Transitional Cell Carcinoma of Urinary Bladder Manifesting as Extensive Retroperitoneal and Axillary Lymph Node Metastasis: An Extremely Rare Case Scenario Detected by ^{18}F-Fluorodeoxyglucose Positron Emission Tomography Scan

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Abstract

Transitional cell carcinoma (TCC) urinary bladder is known to metastasize to regional lymph nodes (LNs), liver, lung, bone, adrenal glands, and intestine. However, an asymptomatic TCC bladder manifesting as metastatic axillary LN mass and extensive retroperitoneal lymphadenopathy is rarely heard of. A 46-year-old male, smoker, presented with 8 cm × 6 cm right axillary swelling of 1-month duration. Aspiration cytology revealed metastatic deposits of poorly differentiated carcinoma favoring TCC. Metastatic evaluation with ^{18}F-fluorodeoxyglucose positron emission tomography (^{18}FDG-PET) scan showed mass lesion urinary bladder, conglomerate right axillary mass and extensive retroperitoneal LNs with significant metabolic activity, biopsy from which revealed deposits of TCC. Transurethral-resection of bladder confirmed TCC and was exhibited palliative chemotherapy on which he progressed. Received palliative radiotherapy to axilla to which he showed significant symptomatic clinical response. He developed obstructive uropathy and was kept on supportive care. Review of literature reveals that our case may be the second case of TCC bladder with generalized lymphadenopathy and the first case of asymptomatic bladder carcinoma manifesting with upfront disseminated abdominopelvic lymphadenopathy detected by ^{18}FDG-PET scan ever reported in world literature.

Keywords: *^{18}F-fluorodeoxyglucose positron emission tomography scan, generalized lymphadenopathy, metastasis, transitional cell carcinoma, urinary bladder*

Introduction

Transitional cell carcinoma (TCC) urinary bladder (UB) metastasizing to supra-diaphragmatic and retroperitoneal lymph nodes (LNs) is extremely rare. ^{18}F-fluorodeoxyglucose positron emission tomography (^{18}FDG-PET) exhibits great importance in LN imaging with ^{18}F-FDG avidly taken up by cells with increased rates of glycolysis.[1] Sensitivity and specificity of ^{18}F-FDG-PET have a proven superiority over computed tomography (CT) scan in detecting malignant LNs.[1] The presence or absence of p53 mutations has been postulated as a determining factor for LN metastasis from TCC bladder but without any prognostic significance.[2,3] Radiotherapy (RT) has been traditionally used in metastatic setting for symptomatic relief of localized disease with satisfactory clinical response.[4]

Case Report

A 46-year-old male, smoker presented with right axillary swelling of 1 month duration. There was no history of fever, night sweats, weight loss, cough, chest lump, gynecomastia, or abdominal pain. Clinical evaluation showed 8 cm × 6 cm erythematous swelling right axilla fixed to underlying structures [Figure 1]. Fine-needle aspiration cytology (FNAC) from the swelling was suggestive of deposits of poorly differentiated carcinoma favoring TCC [Figure 2]. Evaluation with ^{18}F-FDG-PET/CT scan showed a 4.5 cm × 3.2 cm × 4.2 cm soft-tissue density mass lesion UB with maximum standard uptake value (SUV_{max}) of 29.2 [Figure 3], multiple conglomerate axillary LNs largest measuring 6.5 cm × 5.8 cm × 6.4 cm with SUV_{max} 7.7 [Figure 4]. A lymphatic

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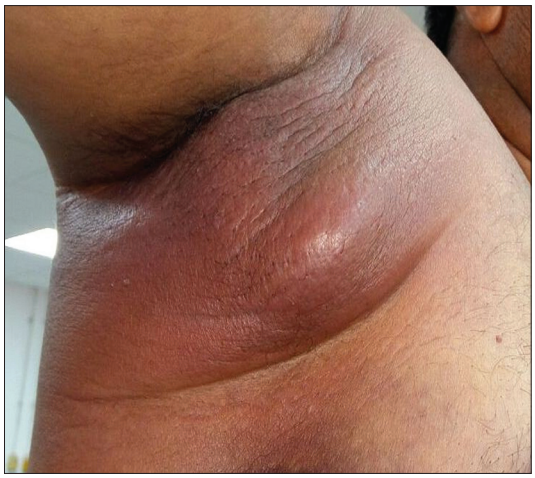

Figure 1: Patient on presentation with right axillary lymph node swelling

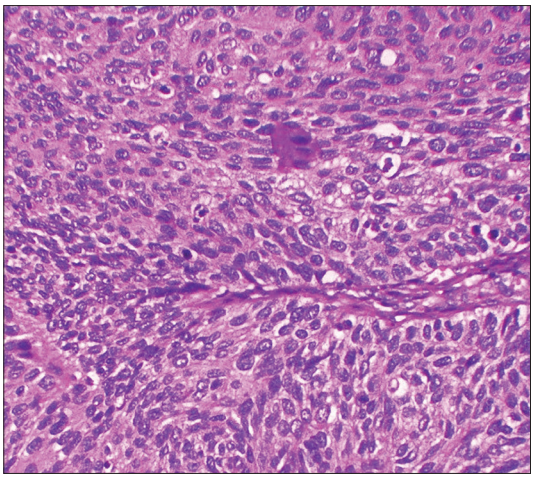

Figure 2: Fine-needle aspiration cytology from the axillary swelling showing deposits of poorly differentiated carcinoma favoring transitional cell carcinoma (H and E, ×100)

