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Case Report

BCG Prosthetic-Joint Infection Months after Intravesical BCG Therapy: A Case Report

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Abstract

Background: Systemic Bacillus Calmette-Guérin (BCG) infection is a rare but well described complication of intravesical BCG administration for the treatment of intermediate- and high-risk non-muscle-invasive bladder cancer. Prosthetic joint involvement is exceedingly uncommon, with only 18 published cases identified in the most recent review.

Case Presentation: An 89-year-old man presented with a two-month history of right hip pain and swelling, months after intravesical BCG for bladder cancer. Imaging and arthrocentesis raised suspicion of prosthetic joint infection (PJI), but conventional cultures were negative. He underwent debridement followed by the first stage of a two-stage revision, with an antibiotic-loaded spacer. Mycobacterial cultures later grew a BCG strain, identified as *Mycobacterium bovis* (*M. bovis*), with pyrazinamide resistance typical of the organism. He received isoniazid, rifampicin and ethambutol for the first 4 months, followed by isoniazid and rifampicin for an additional 12 months, with good clinical and functional recovery. At 18 months he remained infection-free, well adapted to the spacer, and reimplantation was deferred by shared decision.

Conclusion: *M. bovis* PJI should be considered in culture-negative PJI regardless of how remote the BCG exposure. Early mycobacterial culture avoids diagnostic delay and unnecessary antibacterial therapy.

Keywords: Bladder Cancer; Bacillus Calmette-Guérin Immunotherapy; Hip Arthroplasty; *Mycobacterium bovis*; Prosthesis-Related Infections; Two-Stage Revision

Abbreviations

BCG: Bacillus Calmette-Guérin; DAIR: Debridement, Antibiotics and Implant Retention; ITR: Laboratory for Integrative and Translational Research in Population Health; NMIBC: Non-Muscle-Invasive Bladder Cancer; PJI: Prosthetic Joint Infection.

Introduction

Intravesical BCG has been used for more than four decades for the treatment of intermediate- and high-risk non-muscle-invasive bladder cancer, one of the most frequent cancers worldwide and especially in men [1-3]. Although generally well tolerated, it can rarely lead to serious systemic complications [4]. These complications occur in an estimated 2–5% of treated patients and range from a self-limited hypersensitivity-type reaction ("BCGitis") to true disseminated infection ("BCGosis"), which can affect virtually any organ system, including the lungs, liver, kidneys, great vessels and skeleton, and can occasionally be fatal [4-6]. Adverse events may develop at any point from days to several years after instillation, which often obscures the causal relationship with prior BCG exposure. To date, no association has been consistently established between BCG-related complications and specific risk factors such as the number of instillations or cumulative BCG dose [5,6].

Among the systemic manifestations of BCG dissemination, osteoarticular involvement is distinctly uncommon, and prosthetic joint infection (PJI) is rarer still, with fewer than twenty cases reported in the literature [7]. Because conventional bacterial cultures are typically negative, the diagnosis is frequently missed or delayed, and patients may undergo repeated investigations and ineffective antibacterial courses before mycobacterial infection is considered [8,9].

We report a case of *Mycobacterium bovis* (*M. bovis*) PJI involving a total hip arthroplasty which occurred months after intravesical BCG therapy for bladder cancer, illustrating the diagnostic challenges posed by this rare complication and reviewing the current evidence on its recognition and management.

Case Presentation

An 89-year-old man, previously autonomous and living alone, was admitted to another hospital with a two-month history of right hip pain and local swelling. He had no fever and reported no recent infectious episodes, wounds or courses of antibiotic therapy during the preceding six months.

His medical history included dyslipidaemia, arterial hypertension and ischaemic heart disease with a prior myocardial infarction requiring coronary stent implantation, as well as benign prostatic hyperplasia and previous cutaneous malignancies. He had undergone cemented right total hip arthroplasty over a decade earlier. Of relevance, he also had a history of high-grade papillary urothelial carcinoma treated with macroscopically complete resection, followed by a course of intravesical BCG therapy administered over approximately three years, the last instillation six months before this admission.

On admission, the patient presented with local inflammatory signs and swelling of the right hip. Laboratory investigation showed a mildly elevated C-reactive protein of 39 mg/L and a leukocyte count of 10.32×10^9/L, with 24% monocytes and normal neutrophil and eosinophil counts. Computed tomography of the pelvis demonstrated two periarticular collections. Hip arthrocentesis was performed and yielded purulent intra-articular material, raising immediate suspicion of PJI.

