Case Report

Testicular Tuberculosis after Intravesical BCG for Urinary Bladder Cancer: A Role of FDG PET-CT

Abstract

Bacillus Calmette–Guërin (BCG) has been traditionally used as a vaccine against tuberculosis (TB), which contains live, attenuated strain of *Mycobacterium bovis*. However, intravesical BCG administration has been used as an immunological treatment of superficial bladder cancer. Complications after bladder instillation of BCG are rare. We report a case of carcinoma urinary bladder with histopathologically proven granulomatous epididymo-orchitis (TB) after treatment with intravesical BCG.

Keywords: *Bacillus Calmette–Guërin, carcinoma urinary bladder, fluorodeoxyglucose positron emission tomography/computed tomography, tuberculosis*

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Introduction

Urinary bladder cancer is a relatively rare malignancy among Indian population. As per the GLOBOCAN 2020 database, bladder cancer is the 17th common malignancy in India.[1] Bacillus Calmette–Guërin (BCG) has been traditionally used as a vaccine against tuberculosis (TB), which contains live, attenuated strain of *Mycobacterium bovis*. However, intravesical administration of BCG has been used as an immunological treatment of superficial bladder cancer.[2] The therapeutic effect of BCG in bladder cancer is based on contact with tumor cells and subsequent immune stimulation. Immune system activation induces a complex inflammatory response, which selectively affects tumor cells and avoids benign urothelial cells.[3] Complications after bladder instillation of BCG are rare. Local complications are the result of BCG-contaminated urine and can occur anywhere along the genitourinary tract. Systemic effects occur as a result of BCG dissemination to other sites through the bloodstream. The complications reported include cystitis, bladder contracture, granulomatous prostatitis, epididymo-orchitis, pyelonephritis, urethral obstruction, and systemic disease followed by dissemination of bacteria into other organs.[4] We report a case of carcinoma urinary bladder with histopathologically proven granulomatous epididymo-orchitis (TB) after treatment with intravesical BCG.

Case Report

A 73-year-old male with high-grade papillary urothelial carcinoma (muscularis propria free of tumor) underwent chemotherapy followed by transurethral resection of bladder tumor (TURBT) and 5 cycles of intravesical BCG. After 5th cycle of intravesical BCG, the patient developed cystitis and further course of BCG injection was withheld. The patient underwent magnetic resonance imaging abdomen, where the findings suggested possibility of recurrence in the bladder/perivesical region infiltrating the bladder wall and prostate with metastatic right inguinal and iliac lymph nodes.

The patient underwent fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET-CT) to assess the extent of the recurrent disease. PET-CT demonstrated FDG-avid heterogeneously enhancing soft tissue thickening involving the left posterolateral wall of the urinary bladder [Figure 1] with possible involvement of prostate and left seminal vesicle along with two focal FDG-avid heterogeneously enhancing nodular lesions in the right testis [Figure 2]. PET-CT also showed mild FDG-avid prominent lymph nodes in the neck, right hilar, aortocaval,

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retrocaval, right external iliac, and right inguinal regions. Above PET-CT findings suggested the possibility of local recurrent bladder disease. However, in view of FDG-avid enhancing nodular lesions in the right testis and nonregional lymph nodal involvement (lymph nodes in the neck and right hilar region) along with a history of BCG injections, the possibility of coexisting infective etiology (TB) was raised and histopathological correlation was suggested.

Subsequently, the patient underwent cystoscopy + TURBT + fulguration + right orchidectomy. The findings of histopathological examination from TURBT specimen showed polypoid granulation tissue with squamous metaplasia, cystitis glandularis, and noncaseating granulomas. Right orchidectomy specimen showed caseating granulomatous epididymo-orchitis, in keeping with TB.

