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Case Report

Tuberculous Orchi-Epididymitis Following Intravesical BCG Instillation: A Case Managed Conservatively

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ABSTRACT

Bladder cancer is a prevalent malignancy that affects the urinary bladder, and its epidemiology reveals a significant global impact. Based on data from the Surveillance, Epidemiology and End Results (SEER), between the years 2016 to 2020, the age adjusted incidence rate of new cases of bladder cancer was 18.2 per 100,000 individuals (both men and women) annually. Similarly, the age adjusted death rate attributed to bladder cancer was reported at 4.2 per 100,000 individuals, in both genders, per year. The lifetime risk of developing bladder cancer was reported to be approximately 2.3 percent of both men and women. As of 2020, the estimated number of individuals living with bladder cancer in the United States was 725,549. Bladder cancer is more commonly diagnosed in males than females, and the risk of developing the disease increases with age, peaking in individuals over 70 years old. While tobacco smoking is a well-established major risk factor, occupational exposures to certain chemicals, such as aromatic amines and polycyclic aromatic hydrocarbons, also contribute significantly to the disease's development. Moreover, genetic predisposition and chronic bladder infections have been identified as additional risk factors. Awareness of these epidemiological patterns is crucial in formulating preventive strategies and optimizing early detection efforts for bladder cancer.

Keywords: Bladder cancer; Tobacco smoking; Chemicals; Aromatic amines and polycyclic aromatic hydrocarbons

INTRODUCTION

Bladder cancer can present in various ways, and its symptoms often depend on the stage and type of the disease [1]. In its early stages, bladder cancer may be asymptomatic, making it challenging to detect without routine screenings. However, as the disease progresses, common presentations may include blood in the urine (hematuria), which can be visible or microscopic. Visible gross hematuria can cause the urine to appear pink, red, or brown. Other symptoms may include frequent or urgent urination, pain or discomfort during urination, and lower back or abdominal pain. Advanced stages of bladder cancer may lead to unintentional weight loss, fatigue, and bone pain if the cancer has spread to other parts of the body.

CASE PRESENTATION

In the initial diagnosis it is important to differentiate between Non-Muscle Invasive Bladder Cancer (NMIBC) and Muscle Invasive Bladder Cancer (MIBC). These are two distinct stages of bladder cancer with significant differences in their characteristics and treatment approaches. NMIBC refers to cancer that is limited to the inner lining of the bladder and has not invaded the muscle layer. This stage typically includes Carcinoma *In situ* (CIS), papillary tumors, and low-grade non-invasive tumors. NMIBC has a higher likelihood of recurrence but generally carries a more favorable prognosis than MIBC. In contrast, MIBC is characterized by cancer cells that have invaded the muscle layer of the bladder. At this stage, the cancer may have spread beyond the bladder to nearby lymph nodes or other organs. Patients with MIBC may experience more pronounced symptoms, including persistent hematuria, pelvic pain, back

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Received: 25-Jul-2023, Manuscript No. ANO-23-25809; **Editor assigned:** 27-Jul-2023, PreQC No. ANO-23-25809 (PQ); **Reviewed:** 11-Aug-2023, QC No. ANO-23-25809; **Revised:** 13-Jan-2025, Manuscript No. ANO-23-25809 (R); **Published:** 20-Jan-2025 DOI: 10.35248/2167-0250.25.14.337

Citation: Golomb D, Hen E, Brosh-Nissimov T, Maaravi N, Cooper A, Raz O (2025) Tuberculous Orchi-Epididymitis Following Intravesical BCG Instillation: A Case Managed Conservatively. Andrology. 14:337.

pain, and unintentional weight loss. MIBC is associated with a higher risk of disease progression and a poorer prognosis compared to NMIBC. The treatment approaches for NMIBC and MIBC differ significantly. For NMIBC, Transurethral Resection of Bladder Tumor (TURBT) is the standard initial treatment to remove visible tumors from the bladder lining. After TURBT, intravesical therapies, such as Bacillus Calmette-Guerin (BCG) immunotherapy or chemotherapy, are often used to reduce the risk of recurrence and progression [2]. On the other hand, MIBC usually requires more aggressive treatments, such as radical cystectomy or trimodal therapy, which includes a combination of TURBT, radiation therapy, and chemotherapy. The choice of treatment depends on factors such as the extent of cancer spread, the patient's overall health, and their preferences (Figure 1).

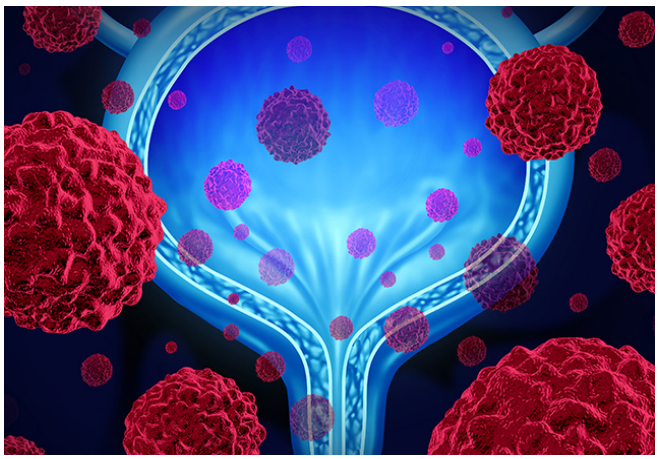

Figure 1: Bladder cancer.