In his local hospital, prosthesis removal was not initially considered and the patient was submitted to debridement, antibiotics and implant retention (DAIR). The patient was started empirically on piperacillin/tazobactam and vancomycin post-operatively. Conventional microbiological cultures of the intra-articular fluid from the arthrocentesis and from the surgery were negative; cytobiochemical analysis of synovial fluid, histology and molecular biology testing were not performed.

After surgery, the patient was transferred to our institution, and the case was subsequently discussed in a multidisciplinary infection prevention and antimicrobial resistance meeting. The wound was closed and without drainage but local swelling persisted and fluctuation could be found on palpation. Loosening of the acetabular component could be seen in hip radiography and a CT scan showed two periprosthetic collections with peripheral enhancement: one peritrochanteric (6.8 x 3.4 x 9.6 cm) and one reaching towards the lower border of the psoas muscle (4.9 x 2.3 x 14.6 cm). The team decided on a two-stage exchange of the arthroplasty and antimicrobial therapy was discontinued to increase the diagnostic yield of intra-operative cultures. Two

weeks later, the patient underwent surgery for extraction of all components followed by extensive irrigation and debridement and implantation of a hip antibiotic-loaded spacer (Figure 1). Multiple intraoperative samples were collected for microbiological investigation and piperacillin/tazobactam and vancomycin restarted afterwards.



Figure 1: Pelvic radiograph showing the right hip antibiotic-loaded spacer implanted.

During the course of treatment, the patient developed persistent cutaneous manifestations, including rash and pruritus, with associated eosinophilia (Figure 2).

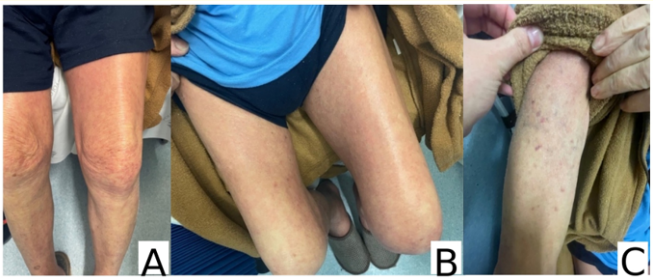


Figure 2: Diffuse maculopapular exanthem attributed to drug hypersensitivity, involving (A, B) the lower limbs, with erythematous, confluent lesions extending from the thigh to the leg, and (C) the forearm, with scattered papular lesions on an erythematous base.

Skin biopsy demonstrated spongiotic dermatitis and superficial angiocentric inflammation with scattered eosinophils. These findings were considered compatible with a hypersensitivity reaction in the appropriate clinical and therapeutic context, and the clinical presentation was considered most consistent with a maculopapular drug-related exanthem.

Conventional intraoperative cultures remained negative. Four weeks after surgery, mycobacterial cultures grew a BCG strain, subsequently identified as *Mycobacterium bovis*. The available microbiological report documented susceptibility to the conventional antimycobacterial agents used for this strain (Figure 3).

GENERAL

MYCOBACTERIOLOGY

MYCOBACTERIOLOGICAL EXAMINATION (generic)

Specimen/Collection site:	Intraoperative

DIRECT EXAMINATION

AFB smear	AFB not observed

CULTURE

A BCG strain was isolated

Identification / AST

Bacillus Calmette-Guérin

Isoniazid (0.1 µg/mL)	**S**
Pyrazinamide (100 µg/mL)	**R**
Streptomycin (1 µg/mL)	**S**
Ethambutol (5.0 µg/mL)	**S**
Rifampicin (1.0 µg/mL)	**S**

AST: antimicrobial susceptibility testing; AFB: acid-fast bacilli;
S: susceptible; R: resistant.

Figure 3: Microbiology report documenting isolation of a BCG strain (*Mycobacterium bovis*) from an intraoperative culture specimen, with the corresponding antimicrobial susceptibility pattern.

Antibacterial therapy was discontinued, and targeted antimycobacterial treatment was initiated with isoniazid, rifampicin and ethambutol for the first 4 months, followed by isoniazid and rifampicin for an additional 12 months, with good clinical and functional recovery. No signs of wound infection were noted one month postoperatively (Figure 4).