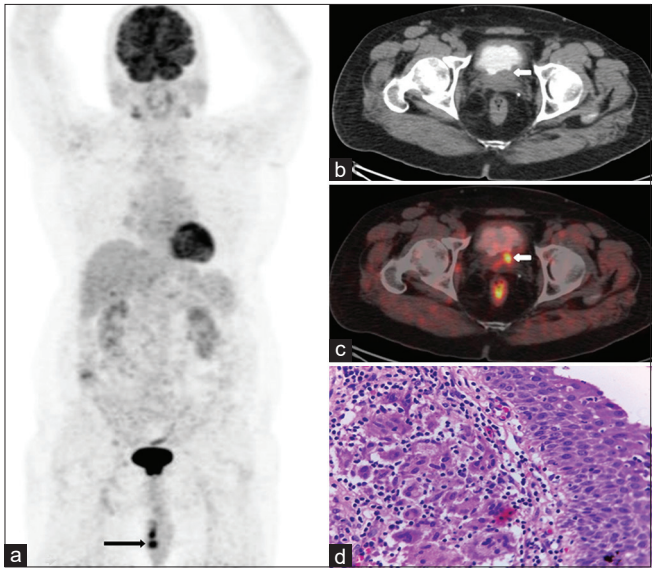

Figure 1: (a) Maximum intensity projection image of 18F-fluorodeoxyglucose positron emission tomography/computed tomography(FDG PET-CT) showing focal FDG uptake in right scrotal region. (b and c) Images showing FDG-avid soft tissue thickening involving left posterolateral wall of the urinary bladder. (d) Biopsy from lesion on the left lateral wall of the bladder showing urothelium on the right with underlying collection of epithelioid histiocytes forming ill-defined granuloma

Discussion

BCG is the attenuated strain of the bovine tuberculous bacterium and consists of living bacilli, dead microorganisms, and subcellular debris. It maintains the immunological properties and antibiotic sensitivities of the parent strain.[2,3]

Toxic side effects post-BCG immunotherapy in cancer patients can be divided into local and systemic categories. Important factors for this toxicity include route of administration, number of repeated injections, and dose of BCG. Patients with superficial bladder cancer including carcinoma *in situ* have been treated with BCG. Intravesical instillation has proved to be the most effective route of administration.

BCG-related epididymo-orchitis is relatively rare. Review of literature revealed incidence in fewer than 1% of complications associated with BCG treatment and may manifest even after 10 years postfinal intravesical BCG instillation.[5,6] The possible route of spread is considered to be prostatic urethroejaculatory duct reflux. Another possibility is traumatic catheterization or concurrent cystitis that result in systemic BCG absorption.[5] Signs and symptoms include fever, leukocytosis, and acute or gradual onset scrotal swelling. When typical antibiotics used for treating urinary tract infections do not respond, granulomatous epididymo-orchitis should be suspected and antimycobacterial agents should be used in the relevant clinical setting.

In addition to identifying the site of disease and evaluating disease burden, FDG PET-CT scans have also been used to assess treatment response in TB by measuring changes in standardized uptake value.[7]

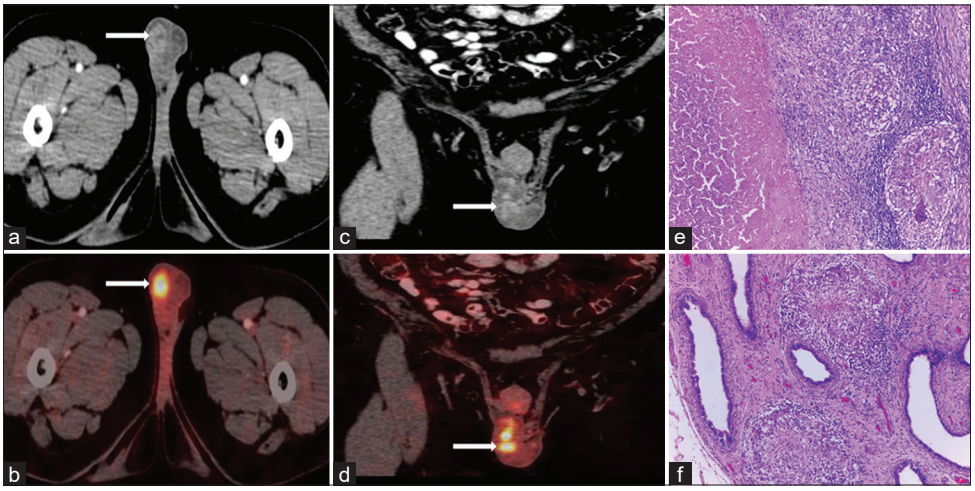

Figure 2: (a-d) 18F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET-CT) images showing two focal FDG-avid heterogeneously enhancing nodular lesions in right testis (white arrows). (e and f) Histopathological examination of the right orchidectomy specimen showing multiple large epithelioid granulomas surrounded by lymphocytic cuffing on the right, caseation necrosis on the left (e), and large epithelioid granulomas in the stroma between epidydimal ducts (f)

This case reinforces the fact that any unusual sites of FDG-avid lesions, which do not match with the metastatic pattern of the disease, should be correlated with the clinical history. Involvement of testis and nonregional lymph nodes along with the history of intravesical BCG injections raised the suspicion of infective etiology in this patient. This case also emphasizes the need for whole body imaging in oncology patients.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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