Mycobacterium bovis Infection of Total Hip Arthroplasty After Intravesicular Bacille Calmette-Guérin Therapy

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Abstract

Bacille Calmette-Guérin (BCG) is a live, attenuated strain of *Mycobacterium bovis*. Intravesicular BCG therapy is the most effective treatment for superficial bladder cancer. The most common complication of this treatment is cystitis; there is a wide range of other complications. The English-language literature includes reports of 3 total hip arthroplasty infections and 1 total knee arthroplasty infection with *M bovis* after BCG therapy. These secondary infections may present either acutely during the therapy, months, or even years later. In this article, we report the case of a patient who presented with a painful right hip 6 years after successful total hip arthroplasty and 3 years after treatment for bladder cancer. Left total hip arthroplasty was performed 2 years after right hip arthroplasty. Surgeons examining a painful joint arthroplasty should be particularly suspicious of infection if the patient has a history of BCG therapy.

Bacille Calmette-Guérin (BCG) is a live, attenuated strain of *Mycobacterium bovis*. Intravesicular BCG therapy is the most effective treatment for superficial bladder cancer.[1] The most common complication is cystitis; there is a wide range of other complications, including hematuria, granulomatous prostatitis, systemic dissemination, osteomyelitis, and hepatitis.[2,3] The English-language literature includes reports of 3 total hip arthroplasty (THA) infections and 1 total knee arthroplasty (TKA) infection with *M bovis* after BCG therapy.[4-7] In this article, we report the case of a patient who presented with a painful right hip 6 years after successful THA and 3 years after BCG therapy for bladder cancer. Left THA was performed 2 years after right THA. The patient provided written informed consent for print and electronic publication of this case report.

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Case Report

A 76-year-old woman presented with right hip pain 6 years after successful right THA and 4 years after left THA. She reported having mild right hip pain for several weeks before presentation with acute exacerbation of right hip pain after a twisting episode. She had a history of superficial bladder cancer diagnosed 3 years earlier and treated with transurethral resection of the tumor and intravesicular BCG therapy once per week for 17 weeks. Physical examination at time of presentation revealed a slightly antalgic gait and increased groin pain with hip rotation. Comparison of immediate postoperative radiographs (Figure 1) and current radiographs (Figure

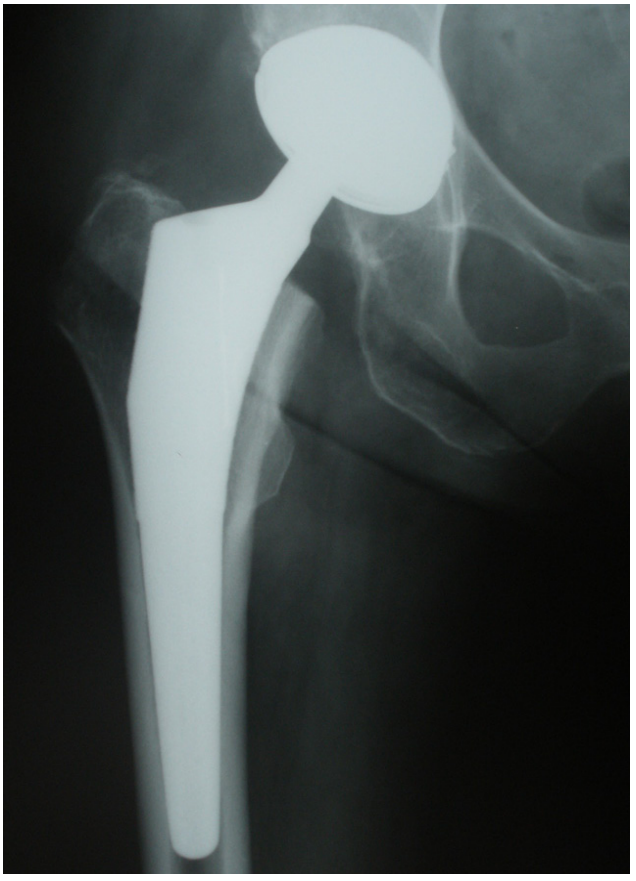

Figure 1. Radiograph after index surgery.