Figure 4: Surgical scar over the right hip, one month after implantation of a hip antibiotic-loaded spacer (first-stage revision procedure), showing no signs of inflammation (no erythema, dehiscence, or discharge).

At follow-up six months after completing treatment (18 months after treatment initiation), he remained clinically stable, with no evidence of recurrent infection. He has remained well adapted to the functional spacer, with satisfactory mobility, and reimplantation of a new prosthesis, although considered, has for now been deferred.

Discussion

PJI is among the rarest manifestations of BCG infection. Gomez., *et al*. (2009) identified only four previously reported cases, with arthroplasty typically preceding BCG therapy by six to twelve years [9]. Williams., *et al*. (2019) expanded this to nine cases, with a latency of 0–48 months from instillation to presentation [10]. The most recent synthesis, by Bosse., *et al*. (2025), reviewed 67 published cases of osteoarticular BCG infection overall, of which only 18 involved a prosthetic joint, occurring almost exclusively in men, with a mean age in the mid-seventies and a median latency of approximately two years [7]. Our patient, an 89-year-old man, is consistent with this demographic pattern, which likely reflects the higher incidence of bladder cancer, and consequently of BCG exposure, among older men [1,2]. His presentation, years after starting BCG and six months after his last instillation, also falls within the recognised, if wide, latency window.

The mechanism underlying such delayed dissemination remains incompletely understood. It has been proposed that mycobacteria may persist locally within the bladder wall for well over a year after the last instillation, with subsequent reactivation and hematogenous dissemination occurring once mucosal or immunological defenses are further compromised — for instance, by age-related immunosenescence or an unrelated intercurrent illness [4,9]. This would explain why prosthetic joint infection can manifest years after BCG exposure, at a site distant from the original genitourinary tract of inoculation, and underscores why a distant history of BCG instillation should never be dismissed as clinically irrelevant regardless of how long ago it occurred.

This case illustrates the central diagnostic challenge reported across the literature: conventional bacterial cultures are typically negative, which can mislead clinicians toward presumed aseptic loosening or culture-negative bacterial PJI [8,10,11]. As in previously published cases, mycobacterial cultures were only pursued once the clinical course — persistent purulence unresponsive to broad-spectrum antibiotics — remained unexplained. The susceptibility pattern provided an important diagnostic clue, with intrinsic pyrazinamide resistance supporting identification as *M. bovis* rather than *M. tuberculosis* [9,10].

A concurrent cutaneous hypersensitivity reaction further delayed recognition, temporarily redirecting attention toward a presumed drug allergy — a diagnostic detour also described elsewhere [8,11,12].

Management combining surgical intervention with prolonged antimycobacterial therapy — typically isoniazid and rifampicin for around twelve months, with ethambutol added initially — is associated with favourable outcomes in the largest published series [7]. As in our patient, diagnostic delay often means repeated procedures and ineffective antibacterial courses before the correct diagnosis is reached [7,9,10].

A two-stage revision strategy, commonly used for chronic PJI, was followed in our patient. Although the patient completed antimycobacterial therapy with good clinical and functional recovery and would be an eligible candidate for second-stage reimplantation, he has, after 18 months of follow-up, not undergone this second procedure. Given his advanced age and the additional surgical risk involved and given that he has remained well adapted to the functional spacer with satisfactory mobility, both the patient and his family have opted to defer definitive reimplantation for the

time being. This illustrates that, in selected elderly patients with good spacer tolerance, definitive reimplantation may reasonably be postponed through shared decision-making, without compromising functional outcome, provided close clinical follow-up is maintained.

Conclusion

Mycobacterium bovis PJI is a rare but potentially serious complication of intravesical BCG therapy and should be considered in patients with a history of BCG treatment for bladder cancer who present with culture-negative PJI, even when BCG exposure occurred years earlier. Early mycobacterial investigation is essential when routine cultures remain negative despite a suggestive clinical presentation.

Although diagnosis may be challenging due to nonspecific clinical manifestations and the slow growth of mycobacteria, appropriate surgical management combined with prolonged antimycobacterial therapy achieved infection control and a good functional outcome in this patient.

Informed Consent

Informed consent was obtained from the patient for publication of this case report and accompanying images.

Conflicts of Interest

The authors declare no conflicts of interest.

Declaration of Generative AI Use

During the preparation of this manuscript, the authors used Claude (Anthropic) to assist with language editing and removal of identifying elements from clinical images. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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