Bacillus Calmette-Guérin Spondylodiscitis after Intravesical BCG Therapy: A Case Report

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Bacillus Calmette-Guérin (BCG) is an attenuated derivative of virulent Mycobacterium bovis (M. bovis). Although intravesical BCG therapy is an effective treatment for non-muscle-invasive bladder cancer (NMIBC), most of spine surgeons do not recognize it. However, this treatment rarely induced complications related to osteomuscular lesion, such as spondylodiscitis.

Here, we report an 80-year-old man with BCG spondylodiscitis. He had back pain without neurological deficit for a few months. He had a history of diabetes, rheumatoid arthritis, prostate cancer, and bladder cancer. Computed tomography revealed vertebral collapse of T9 and T10 (Fig. 1-a). Magnetic Resonance Imaging revealed an osteolytic lesion there and fluid accumulation in the disk space (Fig. 1-b). Blood tests indicated no severe inflammation. The first pathological examination from T10 vertebral biopsy did not...
detect neoplastic cells or general bacteria. However, his back pain and vertebral collapse deteriorated gradually (Fig. 2). We performed a second vertebral biopsy adding acid-fast staining. Acid-fast staining was positive after 3 weeks of culture. Furthermore, genetic sequencing identified *M. bovis*, specifically the BCG Tokyo 172 strain used in Japan (Fig. 3). According to retrospective interview, he had received intravesical BCG therapy (BCG Tokyo 172) for bladder cancer for 13 months before the occurrence of back pain. He was started on isoniazid (INH), rifampicin (RFP), and ethambutol (EB) treatment. Furthermore, the instability between T9 and T10 was getting worse, and anterior-posterior fusion with rib bone grafting in two stages was performed (Fig. 4). The patient required medication for six months. A bony union of T9-T10 was discovered, and there has been no recurrence two years after operation (Fig. 5).

The immunotherapy with intravesical BCG therapy has become the standard treatment for patients with NMIBC7. Domestic incidence rate per 100,000 population of bladder cancer in 2018 is 18.4, and the number is increasing8. Approximately 70% of the cancer are NMIBC. Although the actual incidence of BCG spondylodiscitis was unclear, we found that 25 cases of BCG spondylitis or spondylodiscitis after intravesical BCG therapy have been reported in the English literature in 30 years. A systematic review reported that the average age of patients with BCG spondylodiscitis was 74 years, the average time to onset was 26 months after BCG therapy, and 68% of cases needed to undergo surgery9. BCG spondylitis or spondylodiscitis is thought to result from hematogenous dissemination of BCG infection even many years after initial BCG therapy, and immunocompromised state is associated with the infection10. Our case might be under immunocompromised state: diabetes and rheumatoid arthritis treated with immunocompromised medication, such as methotrexate. For considering diagnosis of *M. bovis*, we need multiplex PCR and DNA sequencing for the rapid and specific identification of BCG6. Specifically, it

![Figure 2. Sagittal plane CT scan before surgery. CT reveals the vacuums in T9/T10 intervertebral disc space. The arrow marks T9.](image)

![Figure 3. Analysis of DNA sequencing of the RD16 region. DNA sequencing reveals the absence in 22 base sequences. It accords with Mycobacterium bovis (M. bovis), BCG Tokyo 172.](image)
Figure 4. Postoperative plain radiographs.
Left: Lateral view. Right: Anteroposterior view.
Radiographs show posterior fusion of T7–L1 and anterior fusion of T9/T10.

Figure 5. Computed tomography (CT) one year after surgery.
Left: Sagittal view. Right: Coronal view.
CT shows bony union of T9–T10 and no recurrence of spondylitis. The arrow marks T9.

is not enough general culture for diagnosis. Following the regimen for TB, treatment with three anti-tuberculosis drugs, such as RFP, INH, and EB, is generally performed because *M. bovis* is intrinsically resistant to pyrazinamide\(^7\). However, RFP-, INH-, and EB-resistant BCG has been reported. Thus, it was recommended to perform a susceptibility test\(^8\). Delay
of diagnosis on spondylodiscitis might lead the patients with progressive neurological deficits and need surgical treat-
ment\(^\text{7}\). Spinal instability due to serious bone destruction, significant deformity, or conservative treatment failure indicates relative surgical intervention\(^\text{8}\).

In conclusion, although BCG spondylodiscitis is a relatively rare complication, we should carefully ask the history regarding BCG therapy in a patient with bladder cancer. Furthermore, spine surgeons should add acid-fast staining and multiplex PCR in the case of spondylodiscitis with intravesical BCG therapy history.

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