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# Urethral fistula and perineal collection during intravesical treatment for non-muscle invasive bladder cancer – A rare complication

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ABSTRACT

Intravesical Bacillus Calmette-Guérin (BCG) immunotherapy for non-muscle invasive bladder cancer (NMIBC) has been used as a treatment since 1976. It is effective in reducing disease recurrence and progression, with mostly self-limiting or mild side effects. Serious complications are rare and thought to be either related to systemic BCG infection (BCG-osis) or a systemic inflammatory response, and often require systemic anti-tuberculous therapy. We report a rare case of urethral fistulation leading to perineal BCG-abscess during intravesical BCG immunotherapy for high grade bladder cancer. This ultimately required systemic anti-tuberculous therapy and cessation of intravesical BCG treatment.

## 1. Introduction

Intravesical Bacillus Calmette-Guérin (BCG) immunotherapy has been used since 1976 for bladder cancer, and it is the preferred treatment for carcinoma in situ (CIS) and high-grade non-muscle invasive bladder cancer (NMIBC).[1] BCG has been shown to reduce recurrence as well as progression of NMIBC to muscle invasive bladder cancer.[1] Patients undergoing intravesical BCG can often experience mild, self-limiting side effects, which include local symptoms such as dysuria, frequency, haematuria and cystitis, as well as systemic symptoms like malaise and fever.[1,2] Although severe complications are rare, they often require long-term treatment and have lasting consequences.[2] Severe complications are usually a result of systemic BCG infection (BCG-osis) which requires systemic tuberculosis therapy.[2]

We describe a rare complication of urethral fistulation leading to a perineal collection that developed during the treatment of NMIBC in an immunocompromised patient that required systemic tuberculosis therapy.

## 2. Case Presentation

A 78-year-old male was worked up for lower urinary tract symptoms (LUTS) and an elevated prostate specific antigen (PSA). An ultrasound revealed an enlarged prostate but also a possible bladder lesion. This was confirmed with flexible cystoscopy and subsequent transurethral resection (TUR) revealed a high grade (TaHG) papillary transitional cell carcinoma (TCC) of the bladder with concurrent carcinoma in situ (CIS). The patient underwent simultaneous transperineal prostate biopsies at time of TUR which revealed Gleason 4 + 5 = 9 prostate cancer, with staging computed tomography (CT) and bone scan revealing skeletal and nodal prostate metastases.

The patient's past medical history included chronic deforming rheumatoid arthritis requiring immunosuppressant therapy, atrial fibrillation, rheumatoid vasculitis and hypertension. The patient was otherwise independent and had a Charlson Comorbidity Index of 4 prior to his cancer diagnoses.

Due to the patient's relative immunosuppression, initial management constituted an induction course of six doses of weekly mitomycin. Upon completion, repeat bladder biopsies demonstrated persistent CIS. After re-discussion at the Urology-Oncology Multi-Disciplinary meeting, the patient trialled intravesical gemcitabine, however suffered a hypersensitivity reaction to this at the first dose and it was ceased. Rheumatological opinion was sought to determine if his immunosuppressive medication could be ceased to facilitate intravesical BCG, at which his methotrexate was discontinued, instead being replaced with oral prednisolone.

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The patient commenced induction intravesical BCG with weekly doses for 6 consecutive weeks. End of induction bladder biopsies were performed which were benign. The patient commenced a monthly BCG maintenance course, but after the sixth dose developed a perineal swelling and further instillations were postponed. Ultrasound and CT demonstrated a large 10cm perineal cystic collection, with microbial culture yielding both *Enterococcus faecalis* and Mycobacterium bovis. Perineal aspirated fluid creatinine levels of 294 suggested a urinary source. An ascending CT urethrogram revealed a fistula at the membranous urethra (see Fig. 1), and a urethral indwelling catheter (IDC) was placed. 3 sets of blood cultures returned negative for Mycobacterium bovis, however given the patient's history of BCG treatment, systemic treatment was commenced for tuberculosis, which included rifampicin 600mg, isoniazid 300mg, ethambutol 25mg/kg and pyridoxine 25mg. The patient self-removed his IDC two weeks after insertion with ultrasound showing an ongoing collection one month later.

Repeat CT cystogram four months following initial diagnosis demonstrated that the collection had largely resolved, with two foci of hyper-attenuation on contrast consistent with ongoing fistulous disease. The patient is completing a six-month course of systemic tuberculosis therapy, remains on surveillance follow-up for bladder cancer and androgen deprivation therapy for prostate cancer.

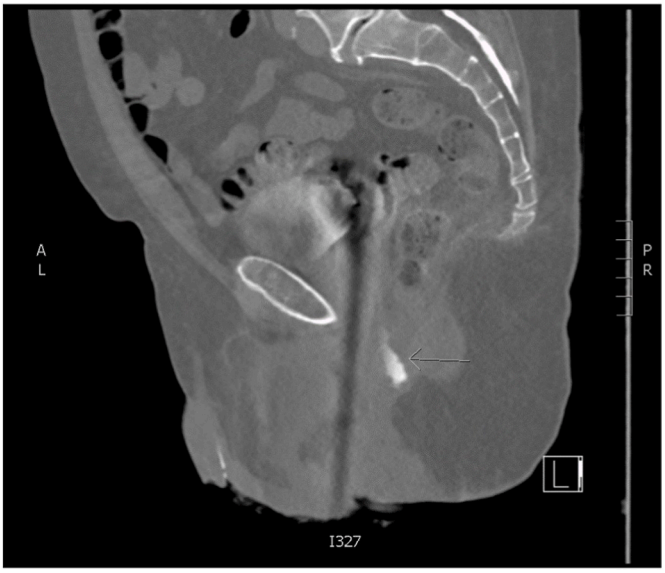


**Fig. 1.** Ascending CT urethrogram demonstrating urethral fistula at the membranous urethra.

## 3. Discussion

Systemic complications are rare in patients undergoing intravesical therapy, occurring in approximately 3–7% of patients.[2,3] There are a wide variety of systemic BCG complications and presentations, including reactive arthritis, spondylodiscitis, vascular mycotic aneurysms, pneumonitis, military tuberculosis, hepatitis, lymphangitis and general sepsis.[2,3]

The pathogenesis of BCG-related complications is not fully understood, with debate regarding whether it represents an inflammatory hypersensitivity reaction, or an infectious complication caused by haematogenous spread of BCG.[3] Current advice is to avoid conditions that may lead to haematogenous spread (such as traumatic urethral catherization, early instillation of BCG within two weeks of TUR, bacterial cystitis or visible haematuria).[2,3] The pre-disposing factors to developing systemic BCG complications are also not well understood, with limited prospective clinical data to demonstrate whether immunosuppression increases the risk of developing systemic BCG complications.[3,4]

A literature review was performed searching PubMed, Google Scholar and Medline for the following terms – 'intravesical BCG', 'bladder cancer', 'BCG', 'perineal abscess' and 'abscess'. Only one other case report by Macleod et al. involved a perineal collection which also demonstrated a fistula between the urethra and collection, requiring percutaneous drainage which was positive for acid-fast bacilli. It was not reported as to whether the patient required systemic tuberculosis therapy.

## 4. Conclusion

Serious complications of intravesical BCG therapy are rare but need to be considered in unusual presentations in any patient who has a history of being treated with BCG. Most of these patients are currently treated with systemic tuberculosis therapy, however the paucity of prospective randomized clinical trials on intravesical BCG therapy for NIMBC with long-term follow-up limits our understanding and management of these complications, and likely underestimates the incidence of BCG complications.

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## Declaration of competing interest

None.

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