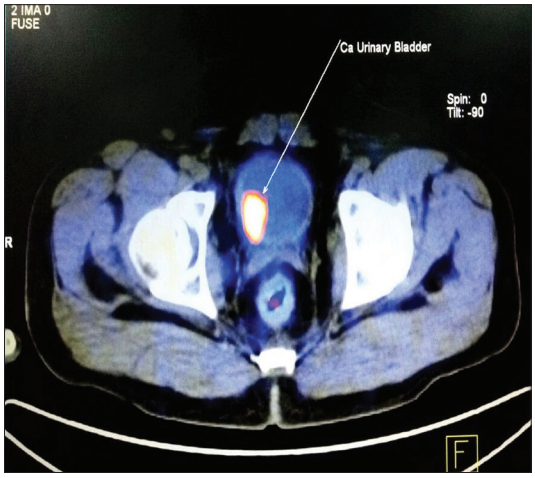

Figure 3: Axial section positron emission tomography scan showing a soft-tissue density mass lesion projecting into the lumen of urinary bladder with irregular eccentric posterolateral wall thickening

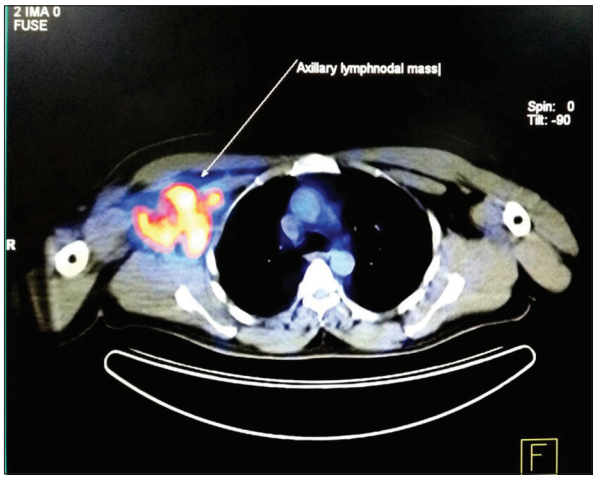

Figure 4: Positron emission tomography scan showing multiple discrete and conglomerate axillary lymph nodes causing contour bulge in the right axillary region

chain involving right para-aortic (largest 1.9 cm SUV_{max} 9.7), paracaval, and aortocaval LNs (largest 2.4 cm, SUV_{max} 11.9) with bilateral right common iliac, internal iliac, and external iliac LNs with significant FDG uptake were seen [Figure 5].

Cystoscopy and transurethral resection of bladder tumor demonstrated high-grade TCC. Deep muscle biopsy was positive for tumor deposits [Figure 6a] with immunohistochemistry (IHC) positive for p53 [Figure 6b]. CT-guided FNAC from the retroperitoneal LNs revealed metastatic deposits of TCC while IHC was negative for CD45, thus excluding lymphoma. The patient was diagnosed as a case of metastatic TCC UB and was exhibited six cycles of palliative chemotherapy gemcitabine and cisplatin. Postchemotherapy ^{18}F-FDG-PET/CT showed an increased size of axillary LN mass to 9.6 cm × 7.8 cm × 7.6 cm and increased SUV_{max} of 9.3. The appearance of the right retrocrural and right retrocaval LNs, increased size, and FDG avidity of retroperitoneal nodes suggested a progressive disease though the size and FDG avidity of the primary was reduced. The patient became symptomatic with swelling, severe pain, and restricted movement right upper limb. He was treated with palliative RT to the right axillary LN mass to a dose of 30 Gy in 10 fractions to which he showed significant symptomatic response with reduction in size of the nodal mass, reduced analgesic requirement, and improved limb movement He was not planned for second-line chemotherapy as he developed obstructive uropathy and deterioration of his general condition and has been kept on symptomatic and supportive care.

