Case Study of the Month

Bacillus Calmette-Guérin Osteomyelitis Mimicking Spinal Metastasis from Urothelial Cell Carcinoma of the Bladder


1. Case report

A 66-yr-old male presented with progressively worsening back pain 5 mo after undergoing radical cystectomy and bilateral extended pelvic lymph node dissection for bacillus Calmette-Guérin–refractory pTisN0M0 urothelial carcinoma of the bladder. Imaging revealed lytic lesions in the 10th and 11th vertebral bodies of the thoracic spine that were suspicious for metastasis and cord compression. The patient underwent computed tomography–guided biopsy of the abnormalities, which showed no evidence of malignancy but revealed chronic inflammatory infiltrate with cultures positive for Mycobacterium bovis. The patient was treated with isoniazid, rifampin, ethambutol, and pyrazinamide.

Abstract

A 66-yr-old male presented with progressively worsening back pain 5 mo after undergoing radical cystectomy and bilateral extended pelvic lymph node dissection for bacillus Calmette-Guérin–refractory pTisN0M0 urothelial carcinoma of the bladder. Imaging revealed lytic lesions in the 10th and 11th vertebral bodies of the thoracic spine that were suspicious for metastasis and cord compression. The patient underwent computed tomography–guided biopsy of the abnormalities, which showed no evidence of malignancy but revealed chronic inflammatory infiltrate with cultures positive for Mycobacterium bovis. The patient was treated with isoniazid, rifampin, ethambutol, and pyrazinamide.
mid- to lower back pain requiring narcotics. He had difficulty sleeping in the supine position due to the pain. On physical examination, he had no neurological deficits. A computed tomography (CT) scan of the thoracic, lumbar, and sacral spine revealed lytic lesions at T10–T11 vertebral bodies that were suspicious for bony metastasis, although they were atypical, as the lesions were sharply maginated (Figs. 1 and 2). A follow-up technicium-99m bone scan demonstrated increased tracer uptake at T10–T11 (Fig. 3). Chest x-rays revealed clear lung fields but also wedge compression deformities at the T10–T11 vertebral bodies. Spinal MRI revealed apparent bony metastasis to T10 and T11 vertebrae, with prevertebral and epidural soft-tissue involvement causing severe cord compression at the T10 and T11 levels (Figs. 4 and 5).

Given the atypical presentation of progressive metastatic bladder cancer in the setting of pTisN0M0 bladder cancer at cystectomy, a CT-guided biopsy was obtained of the right T10 pedicle prior to palliative spinal radiation therapy and systemic chemotherapy. Pathology revealed fibrosis and chronic inflammatory infiltrate with no evidence of malignancy. Fluorochrome stain of the body fluid was positive for few acid-fast bacilli. Empiric therapy with isoniazid, rifampin, ethambutol, and pyrazinamide was administered. Culture results showed *Mycobacterium tuberculosis* complex (including *Mycobacterium bovis*) by sequence identification, which was subsequently confirmed as *M. bovis* by biochemical tests (Fig. 6). The pyrazinamide was stopped from the regimen (*M. bovis* is usually resistant to pyrazinamide). Notably, the patient never had fevers, chills, or leukocytosis, which lowered the likelihood of an infectious process in the differential diagnosis. The patient subsequently had a negative tuberculin skin test and a negative γ-interferon blood test for tuberculosis. He was also negative for HIV. The patient is now in his third month of a planned 12-mo course of treatment, with marked improvement of symptoms.
2. Discussion

The standard treatment options for CIS of the bladder are intravesical BCG immunotherapy or immediate cystectomy for selected patients. Complications of BCG immunotherapy include cystitis (up to 90%), fever (3%), and hematuria (up to 34%) [1,2]. Symptoms of cystitis, including frequency, dysuria, hematuria, and low-grade fevers, usually occur after the third dose and are usually managed with supportive therapy. Local granulomatous infections can include granulomatous prostatitis (clinically 1%, although up to 40% can have biopsy-proven disease) and epididymo-orchitis (<1%). Severe complications, including sepsis and systemic infections, are rare (<1%). Late organ-specific manifestations (pneumonitis, hepatitis, pyelonephritis, osteomyelitis, and bone marrow infection) are due to a reactivation of BCG infection. Symptoms can include high fever, chills, hypotension, and mental confusion. Severe systemic disease can also present with disseminated intravascular coagulopathy, respiratory failure, jaundice, and leukopenia [2].

Risk factors for complications from BCG instillation include traumatic catheterization, hematuria, active infection, immunosuppression, bladder outlet obstruction, radiation cystitis, and transurethral resection of the prostate and bladder within 2 wk of instillation [2,3]. Additionally, BCG organisms have been known to persist in the bladder up to 16 mo after completion of BCG instillation, although they have not been shown to increase complications from BCG immunotherapy [4].

At least nine cases of M. bovis osteomyelitis have been reported following intravesical therapy [5–10]. The range for presentation postinstillation varies between 2 wk and 12 yr in these reports. Notably, six of nine patients with vertebral osteomyelitis required surgical intervention with debridement and spinal stabilization. One of these cases received a presumptive diagnosis of metastatic lung cancer and underwent empiric radiation therapy to the back and chest [7].

Our case also presented with back pain and imaging that was clinically regarded as bony metastases—a very different manifestation than the reports of osteomyelitis—and had been prepared for radiation therapy to the spine for suspected metastatic disease, pending the biopsy result. With the rapid return of the acid-fast bacilli culture from fluorochrome staining, the patient received the appropriate treatment. This case report demonstrates the importance of clinical history in patients who have received intravesical BCG immunotherapy and present months or years later with back pain. BCG-related osteomyelitis or other skeletal infection must always be considered in the differential diagnosis in this population in order to initiate appropriate and expeditious therapy.

Conflicts of interest: The authors have nothing to disclose.

EU-ACME question

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Question:

Intravesical bacillus Calmette-Guérin (BCG) is absolutely contraindicated for all of the following patients except:

A. The patient who is on immunosuppressive medication.
B. The patient who has a traumatic catheterization and develops hematuria prior to instillation.
C. The patient with a history of BCG sepsis.
D. The patient with a history of tuberculosis.
References