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Pulmonary Granulomatosis Revealing BCGitis after Immunotherapy for Bladder Cancer

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Abstract

Intravesical instillation of Bacillus Calmette-Guérin (BCG) is an established treatment for non-muscle-invasive bladder cancer, but rarely leads to systemic complications. We report the case of a 53-year-old male, a chronic smoker and cannabis user, who developed respiratory symptoms including productive cough, dyspnea, and deterioration in general health three months after completing intravesical BCG therapy for urothelial carcinoma. Chest CT revealed multiple pulmonary nodules and masses, while a lung biopsy showed non-caseating epithelioid granulomas. Differential diagnoses, including tuberculosis and sarcoidosis, were excluded based on negative microbiological tests and clinical assessments. A strongly positive tuberculin skin test (21 mm induration), the temporal relationship with BCG therapy, and exclusion of alternative causes supported the diagnosis of BCG-induced pulmonary granulomatosis. The patient responded favorably to antitubercular therapy (isoniazid, rifampicin, and ethambutol). This case highlights the importance of a thorough diagnostic evaluation in granulomatous lung disease and underscores BCGitis as a potential delayed complication of intravesical BCG therapy, even in immunocompetent patients. Intravesical Bacillus Calmette-Guérin (BCG) immunotherapy remains the gold standard for intermediate- and high-risk Non-Muscle-Invasive Bladder Cancer (NMIBC), significantly reducing tumor recurrence and progression by triggering a local immune response. BCGitis, defined as systemic manifestations secondary to intravesical BCG therapy, can arise either from hematogenous dissemination or from hypersensitivity immune reactions, posing diagnostic challenges due to its nonspecific clinical presentation. This case report illustrates a rare but serious complication of intravesical BCG therapy, describing the clinical context, diagnostic approach, therapeutic management, and outcomes of a patient developing pulmonary granulomatosis following BCG treatment.

Keywords

BCGitis, Pulmonary Granulomatosis, Bladder Cancer, Immunotherapy, Tuberculin Skin Test

1. Introduction

Intravesical Bacillus Calmette-Guérin (BCG) immunotherapy remains the gold standard for the treatment of intermediate- and high-risk Non-Muscle-Invasive Bladder Cancer (NMIBC). It significantly reduces tumor recurrence and progression by triggering a local immune response within the bladder mucosa.

Although the therapy is generally well tolerated, a subset of patients may develop local or systemic adverse effects. Local complications are more common and typically include irritative urinary symptoms. Systemic complications, though rare, can be severe and include disseminated infections affecting the lungs, liver, bones, and vascular system.

BCGitis refers to systemic manifestations induced by BCG therapy, which may arise from hematogenous spread of the attenuated mycobacteria or a hypersensitivity immune reaction. The clinical presentation is variable and may mimic other granulomatous or infectious diseases, making the diagnosis particularly challenging.

This case report aims to illustrate a rare but serious complication of intravesical BCG therapy, where a patient developed pulmonary granulomatosis after treatment for bladder cancer. We discuss the diagnostic approach, including differential diagnoses, and therapeutic strategies, emphasizing the need for clinical vigilance and timely management in such cases.

2. Case Report

We report the case of a 53-year-old man with no personal history of pulmonary tuberculosis or known recent exposure. He was a chronic smoker (45 pack-years) and had a long-standing history of cannabis use. The patient had been under urological follow-up since 2021 for high-grade invasive papillary urothelial carcinoma of the bladder, diagnosed by transurethral resection. He subsequently received six sessions of intravesical BCG instillation, completed on February 22, 2022.

Approximately three months following the final BCG session, he developed a dry cough, exertional dyspnea, night sweats, and a progressive decline in his general condition. The cough became productive, and dyspnea worsened. On clinical examination, he was afebrile, with a respiratory rate of 20 breaths per minute, an oxygen saturation of 92% on room air, and bilateral crackles on auscultation. The remainder of the systemic examination was unremarkable.

A chest X-ray revealed bilateral interstitial nodular opacities, predominantly in the lower zones, along with left hilar-basal infiltrates and a reduced cardiac silhouette (**Figure 1**).

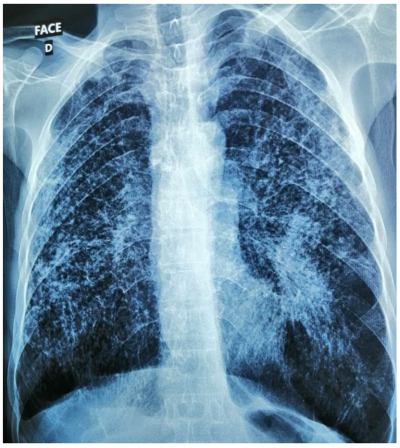

Figure 1. Chest X-ray showing bilateral diffuse interstitial and nodular opacities with left hilar infiltrates, consistent with granulomatous pulmonary involvement following intravesical BCG therapy.

High-resolution chest CT showed numerous bilateral pulmonary micronodules with hematogenous distribution, dense peripheral pulmonary masses with irregular borders (including a large calcified mass measuring 37.5 × 29 mm), and an excavated apical mass on the right measuring 37 × 24.8 mm. There were also areas of bilateral septal and non-septal thickening and calcified mediastinal lymphadenopathy, the largest node measuring 11 mm in short axis (**Figure 2**).

