



Inflammation and infection

Penile granulomas after BCG instillations. A case report and review of literature

A. Eguibar^{a,*}, M.A. Portilla^a, J.A. Mainez^a, J. Lopez-Tello^a, R. Cansino^a, S. Fernandez^b

^a Department of Urology, Quironsalud, Madrid, Spain

^b Pathology Anatomy, Spain

ARTICLE INFO

Keywords:

Intravesical instillations
Bacillus Calmette-Guerin
Penile granulomas
Cryotherapy

ABSTRACT

Penile granulomas has been rarely reported in the setting of BCG instillations. We present a 70 year-old male with multiple penile granulomas during BCG instillations due a high-grade urothelial bladder cancer. Histopathological study revealed granulomatous structures with central necrosis as seen after BCG therapy. Local treatment with cryotherapy has been shown to be effective. This case emphasizes the importance to suspect this adverse effect in patients under BCG treatment.

Introduction

Bacillus Calmette-Guerin (BCG) is a live attenuated strain of *Mycobacterium bovis* that has been used to treat urothelial carcinoma since 1976. Nowadays has become the gold standard adjuvant therapy for the treatment of high-risk non-muscle-invasive bladder cancer. Although the mechanism of its therapeutic effect is still under investigation, BCG has been shown to decrease the risk of recurrence and progression after transurethral bladder resection TURBT.¹

Treatment with intravesical BCG is generally safe and the risk of complications associated with this treatment is estimated to be 5–10%. The most common side effects consist of cystitis associated with dysuria in 80% of cases and macroscopic haematuria in 40% of cases. Low-grade fever (38.5 °C) has been shown to develop in about 30.5% of patients, without significant systemic effects, and usually subsides within 48 hours.²

Systemic side effects account for a smaller proportion of reactions to intravesical BCG and can rarely be life-threatening. It includes general malaise (15.5–24.8%), rash (2.2–2.7%), fever (7.5–17.1%), and infections including sepsis.

Around 5% of patients can experience significant morbidity, typically noncaseating granulomatous inflammation of either local structures within the genitourinary tract or systemic organs, including the lung, liver, and osteomuscular structures.³

We report here a case of a 70-year-old man who was diagnosed with penile granulomas after intravesical BCG instillations.

Case presentation

We present a 70 year old man with past medical history of hypertension, diabetes mellitus and gastroesophageal reflux. Smoker of 20 cigarettes per day. He has a history of TURBT reporting a high-grade urothelial bladder cancer. He completed six weeks of induction therapy and maintenance during 3 months. During the maintenance instillation we noticed multiple penile mucosal lesions located in glans and bridle. The physical examination revealed 4–5 mm firm, painful and erythematous nodules, during the exploration (Fig. 1).

A skin biopsy was performed. During the biopsy we noticed purulent fluid. Histopathology revealed: Granulomatous structures in the dermis, with central necrosis, as seen after BCG therapy (Fig. 2). No bacteria were found in sample with Ziehl Nielsen (Fig. 3).

After the diagnosis we proceeded to the local treatment of the lesions with cryotherapy. During follow up no new lesions were observed and the treated lesions disappeared.

Discussion

The mechanism by which BCG asserts its antitumor effect is still unclear. It has been suggested that non-specific immune response with formation of granulomas, accumulation of macrophages and the subsequent activation of T helper 1 cells supports BCG treatment success.⁴

BCG instillations in high-grade bladder cancer have been shown to be effective preventing the risk of progression and recurrence. Despite instillations are generally well tolerated, there are some specific risk that

* Corresponding author.

E-mail address: aeguibar005@gmail.com (A. Eguibar).

<https://doi.org/10.1016/j.eucr.2021.101716>

Received 4 April 2021; Received in revised form 5 May 2021; Accepted 11 May 2021

Available online 16 May 2021

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Fig. 1. Penile mucosal lesions located in glans and bridle.

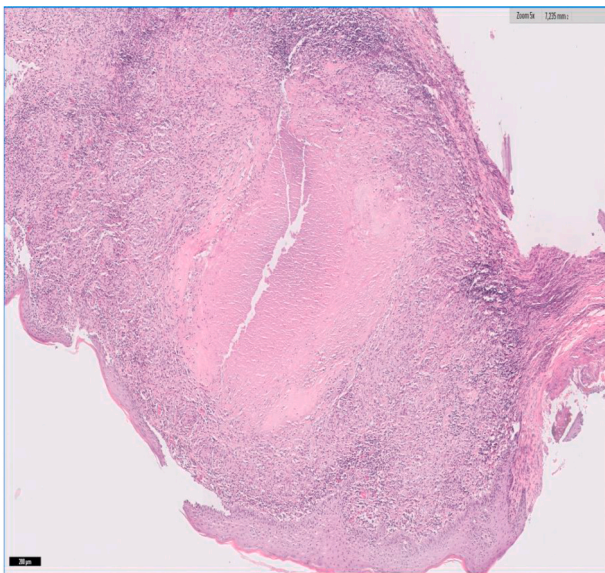


Fig. 2. Microphotograph of the lesion showing granulomatous structures in the dermis, with central necrosis. Hematoxylin-eosin stain, 100 \times .

results from the virulence of the attenuated bacillus and the immune response.

Serious complications including granulomatous pneumonitis, lymphadenitis, distant intramuscular and bone abscesses, hepatitis, sepsis and mycotic aneurysm have been reported. Regarding local reaction, granulomatous inflammation of the mucosal glans is rare with limited reports in literature.⁵ The symptoms are mainly local with itchiness and discomfort in the glans. The diagnosis requires an

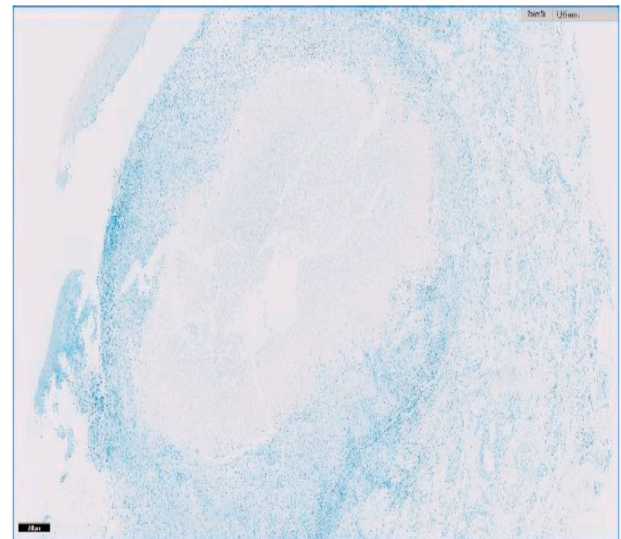


Fig. 3. Ziehl Nielsen stain, showing no bacteria on light microscopy (200 \times).

exhaustive physical examination. Differential diagnoses include soft tissue infections and fungal infections, being the histological analysis fundamental for the outcome of the case.

Similar to other BCG noncaseating granulomatous inflammation, these reactions were initially believed to be aseptic due to hypersensitivity response and rarely microorganisms could be cultured or identified with acid-fast stains of the affected tissue.

Treatment is necessary to prevent superinfection and inflammatory reactions over the meatus, which can cause meatal stenosis. In this case, a dermatologist collaboration, cryoablation with liquid nitrogen was chosen. The result after two weeks was positive with disappearance of the treated lesions.

Conclusion

Penile granulomas after BCG therapy is an uncommon reaction, rarely described in the literature that we have to suspect in patients under BCG treatment with glans discomfort. Treatment with liquid nitrogen has been shown to be effective against this type of lesions.

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