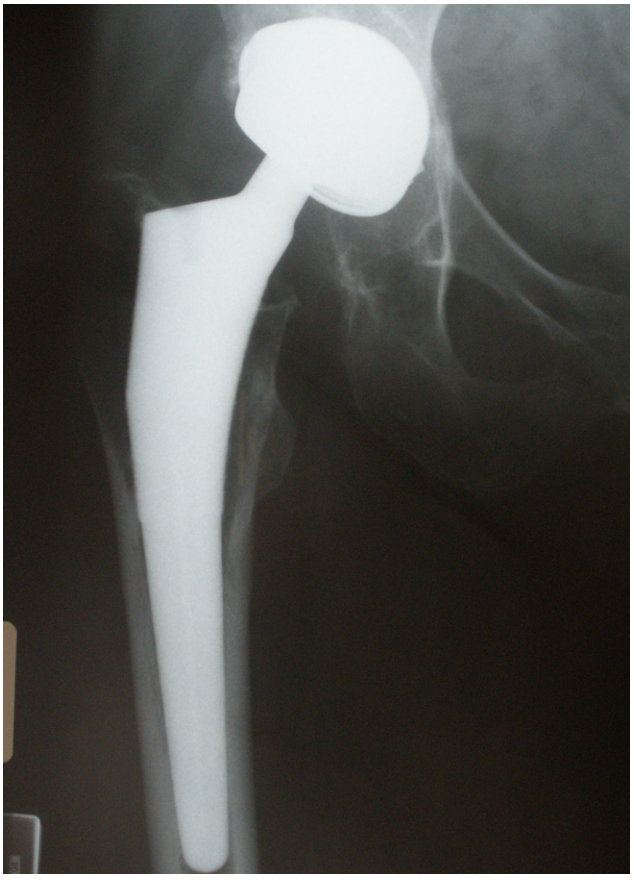

Figure 2. Radiograph 6 years after surgery but before revision.

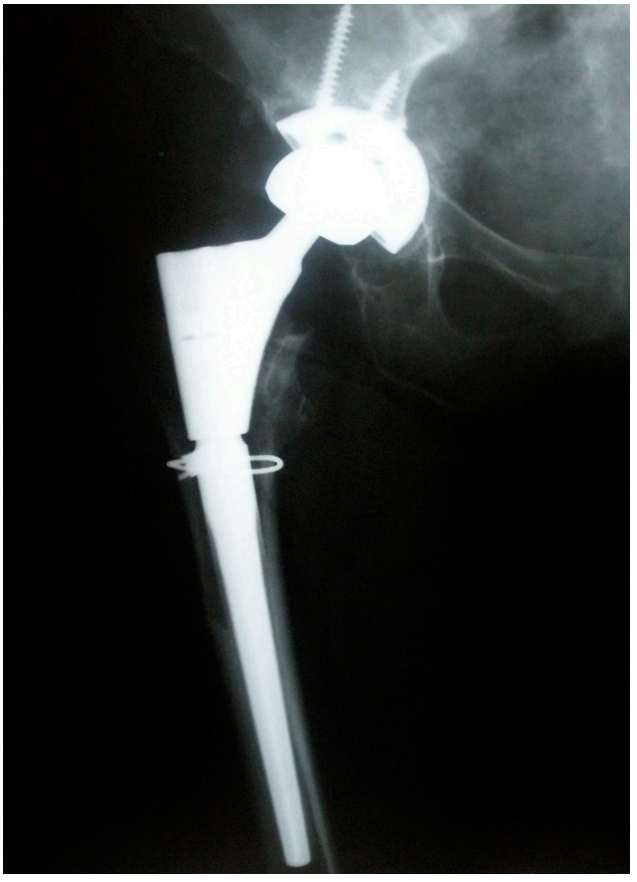

Figure 3. Radiograph 2 months after revision.

2) revealed acetabular component migration, which suggested loosening. Approximately 2 weeks later, the patient presented with signs of systemic illness. Laboratory test results showed evidence of infection: white blood cell (WBC) count of 7800 cells/mm^3 (normal, 4.5-10 cells/mm^3), C-reactive protein (CRP) level of 146 mg/L (normal, 0-12 mg/L), and erythrocyte sedimentation rate (ESR) of 115 mm/h (normal, <20 mm/h). Given the possibility of infection, aspiration of the hip was performed. A test for synovial fluid cell count was not performed because the fluid could not be obtained in sufficient quantity. Gram stain and culture results were negative for microorganisms.

