

### ABSTRACT

Intravesical bacillus Calmette-Guerin (BCG) instillation is a commonly used treatment for urothelial bladder carcinoma. Soft tissue manifestation of Mycobacterium tuberculosis (M. tuberculosis) following administration of BCG is exceedingly rare. Few cases of periprosthetic M. tuberculosis infections have been reported, however they have been isolated to the hip and knee. This case study presents a well-healed total ankle arthroplasty subsequently infected with M. tuberculosis resulting in a non-salvageable limb.

### LITERATURE REVIEW

Intravesical application of BCG immunotherapy is a proven and commonly recognized treatment in reducing both progression and recurrence of urothelial bladder cancer<sup>1</sup>. BCG is administered directly into the bladder via a catheter which stimulates an immune response. This immune response is not fully understood. It is believed that the BCG vaccine has a predilection for entering bladder cancer cells. The BCG vaccine proteins are broken down and are combined with histocompatibility antigens and are displayed on the cell surface. This induces a cytokine-mediated and direct cell-to-cell cytotoxicity response which targets the cells for destruction<sup>1</sup>.

Adverse effects resulting from BCG administration for bladder cancer are rare and primarily consist of irritative bladder symptoms and mild flu-like symptoms which last from 1-3 days<sup>2</sup>. True infection is an exceedingly rare complication, and periprosthetic infections are even rarer. It has only been described in total hip<sup>3,5,6,7</sup> and knee<sup>3,4</sup> arthroplasty. There are no reported incidents in a total ankle arthroplasty.

In a large study of 1045 patients with a prosthetic device such as a pace maker, artificial heart valve, or joint replacement, who received BCG to treat bladder carcinoma, there were no instances of infective endocarditis or periprosthetic infection<sup>2</sup>.

Aitchison and colleagues summarized the literature and found two total knees and six total hips that developed Mycobacterium infection following BCG administration. They reported that six of the eight prostheses were explanted and there were no mortalities as a result of the infection<sup>8</sup>.

### CASE STUDY

A 79 year old male with past medical history of bladder carcinoma, CAD, CABGx4, HTN, HLD, AAA, L CIA aneurysm, and previous DVT presented to the hospital with right lower extremity redness and swelling and a small pinpoint wound on the posterolateral ankle. He has noticed clear drainage coming from the wound for about 1 week. He underwent total ankle arthroplasty approximately 10 years ago. Of note, he received the BCG vaccine to treat his bladder cancer 1 year prior. He states that although he always had a mild degree of chronic swelling around his ankle, it became much more noticeable after the BCG treatment.

On physical examination, he was noted to have a full thickness wound to the right lateral ankle without exposed hardware or bone. His pulses were biphasic on all 3 pedal vessels with 2+ pitting edema distal to the knee. His epicritic sensation was grossly intact. He had pain with range of motion of the ankle only. He was an independent ambulator. His vital signs were stable and he was not experiencing any constitutional symptoms.

Due to suspicion of a chronic infection of the ankle implant, he was admitted to the hospital and was taken to the operating room for an incision and drainage. The right ankle joint was tapped which revealed clear synovial fluid. The wound overlying the fibula was debrided which revealed exposed hardware (Figure 1). The fibular plate and 2 screw screws were removed (Figure 2). There was caseous material anterior to the fibula which was sent for culture and path. On the same admission, the patient went for an additional surgical debridement. Posteriorly, more caseous material was found and after aggressive debridement (Figure 3), the wound was closed primarily. The pathology report read "fragments of necrotic tissue mixed with inflammatory granulation tissue." The deep cultures showed MSSA and enterococcus.



Figures 1 & 2. Right ankle X-ray before and after fibula plate and screw removal.  
Figure 3. Intra-operative photograph of caseous material in the posterolateral ankle.



Figure 5. Intraoperative photograph after explantation  
Figure 6. Right ankle X-ray with cement spacer

The patient was discharged and followed closely as an outpatient. He was placed on intravenous vancomycin and piperacillin-tazobactam. Three weeks after the second debridement was performed, the cultures became positive for AFB. One month later the culture became morphologically consistent with M. tuberculosis complex. A DNA probe was performed and it was positive for M. tuberculosis complex, as well. The patient was started on rifampin and isoniazid.

Despite continued antimicrobial therapy and local wound care, the wound failed to heal. It was determined that he needed to be re-admitted for surgical intervention. In the operating room it was discovered that the lateral wound probed to the ankle implant and more caseous material was found. The prosthesis was explanted (Figure 5) and it was found to be loose and surrounded by non-viable tibial and talar bone. The wound was debrided and a gentamicin-impregnated antibiotic spacer was inserted (Figure 6).

Limb salvage options were discussed with the patient and it was decided that a below-knee amputation would benefit the patient the most. The procedure was successful (Figures 7 & 8), there were no further caseous granulomas proximally and the deep tissue cultures were negative for any growth. The patient healed without incident and now ambulates independently with a custom below-knee prosthesis.



Figure 7. Intraoperative photograph of the below-knee amputation  
Figure 8. Below-knee amputation healing well

### DISCUSSION & CONCLUSION

This patient's case is the first confirmed case of a total ankle infected by Mycobacterium as a direct consequence of BCG administration. This case is also unusual for several other reasons. Infection is a large concern when discussing total ankle implants, but the risk of infection is typically in the immediate perioperative period, not 10 years after a successful implantation. Cutaneous manifestation of M. tuberculosis is rare and typically found in immunocompromised patients. Although the patient has a complicated medical history, he was immunocompetent.

This case highlights the importance of testing for AFB and fungus in addition to the standard aerobic and anaerobic cultures in an atypical infection case. It is almost important to note how long it took for the AFB to come back positive, nearly 3 weeks after the sample was collected. If a patient does have a TB infection, they must start a course of oral rifampin and isoniazid. It is also critical to confirm the result via DNA probe, but treatment should be initiated before these results are finalized.

Intraoperatively, when the caseous material was encountered and cutaneous TB was suspected, there was immediate concern about contracting TB. After discussing with our infectious disease specialist, because cutaneous TB is not airborne, there is no risk of contracting TB via respiration. However, it is important to avoid instrumentation that could potentially aerosolize it, such as electrocautery, hydroscalpel or a rotary burr.

Based on our experience, a surgeon planning on performing total ankle arthroplasty may consider screening patients for history of receiving the BCG vaccine. It is unclear whether or not TAR should be avoided in this subset of patients or if prophylactic antibiotics are appropriate.

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