RESULTS AND DISCUSSION

BCG has been the most widely administered vaccine globally for the prevention of tuberculosis for over a century. The use of BCG in the treatment of NMIBC has been highly successful. Early studies demonstrated BCG's ability to induce a delayed hypersensitivity response in guinea pig bladders [3]. In the 1970's, Alvaro Morales developed the BCG protocol still used today [4], consisting of six weekly instillations based on vial availability and short adverse events duration. Landmark studies in the mid-1970's showcased BCG's efficacy, leading to randomized trials confirming its superiority in reducing tumor recurrence compared to surgical resection alone [5]. BCG has also been found to prevent or delay progression to invasive disease [6]. Despite its success, BCG fails in a significant number of patients, and adverse effects can limit treatment schedules [7]. BCG's mechanism of action involves attaching to the urothelium, stimulating innate and adaptive immune responses, leading to cytotoxicity of bladder cancer cells [8].

Although BCG is an attenuated strain of *Mycobacterium bovis*, it can still lead to invasive mycobacterial infections [9]. BCG instillation can still lead to local and systemic invasive mycobacterial infections. The incidence of genitourinary complications following BCG instillation is low, and tuberculous orchi-epididymitis is a rare manifestation [10]. The infection usually involves the epididymis first, with the testis secondarily affected. Tuberculous orchi-epididymitis, a rare complication of BCG instillation, poses diagnostic challenges and may mimic malignancy or other bacterial infections.

We present the case of an 83-year-old man with high-grade urothelial cell carcinoma who developed tuberculous orchi-epididymitis following BCG therapy. The patient was managed conservatively with a combination of anti-tuberculotic medications, leading to successful resolution of symptoms and preservation of testicular structures. In the case report, we presented an 83-year-old man with high grade urothelial cell carcinoma received BCG instillation as part of his treatment. Following two out of six planned instillations, he presented with left-sided epididymitis. Empirical treatment with oral co-trimoxazole was initiated, but purulent discharge from the right hemi-scrotum prompted further investigation. Scrotal ultrasound revealed a heterogeneous mass in the right testicle, continuous with the epididymal tail. Swabs and tissue samples tested positive for *Mycobacterium tuberculosis* complex, specifically *M. bovis*. Conservative management with a combination of isoniazid, rifampin, ethambutol, and vitamin B complex was chosen. Due to drug induced hepatitis, the treatment was modified to isoniazide, ethambutol, and levofloxacin. Twelve months after diagnosis and three months post-treatment, physical examination showed no purulent discharge, and ultrasound confirmed complete resolution.

The diagnosis of tuberculous orchi-epididymitis is challenging and can be mistaken for malignancy or other bacterial infections. In cases of non-responsive orchi-epididymitis following BCG therapy, surgical intervention might be considered. Collecting appropriate cultures is essential to identify mycobacterial infections in such cases. BCG, originally developed as a tuberculosis vaccine, has proven effective in NMIBC treatment after TURBT. Despite its attenuated state, BCG can cause invasive infections.

Adverse effects of intravesical BCG instillation are rare, and they can be categorized as systemic or local. Systemic complications result from BCG dissemination through the bloodstream, while local effects occur due to BCG-contaminated urine in the genitourinary tract. Mild symptoms following BCG instillation are common and include urinary irritative symptoms, malaise, and low-grade fever. Severe complications, although rare, may include sepsis, pneumonitis, granulomatous hepatitis, lymphadenitis, spondylodiscitis, and vascular issues. The incidence of severe complications can be reduced by avoiding BCG instillation under specific conditions. While previous reports mostly describe surgical management of tuberculous infections of the epididymis and testis, our case demonstrates the success of conservative management with anti-tuberculotic medications. This approach preserves the epididymis and testicle, which would have been excised with a surgical approach. We advocate for adopting a conservative approach initially and considering surgery only for non-responsive cases.

CONCLUSION

Tuberculous orchi-epididymitis following BCG instillation is a rare complication that requires careful consideration in patients

presenting with epididymitis after BCG therapy. This case illustrates the feasibility of conservative management with anti-tuberculotic medications to spare testicular structures and avoid unnecessary surgical interventions. Early diagnosis, appropriate culture collection, and prompt initiation of conservative treatment lead to favorable outcomes in patients with this rare complication. Further research is needed to establish guidelines for optimal management after BCG therapy, aiming to preserve testicular function and improve patient outcomes.

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