



Prosthetic joint infection due to *Mycobacterium bovis* 5-years after BCG-instillations

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The Bacillus Calmette-Guerin (BCG) has been used as intravesical immunotherapy for superficial urothelial bladder carcinoma in preventing its recurrence. Prosthetic joint infections due to those instillations are very rare and few practitioners know this side effect.

We report the case of a 77-year old male with a medical history of right hip replacement and superficial urothelial bladder carcinoma treated with BCG-instillations. He presented with a painful hip joint and extreme difficulty at walking. Because of high suspicion of prosthetic joint infection, a 2-stage arthroplasty was performed. Microbiological culture revealed *Mycobacterium bovis* so he was kept on antituberculous therapy for twelve months.

Remarkable is the delay between the instillations and the acquisition of the prosthetic joint infection. A medical history of BCG instillations should warrant the practitioner for a possible joint infection. There are no current guidelines concerning the therapy.

Keywords : hip prosthesis ; infectious arthritis ; intravesical instillation ; *Mycobacterium bovis* ; prosthetic joint infection ; BCG.

INTRODUCTION

The Bacillus Calmette-Guerin (BCG) is used as intravesical immunotherapy for superficial urothelial bladder carcinoma in preventing its recurrence

(6). Those BCG instillations can cause local and systemic side effects. Osteo-articular complications can present as infectious and noninfectious, the latter being the most common (4,5). Prosthetic joint infection due to *Mycobacterium bovis* after intravesical BCG instillations are very rare, there are only 8 previous cases known (1). Few practitioners know this side effect and there are no guidelines regarding how to treat this complication.

CASE REPORT

We report the case of a 77-year old male with a history of a left hip replacement in 1998 and a revision because of assumed aseptic loosening in February 2016. The initial rehabilitation was uneventful, but six months later the hip became painful and he needed a cane to walk. In January 2017 he presented at our outpatient clinic for the first time with a painful hip joint and extreme difficulty at walking. He presented with a Trendelenburg gait

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No benefits or funds were received in support of this study. The authors report no conflict of interests.

Acta Orthopædica Belgica, Vol. 86 - 2 - 2020



Figure 1. — Pre-operative total hip prosthesis.



Figure 2. — Removal of the prosthetic components (1st stage revision).

and hip rotation was very painful. The incision was well healed and showed no signs of infection. His medical history was notable for superficial urothelial bladder carcinoma in 2011 which had been treated with multiple transurethral resections, BCG instillations and radio-chemotherapy.

The radiological workup revealed destruction of the acetabulum with intrapelvic migration of a trabecular metal cup and possible pelvic dissociation. A blood sample showed elevated C-reactive protein (CRP) (70.3 mg/l), elevated erythrocyte sedimentation rate (46 mm/hour) and a normal white blood cell count. CT-scan of the pelvis confirmed anterosuperior intrapelvic protrusion of the cup but the posterior column of the acetabulum was intact (Paprosky 3B).

After careful discussion, the decision was taken to perform a two-stage procedure to remove loose components and sample cultures and biopsies.

During surgery, there was drainage of a purulent fluid from a collection posteriorly to the hip joint. Both synovasure test (alpha-defensin +) and frozen section biopsies (high power field neutrophil count (HPF) >50, no signs of malignancy) were positive for infection. As planned, a two-stage procedure was performed with removal of the components and a thorough debridement of infected tissue. A moulded antibiotic loaded acetabular spacer was placed and IV antibiotics were initiated. (vancomycin 2g bolus and continuous infusion with plasma levels between 20 to 30mg/l and ceftazidime 6g/24h continuous infusion).

Postoperatively there was a good healing of the wound and the CRP decreased to a value of 16.3 mg/l at discharge. Cultures were negative and even PCR (16s RNA) could not reveal microbiological tissue. The patient left the hospital on day 18 postoperatively. The treatment at discharge was analgesia, antibiotic switch to ciproxin 500mg twice a day and clexane 40mg daily. The general practitioner was asked to check the CRP level twice a week with an early referral to the orthopaedic department if the CRP would incur (>30 mg/l).

After 3 weeks, microbiological culture revealed *Mycobacterium bovis*. The original PCR sample was checked again and found to be positive on *M. bovis* (a weak signal, initially considered too weak to be positive). The antibiotic therapy was replaced with rifampicin 300mg twice a day, isoniazid 300mg daily and ethambutol 400mg three times daily. Since his malignancy, he had a non-evolutive lung nodule, which in light of the current clinical setting could be the primary metastatic lesion of the *M. bovis* instillation. Bronchial aspirates showed negative cultures and were not suspicious for malignancy. Lung biopsies were not taken because the patient refused it.

After 2.5 months of antituberculous therapy the second stage of the arthroplasty was performed. The tissues were sound but peroperative fresh frozen section biopsies revealed 5-20 neutrophils per high power field. An uncemented femoral component was placed. For the acetabulum, antibiotic loaded



Figure 3. — Kerboull cross reconstruction (2nd stage revision).

structural allografts were used and the construction was protected with a Kerboull cross and an Avantage cemented double mobility liner. (7,8) He was kept non-weight bearing for 6 weeks, allowed partial weight bearing for another 6 weeks and from then onwards, full weight bearing was allowed. The postoperative CRP levels quickly dropped to remain stable around 15mg/l. He was kept on triple therapy for at least 12 months. At 8 months, the hip remained painfree and he ambulated with a cane outside and without support inside his house. Follow-up cystoscopy with urine cultures could not reveal persistent *M. bovis*.

The patient presented him at the outpatient clinic 1 year after the first stage operation and the start of tuberculostatic drugs. His general condition was good, he experienced little discomfort and walked with canes. Radiological and biochemical findings were normal (CRP 4.2mg/l). The lung nodulus retained its dimensions on CT-scan after months of tuberculostatic drugs.

DISCUSSION

Prosthetic joint infection and septic arthritis due to *M. bovis* is an extremely rare complication after BCG instillations for urothelial bladder carcinoma. Most likely the *M. bovis* was introduced during the instillation for the superficial bladder carcinoma. Remarkable is the delay between the instillations and the acquisition of a joint infection. It can be

assumed that also the first ‘asymptomatic loosening’ has been due to this low grade *M. Bovis* infection. Seeding to the lungs and the formation of a non-evolutive tuberculoma could explain this delay. Bowyer et al. found persistent mycobacteria in the urine up to 16.5 months after the instillations (3). Böhle et al. described an early dissemination of BCG from the bladder, seeding the lungs with reactivation years later (2).

A recent literature review made by Aitchison et al. concluded there are 8 previous cases known with prosthetic joint infection due to BCG instillations. Three of them were treated with a two-stage revision, 1 died before performing the 2nd-stage, 2 with a one-stage revision and 2 with debridement, antibiotics and implant retention (DAIR-strategy) (2).

Based on the current literature there is no consensus regarding the duration of the anti-tuberculous therapy and whether you should perform surgery or not (DAIR-strategy or one-stage/two stage arthroplasty). The previous cases used at least a bi-therapy tuberculostatica for at least 9 months (mostly 1 year) (1).

A history of urothelial carcinoma and BCG instillation should warrant the orthopaedic surgeon in the event of a (periprosthetic) joint infection and specific cultures should be taken. Antibiotic regimen should be long and prolonged and regular follow up is required if a successful outcome is desired.

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