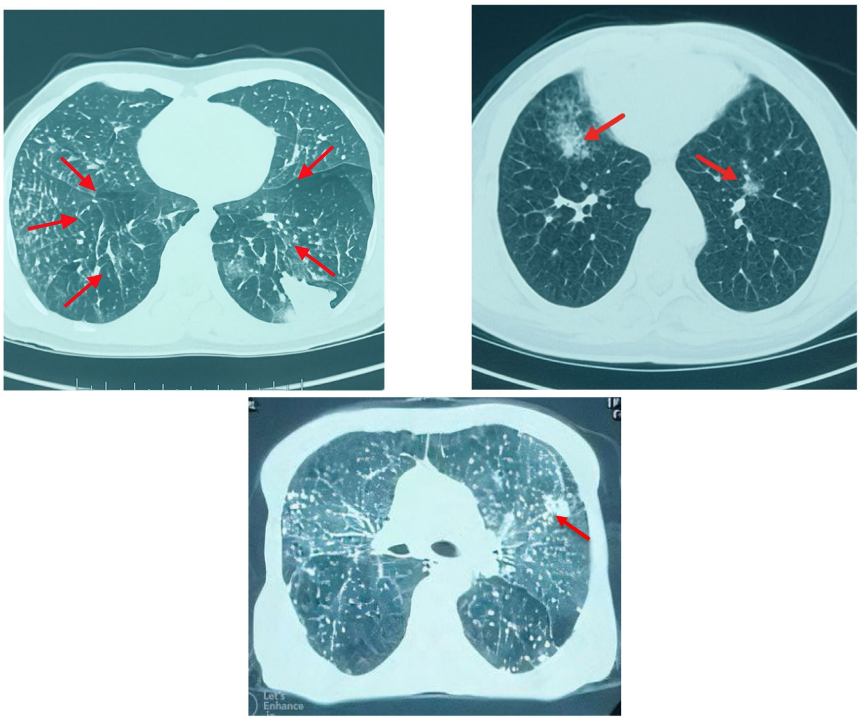

Figure 2. Axial chest CT images showing multiple bilateral micronodules with hematogenous distribution, peribronchovascular thickening, and subpleural masses with calcification. These findings are consistent with BCG-induced granulomatous pulmonary involvement.

Laboratory evaluation was within normal limits except for a mild thrombocytosis. Microbiological analysis, including direct examination, culture for acid-fast bacilli, and PCR testing, was all negative. Pulmonary biopsy demonstrated non-caseating epithelioid granulomas with no evidence of malignancy. An 8-month-old CT urogram performed after BCG treatment showed no evidence of retroperitoneal or pelvic disease. Ophthalmologic and hepatic evaluations were unremarkable, and there were no musculoskeletal complaints. Serum Angiotensin-Converting Enzyme (ACE) testing was performed to rule out sarcoidosis.

The tuberculin skin test showed a strong reaction, with 21 mm of induration. Given the absence of microbiological confirmation but a supportive clinical history, histological findings, and exclusion of other causes, a diagnosis of BCG-induced pulmonary granulomatosis was established. The patient was initiated on antituberculous therapy with isoniazid, rifampicin, and ethambutol. He showed marked clinical improvement with resolution of symptoms and no adverse effects were reported during follow-up.

3. Discussion

BCG (Bacillus Calmette-Guérin), an attenuated strain of Mycobacterium bovis, is widely used for intravesical immunotherapy in patients with NMIBC [1]. While generally well tolerated, BCG instillation may lead to complications, especially in predisposed individuals.

The mechanism of action involves local immune activation via macrophages, neutrophils, and cytokines [2]. Common side effects include fever and dysuria; however, systemic dissemination may lead to serious conditions, including pneumonitis, hepatitis, osteomyelitis, or vascular involvement .

In our case, the delayed onset of pulmonary symptoms and granulomatous inflammation without microbiological confirmation suggested disseminated BCGitis. Such cases often require clinical judgment and histopathological support.

Proposed mechanisms include hematogenous spread or hypersensitivity. Risk factors such as bladder trauma, recent instrumentation, immunosuppression, and diabetes mellitus may increase vulnerability [3].

Antitubercular therapy (isoniazid, rifampicin, ethambutol) is the mainstay of treatment. Mycobacterium bovis is naturally resistant to pyrazinamide. Corticosteroids may be used in severe cases.

This case highlights the need for awareness of atypical pulmonary presentations of post-BCG instillation and prompt diagnostic evaluation to guide therapy.

4. Conclusions

This case underscores the importance of considering BCG-related complications in the differential diagnosis of patients presenting with unexplained pulmonary symptoms following intravesical immunotherapy. Although rare, BCG-induced pulmonary granulomatosis can mimic infectious, neoplastic, or inflammatory diseases, posing a diagnostic challenge.

A comprehensive clinical evaluation, appropriate imaging, histological confirmation, and exclusion of alternative causes are essential to establish the diagnosis. Despite negative microbiological results, clinical context and histopathological findings can be sufficient to initiate treatment.

Early recognition and initiation of appropriate antimycobacterial therapy are crucial to avoid progression and improve patient outcomes. This case also highlights the need for increased awareness of systemic BCG-related adverse events, even in immunocompetent individuals.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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