Discussion

The most common primary site with upfront metastatic axillary LNs is an occult breast primary in both females and males. Other primary sites include thyroid, lung, pancreas, and colon while UB as the primary site is least heard of. Pelvic LN metastasis from TCC UB occurs most commonly in about 78% cases followed by liver, lung, bone, adrenals, and bowel.[5,6] TCC metastasizing to heart,

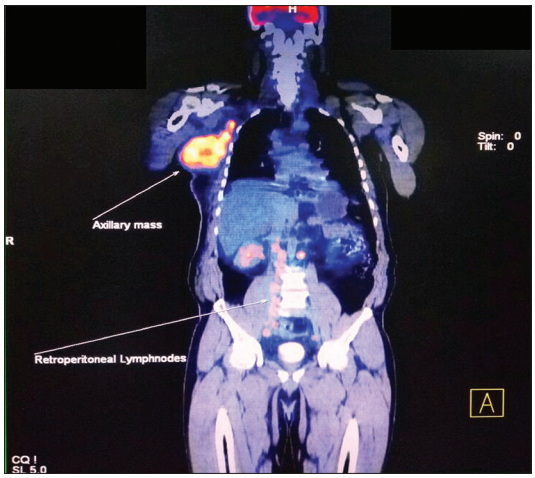

Figure 5: Whole body positron emission tomography scan showing the axillary lymph nodes along with the retroperitoneal and pelvic lymph nodes

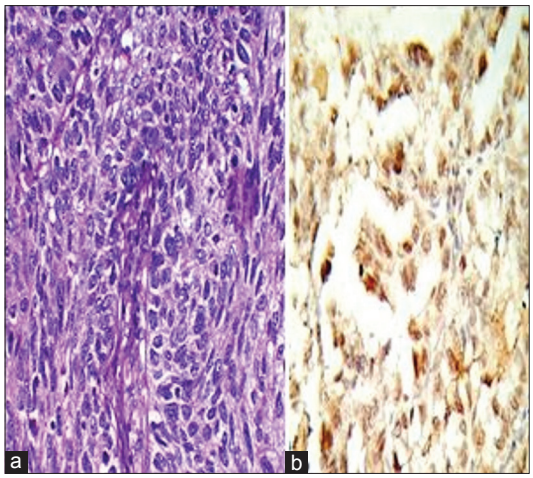

Figure 6: (a) Biopsy bladder mass showing transitional cell carcinoma (H and E, ×100). (b) Immunohistochemistry from bladder tissue showing positivity for p53

spleen, pancreas-kidney, ovary, uterus, testes, and even prostate are known but none to axillary or retroperitoneal LNs.[5]

Kancharla *et al*.[7] in 2010 reported the first case of TCC bladder with retroperitoneal and axillary lymphadenopathy where the patient had initially presented with hematuria and was later diagnosed to have disseminated lymphadenopathy. Our case is the first case where an asymptomatic patient presented with upfront massive axillary LN metastasis and retroperitoneal lymphadenopathy detected by ^{18}F-FDG PET.

TCC bladder often exhibits multifocality with multiple primary tumors and frequent recurrences that can occur anywhere in the urinary tract from the renal pelvis to the urethra suggesting field cancerization, where the whole urothelium gets exposed to the same carcinogens, leading to the transformation of many independent urothelial cells and resulting in multiple tumors developing independently in multiple sites. This concept may explain the occurrence of upfront widespread lymphatic metastasis from bladder primary in our case. Overexpression of p53 is predictive of lymphatic spread and highly aggressive behavior with more invasiveness and distant dissemination as compared to tumors which remain confined to UB.[2,3] Cancer stem cells do appear to play a role in disease dissemination, but their true significance is yet to be clarified.[8]

As compared to the cross-sectional view of LNs, PET has acquired great importance in LN imaging, primarily with the glucose analog ^{18}F-FDG which is phosphorylated to ^{18}F-FDG-6P, and gets trapped in tumor cells that are relatively deficient in glucose-6-phosphatase denoted by their SUVs. Both sensitivity and specificity of ^{18}F-FDG PET have been superior to CT and magnetic resonance imaging (MRI) in detecting malignant LNs due to low accuracy of size parameters evaluated my CT/MRI.[1] CT imaging of normal ovaries can mimic external iliac LNs, small intestinal loops close to retroperitoneum can resemble nodal disease while peritoneal nodules can mimic pelvic LNs. Even MRI with intravenous gadolinium administration has not been effective in differentiating benign from malignant LNs.[1]

Extensive randomized studies have demonstrated the superiority of cisplatin-based combination systemic chemotherapy over those containing other drugs or cisplatin alone.[4] Methotrexate/vinblastine/adriamycin/cisplatin[4] and gemcitabine/cisplatin[9] have proven to be superior to other combinations and broadly similar in efficacy to each other. Palliative RT provides pain relief, preservation of organ function, skeletal integrity, and rehabilitation.[4] Radiation dose ranges from 21 Gy in 3 fractions to 35 Gy in 10 fractions with no evidence of a difference in efficacy or toxicity between the schedules.[4,10]

Conclusion

By reporting this exceedingly rare case, we recommend that the diagnosis of primary TCC bladder should always be considered in patients presenting with an axillary LN mass so as to initiate an appropriate evaluation strategy. ^{18}FDG-PET/CT provides the extent of metastases by providing whole body scan information. In our case, ^{18}FDG-PET/CT gave information of extensive retroperitoneal lymphadenopathy in clinically hidden metastases.

Acknowledgments

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Conflicts of interest

There are no conflicts of interest.

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