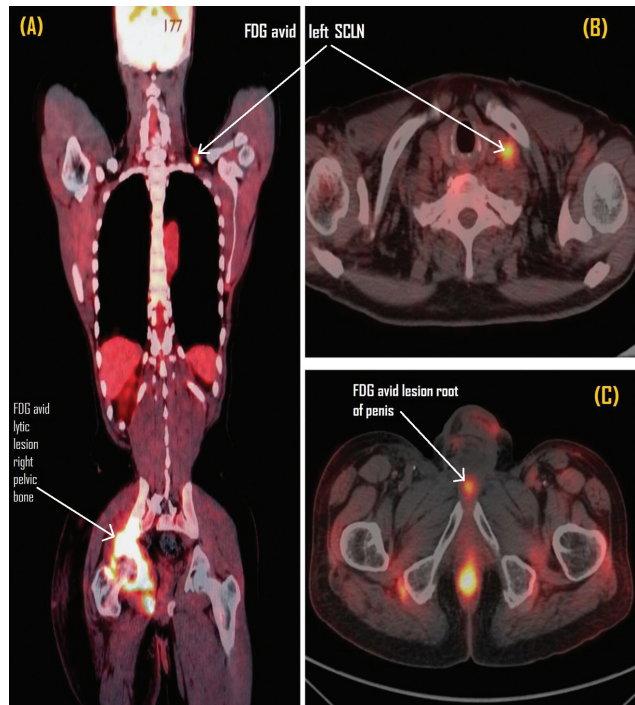


Fig. 3 Whole body ¹⁸F-fluorodeoxyglucose positron emission tomography computed tomography (¹⁸F-FDG-PET/CT) scan (A) of coronal section showing FDG avid left supraclavicular lymph node (SCLN) and FDG avid destructive lytic lesion of right pelvic bone; (B and C) axial section showing FDG avid left SCLN and lesion root of penis.

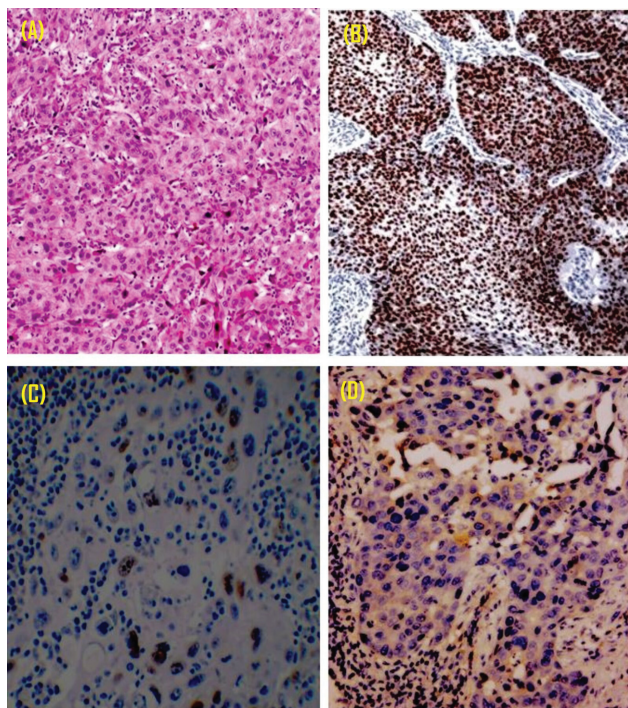


Fig. 4 Image-guided biopsy from penile root lesion showing (A) squamous cell carcinoma penis (hematoxylin and eosin 100 \times); (B) immunohistochemistry detecting p53, (C) cyclin D1, and (D) epidermal growth factor receptor.

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

Discussion

PCs are very rare malignancies with an incidence of 0.5 to 1% in developed nations and approximately 1 to 10% in poor socioeconomic nations, associated with HPV through viral oncogenes E6 targeting p53 and E7 attacking RB1 tumor-suppressor genes, that are actively transcribed by HPV-DNA⁶ culminating into widespread dissemination and grave prognosis.⁷ SCC is the most common malignant histology affecting 50 to 70 years old men, apart from sarcoma, basal cell carcinoma, and malignant melanomas.¹ SCC of penis generally metastasizes distantly to lung, liver, brain, bones, heart, adrenals, eye,¹ and skin,² 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,^{8,9} while noncancerous affection occurs from tuberculosis, sarcoidosis, and toxoplasmosis.¹⁰

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

patient. Pain and discharge from penis are the late symptoms indicative of invasive disease that actually bring patients to a physician. Distant metastasis is usually late with an incidence of less than 3%.¹ PC metastasizes to inguinal LNs in approximately 47 to 85% cases⁶ and to pelvic LNs in 19 to 48% cases³ however, a thorough review of literature did not reveal reported incidence of direct SCLN spread. Bilateral or multiple nodal involvement, pelvic LN spread (vis-à-vis inguinal), and extranodal dissemination are the harbingers of poor disease outcome.³ Bone metastasis to axial skeleton was also seen in this case that is also very rare with poor prognosis.¹ Tissue diagnosis with fine-needle aspiration cytology, incision/excision biopsy, sentinel node biopsy are the gold standards to diagnose primary and secondary malignancies. IHC showing p53 overexpression is predictive of both local and distant lymphatic dissemination, extranodal spread, and fulminant behavior of PC.⁷

In addition to the invasive techniques stated above, noninvasive diagnostics like CT scan and magnetic resonance imaging have improved the detection of primaries; ¹⁸F-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.¹⁰ In PC, high FDG uptake has been reported both in primary lesion and metastatic LNs, though with lesser sensitivity in nonpalpable cN0 inguinal LNs, albeit higher specificity and increased false-positives in inflammatory reactive LNs.^{5,10} ¹⁸F-FDG-PET/CT has shown a sensitivity of 91% and specificity of 100% for pelvic LNs and approximately 85 and 86%, respectively, for distant metastatic sites in PCs,^{5,10} while such data on SCLN is 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 ¹⁸F-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. ¹⁸F-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 multidisciplinary approach.

Authors' Contribution

Purkayastha Abhishek conceptualized, designed and prepared the manuscript. Purkayastha Abhishek and Suhag Virender were involved in definition of intellectual content and literature search. Purkayastha Abhishek, Suhag Virender, and Taneja Sachin contributed substantially in clinical studies, data analysis, and statistical analysis. Purkayastha Abhishek, Suhag Virender, and Husain Azhar helped in data acquisition. Purkayastha Abhishek, Suhag Virender, Taneja Sachin, and Husain Azhar were involved

in manuscript editing and review. Purkayastha Abhishek, Suhag Virender, Taneja Sachin, and Husain Azhar provided guarantee. The manuscript has been read and approved by all the authors, the requirements for authorship have been met, and each author believes that the manuscript represents honest work.

Ethical Approval

Written informed consent to publication was obtained from the patient.

Funding

None.

Conflict of Interest

We have no conflicts of interest to declare.

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