Mycobacterium bovis Infection of Total Knee Arthroplasty After Bacillus Calmette-Guérin Therapy for Bladder Cancer

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Intravesicular instillation of bacillus Calmette-Guérin (BCG), an attenuated form of Mycobacterium bovis, is the most effective treatment for superficial bladder cancer.\(^1\),\(^2\) Minor local reactions to this treatment, such as cystitis and hematuria, are common, but more severe systemic complications\(^3\),\(^4\) have also been documented, including sepsis, pneumonitis, granulomatous hepatitis, vertebral osteomyelitis,\(^5\),\(^6\) and rarely, total joint infection.\(^7\)-\(^11\)

We present a case of *M. bovis* infection of a total knee arthroplasty (TKA) after BCG immunotherapy for bladder cancer that was successfully treated with antitubercular chemotherapy and retention of implants. We include a review of the literature addressing this rare mode of infection. The patient provided written informed consent for print and electronic publication of this case report.

Case Report

A 66-year-old man presented with a chief complaint of progressive left knee stiffness over several months. Five years earlier, he underwent uncemented left TKA. His knee was functioning well with active range of motion from 0° to 126°, and he had returned to strenuous cycling. One year after his TKA and 4 years prior to the onset of stiffness, he had been diagnosed with superficial transitional cell carcinoma of the bladder. His treatment included intravesicular BCG therapy weekly for 6 weeks followed by semi-annual maintenance therapy.

Initial examination upon presentation with left knee stiffness showed a significant effusion and diminished range of motion but little discomfort. The patient denied fever, chills, night sweats, and weight loss. Radiographs were normal with good component positioning and normal-appearing bone-implant interfaces (Figures A, B). Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and white blood cell count (WBC) were within normal limits, and aspirate of the knee revealed no organisms. Based on these findings, the presumptive diagnosis was an adverse reaction to polyethylene wear. Because of persistent stiffness, the patient underwent an
examination under anesthesia, arthroscopy, and major synovectomy with biopsy. Intraoperative findings included normal polyethylene but a marked hypertrophic synovitis and abnormal, semi-turbid fluid. The fluid WBC count was 5.35×10^9/L but no organisms were isolated initially. Histologic samples showed chronic inflammation with patches of acute inflammation. Approximately 6 weeks after surgery, cultures became positive for acid-fast bacillus, which was identified as *M. bovis*.

Maintenance BCG therapy was discontinued, and antitubercular chemotherapy was initiated, consisting of 12 months of rifampin 600 mg daily and isoniazid 300 mg daily. Because symptoms significantly improved after arthroscopic incision and drainage and synovectomy, the TKA implants were maintained and symptoms closely monitored. Subsequent cultures and biopsies remained negative, and the patient continued to do well clinically with no residual stiffness.

At 7½-year follow-up, there is no clinical evidence of infection, and the patient continues to enjoy a high level of function with no pain and no recurrent stiffness. He has returned to cycling, logging more than 40,000 miles. However, a recurrence of bladder cancer is being treated with mitomycin C and gemcitabine, alternative to BCG.

**Discussion**

Mycobacterial infection in total joint arthroplasty (TJA) is uncommon;12 *M. bovis* infection of joint arthroplasty after intravesicular BCG therapy is exceedingly rare. Joint infection is thought to be the result of dissemination of BCG throughout the bloodstream.13

A review of the literature of BCG infection of TJA after intravesicular therapy for bladder cancer revealed only 5 case reports (Table). The average age on presentation was 77 years, and all patients were men, with 4 total hip arthroplasties (THAs) and 1 TKA. The average time from index procedure to initial presentation was 7.8 years, and the average time from cancer diagnosis to initial presentation was 20 months. Patients received an average of 8.6 consecutive weeks of BCG treatments, and maintenance therapy was not noted in any of the published reports. The average duration of antitubercular therapy was 13 months, and it comprised either 2- or 3-agent therapy. All reported cases were treated with removal of primary implants in either a 1- or 2-stage fashion. To our knowledge, this is only the second case of BCG infection of TKA reported in the literature and the first report of successful treatment with retention of primary implants.

There are several possible explanations for the success of a more conservative treatment approach in our patient.
First, this TKA was uncemented. Second, BCG is an attenuated form of *M bovis*, which is itself a relatively less virulent species than *M tuberculosis*. Finally, mycobacterial species do not produce the biofilm that is seen in other bacterial arthroplasty infections, which typically necessitate removal of implants in cases of chronic infection.\(^\text{14}\)

This case was unique because the patient lacked signs of infectious symptoms, there were normal inflammatory markers, and arthroscopy was necessary to aid in the diagnosis. The definitive diagnosis in this case was significantly delayed to attain a positive *M bovis* culture. Definitive treatment was provided by arthroscopy, implant salvage, and antitubercular chemotherapy only. The standard of care for an infected modular TKA normally involves revision of the polyethylene tibial insert with irrigation and débridement, or removal of components and insertion of new implants in a 1- or 2-stage procedure. Despite the unusual algorithm to reach a definitive diagnosis of an infected joint arthroplasty in this case, we do not recommend arthroscopic biopsy, washout, and antimicrobial therapy as definitive treatment for infected joint arthroplasty, and we continue to support the removal of infected components in a staged manner.

**Conclusion**

Joint replacement patients with bladder cancer represent a relatively small cohort. Based on current demographics and the increasing demand for joint arthroplasty, it is likely that this unique subset of patients will grow. No current standard of care exists for the treatment of these patients. One preventative measure is to consider alternative types of chemotherapy for bladder cancer treatment, such as mitomycin. Another potential solution would be administration of prophylactic doses of antitubercular agents concomitantly with intravesicular BCG, which would allow for the local effects of BCG immunotherapy while controlling the potential for systemic dissemination. The optimal dose range to achieve this dual effect is not known and is an area for research.

It is important for both arthroplasty surgeons and urologists to be aware of this potential complication in order to appropriately counsel this unique subset of patients. Our case report is the first to demonstrate that a successful outcome can be obtained with retention of primary components. Through research and continued data acquisition, a more concrete standard of care can be established. Until then, we recommend a collaborative approach between informed parties to devise a patient-specific plan of care.

**Key Info**

**Figures/Tables**

**References**
References


**Multimedia**

**Product Guide**

**Product Guide**

- STRATAFIX™ Symmetric PDS™ Plus Knotless Tissue Control Device
- STRATAFIX™ Spiral Knotless Tissue Control Device
- BioComposite SwiveLock Anchor
- BioComposite SwiveLock C, with White/Black TigerTape™ Loop

**Citation**