For possible infection in the hip joint, 2-stage revision arthroplasty was performed. In the first stage, exploration of the joint revealed a loose acetabular component and purulent fluid in the acetabulum. The acetabular component was removed. Removal of the well-fixed femoral component required an extended trochanteric osteotomy. Gram staining results were still negative for a causative organism. Although no organism was found, the purulent fluid suggested infection was the likely cause of loosening. The joint was treated with an antibiotic-loaded acrylic cement spacer (Prostalac; DePuy, Warsaw, Indiana) implanted into the acetabular and femoral sides. The trochanteric osteotomy was repaired with circlage wire. Intravenous vancomycin was administered after surgery until an intraoperative culture specimen was reported as positive for growth of *M bovis*. Antituberculosis medications were then started and continued for 9 months, at which time ESR, CRP level, and WBC count were found to be normal.

In the second stage, the antibiotic-loaded acrylic cement spacer was removed, and revision surgery was performed using a trabecular metal acetabular component and a porous-coated uncemented femoral component (Figure 3). Five months later, the patient was ambulating without pain.

Discussion

BCG was isolated as the causative organism of bovine tuberculosis in 1921.[8] Use of BCG therapy in managing bladder cancer was described by Morales and colleagues[9] in 1976. Intravesicular instillation of BCG results in an early influx of granulocytes into the bladder wall, followed by an influx of mononuclear cells and a cytokine response (interleukins 2 and 12, interferon).[1] BCG therapy is the most effective immunotherapy.[10] Most adverse events are related to dose administration and result from a bladder inflammatory response leading to cystitis.[2] Nadasy and colleagues[3] reported 4 cases of systemic dissemination after BCG therapy for bladder cancer. Although many other complications have been reported,[2,11] intravesicular BCG is generally well tolerated. Such therapy produces no

complications in more than 95% of patients.[2]

The literature includes 3 case reports of *M bovis* infection of THA and 1 report of *M bovis* infection of TKA in patients with bladder cancer treated with intravesicular BCG. Guerra and colleagues[6] were the first to report *M bovis* infection of THA after BCG therapy (17 months after last dose), Reigstad and Seiwers[4] reported a THA infected 6 months after last dose of BCG, and Segal and Krauss[5] reported a THA infected 4 years after therapy. Chazerain and colleagues[7] reported a TKA infected after the eighth weekly dose of BCG.

All 4 THA infections (3 previous plus present case) were delayed; they occurred 6 months to 4 years after BCG therapy. Bowyer and colleagues[12] reported BCG can persist in the bladder wall and early-morning urine up to 16.5 months after completion of intravesicular BCG therapy. Therefore, the period of BCG exposure may extend long after therapy. It is possible that subsequent bladder trauma or bladder infection can trigger the spread of the dormant bacilli and cause infection. Laboratory test results may or may not indicate ongoing infection. A high index of suspicion for infection and a history of BCG therapy may be the most important factor in correct diagnosis.

Over the past 30 years, intravesicular BCG therapy has been the most effective treatment for superficial bladder cancer.[1] With THAs and TKAs being performed in increasing numbers, and with BCG therapy being the standard of care for bladder cancer, there is a potential for more THAs and TKAs to be infected with *M bovis*. Prophylactic chemotherapy after BCG therapy may be insufficient for prevention of systemic dissemination of *M bovis*; for example, vertebral osteomyelitis[13] and granulomatous hepatitis[14] developed despite use of such prophylaxis. Additional data are needed to conclude that a patient who has an endoprosthesis and undergoes intravesicular BCG therapy should be administered prophylaxis to prevent dissemination of BCG to the prosthesis. More surveillance is needed to elucidate the relationship between these events.

Conclusion

M bovis infection is possible in patients who undergo THA or TKA and intravesicular BCG therapy. Laboratory test results or hip aspirations are unlikely to reveal *M bovis* infection. Testing an intraoperative specimen for culture and sensitivity is the most reliable diagnostic method. There is no evidence that medication prophylaxis is effective, but all patients who undergo THA or TKA and BCG therapy should be informed that acute and delayed infections are possible, and they should be educated about these infections.

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The authors report no actual or potential conflict of interest in relation to this article.

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This paper will be judged for the Resident Writer's Award.