

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

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### Keywords:

Bacillus Calmette-Guérin spondylodiscitis, intravesical BCG therapy, non-muscle-invasive bladder cancer, immunocompromised state, case report

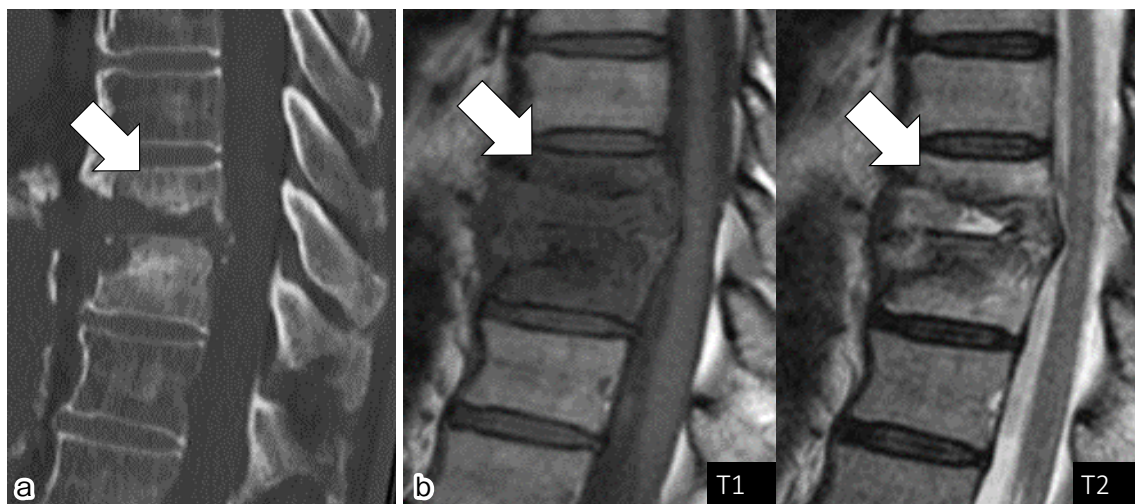
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Bacillus Calmette-Guérin (BCG) is an attenuated derivative of virulent *Mycobacterium bovis* (*M. bovis*). Although intravesical BCG therapy is an effective treatment for non-muscle-invasive bladder cancer (NMIBC)<sup>1)</sup>, most of spine surgeons do not recognize it. However, this treatment rarely induced complications related to osteomuscular lesion, such as spondylodiscitis<sup>2)</sup>.

Here, we report an 80-year-old man with BCG spondy-

lodiscitis. 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



**Figure 1-a.** Sagittal plane computed tomography (CT) scan at first visit.

CT shows osteolytic lesion on T9–T10. The arrow marks T9.

Fig. 1-b Sagittal magnetic resonance imaging (MRI) images at first visit.

Left: T1-weighted image. Right: T2-weighted image.

MRI shows fluid accumulation in the disk space of T9/10. The arrow marks T9.

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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 in-



**Figure 2.** Sagittal plane CT scan before surgery. CT reveals the vacuums in T9/T10 intervertebral disc space. The arrow marks T9.

travesical 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).

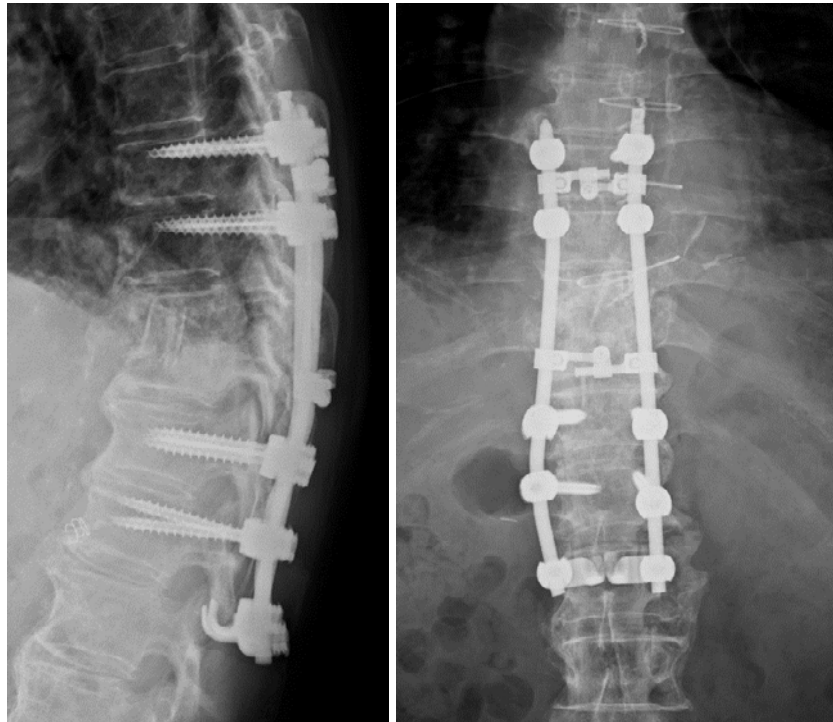
The immunotherapy with intravesical BCG therapy has become the standard treatment for patients with NMIBC<sup>(1)</sup>. Domestic incidence rate per 100,000 population of bladder cancer in 2018 is 18.4, and the number is increasing<sup>(3)</sup>. Approximately 70% of the cancer are NMIBC. Although the 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 surgery<sup>(4)</sup>. 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 infection<sup>(5)</sup>. 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 BCG<sup>(6)</sup>. Specifically, it

Mycobacterium tuberculosis strain DKC2 genome assembly, chromosome: 1  
 Sequence ID: [LR027516.1](#) Length: 4409544 Number of Matches: 1

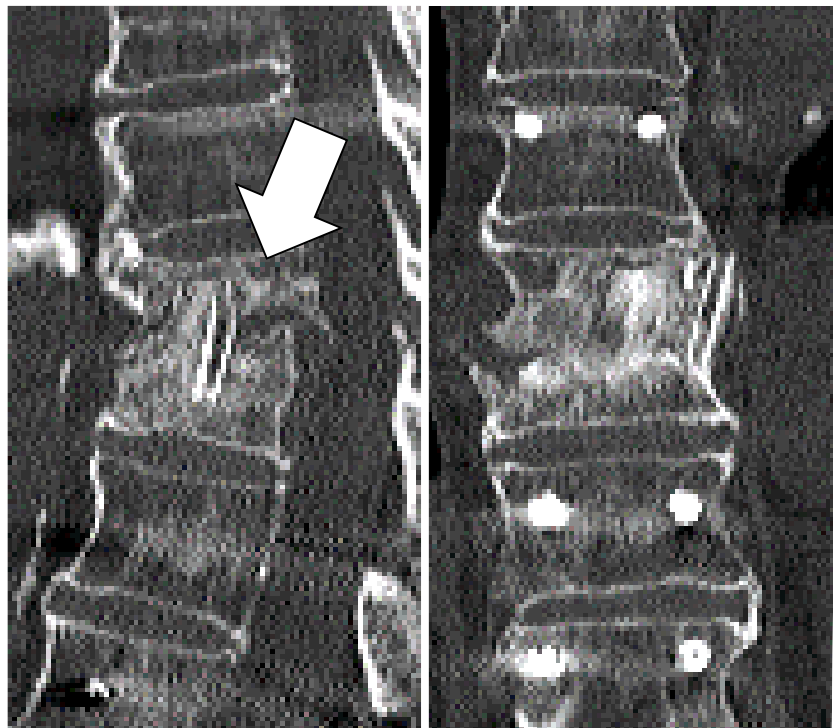
Range 1: 3824230 to 3824578

Score	Expect	Identities	Gaps	Strand
503 bits(272)	2e-138	327/349(94%)	22/349(6%)	Plus/Pl
Query 1	TCGATACCCGTCGCCGAGCGCAGCATGGGCGCAAAGAGCCGCCAACCGAATTGCAGCGCA	60		
Sbjct 3824230	TCGATACCCGTCGCCGAGCGCAGCATGGGCGCAAAGAGCCGCCAACCGAATTGCAGCGCA	3824289		
Query 61	AGGGCGTGCCGACCCGCCAGCCGCGGCCAAAGTCGCTGCTAGCGAGGCCGTACCGCG	120		
Sbjct 3824290	AGGGCGTGCCGACCCGCCAGCCGCGGCCAAAGTCGCTGCTAGCGAGGCCGTACCGCG	3824349		
Query 121	TCGAGCAGCTCCGCAACATTGGGAAATCGCTGTTGCAGCTGGCCACGGGATATCCGTCC	180		
Sbjct 3824350	TCGAGCAGCTCCGCAACATTGGGAAATCGCTGTTGCAGCTGGCCACGGGATATCCGTCC	3824409		
Query 181	AGCAGTGCCCGGGCTAAGACCCGCCCATGTGGTTCGAGAGCCCGTTCGATGATGTCAGCG	240		
Sbjct 3824410	AGCAGTGCCCGGGCTAAGACCCGCCCATGTGGTTCGAGAGCCCGTTCGATGATGTCAGCG	3824469		
Query 241	GGCGCCTCGA-----GTCCAGGTGATCGAGCACGGCCCCA	278		
Sbjct 3824470	GGCGCCTCGAAGTGAACAGTCTGGTCAGTTCCGCCCAGGTGATCGAGCACGGCCCCA	3824529		
Query 279	ACCAGTTGGTCTTGGTGCCGAAGTGACGAAACACCAGCCCGTGGTTGA	327		
Sbjct 3824530	ACCAGTTGGTCTTGGTGCCGAAGTGACGAAACACCAGCCCGTGGTTGA	3824578		

**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.



**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<sup>7</sup>. However, RFP-, INH-, and EB-resistant BCG has been reported. Thus, it was recommended to perform a susceptibility test<sup>8</sup>. Delay

of diagnosis on spondylodiscitis might lead the patients with progressive neurological deficits and need surgical treatment<sup>9</sup>. Spinal instability due to serious bone destruction, significant deformity, or conservative treatment failure indicates relative surgical intervention<sup>10</sup>.

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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**Author Contributions:** Sachiko Kawasaki, Akihito Kawai, and Masato Tanaka operated the case and contributed to the acquisition, analysis, or interpretation of data for the work. Tomoko Nishimura helped to treat the case and confirmed the content. Hideki Shigematsu contributed to drafting the work or revising it critically for important intellectual content. Yasuhito Tanaka contributed to the final approval of the version to be published.

**Ethical Approval:** The authors have no approval code because this manuscript is a case report.

**Informed Consent:** A statement that appropriate informed consent was obtained.

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