

Parapharyngeal tuberculoid mass: a rare complication of Bacillus Calmette-Guerin therapy for urothelial carcinoma in situ

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Abstract

Bacillus Calmette-Guerin (BCG) is commonly used in treating superficial urothelial carcinoma. Though rare, local and systemic disseminated BCG infections are important to recognize as they require prolonged antimicrobial therapy and surveillance. We present an unusual case of a parapharyngeal space mass as manifestation of disseminated BCG following urothelial carcinoma treatment.

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Key Clinical Message:

Local and systemic complications of Bacillus Calmette-Guerin therapy are important to recognize as they require prolonged antimicrobial therapy; molecular genomic testing may be key to diagnosis when culture data is inconclusive.

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Bacillus Calmette-Guerin (BCG) is commonly used in treating superficial urothelial carcinoma. Though rare, local and systemic disseminated BCG infections are important to recognize as they require prolonged antimicrobial therapy and surveillance. We present an unusual case of a parapharyngeal space mass as manifestation of disseminated BCG following urothelial carcinoma treatment.

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Introduction

Bacillus Calmette-Guerin (BCG), a live-attenuated strain of *Mycobacterium bovis*, has been successfully used as intravesical immunotherapy in superficial (muscle-sparing) bladder cancer for over 40 years.¹ It is the treatment of choice in patients with urothelial carcinoma *in situ* (Tis) and early-stage disease (Ta-T1), and has been shown to reduce both its recurrence and progression.² While its precise mechanism of action remains poorly defined, BCG infection of the urothelium stimulates a cytokine-mediated immune response and confers anti-tumor activity by cytotoxic T lymphocytes.³

Local and systemic infectious complications of BCG intravesical therapy are rare; the most common of these is BCG cystitis, but reported manifestations include orchitis, sepsis, granulomatous hepatitis, pneumonitis, osteomyelitis, arthritis, and mycotic aneurysms. In this report, we describe a rare case of a 71 year old male with bladder carcinoma *in situ* treated with two courses of intravesical BCG who presented with development of a parapharyngeal mass, ultimately found to be distant mycobacterial infection.

Case Report and Discussion

This study was exempt from review by the UCSF Institutional Review Board. A 71 year old man presented to clinic with a six month history of a left-sided soft, compressible neck mass. He denied any associated pain or dysphagia, compressive symptoms, hoarseness, or globus. His past surgical history was notable for a childhood adenotonsillectomy; urothelial carcinoma *in situ* status post two transurethral resections of bladder tumors and two therapeutic courses with one maintenance intravesical immunotherapy with BCG. His treatment was complicated by BCG cystitis, for which the patient was treated with a three weeks of isoniazid and rifampin, and his symptoms resolved. The last intravesical BCG therapy was completed six months prior to developing a neck mass and 12 months prior to presentation in clinic.

Outside hospital workup of the mass included an ultrasound of the neck and an MRI. These showed a left level II/III 6.6 x 2.8 cm complex cystic mass with a mural soft tissue component and an unusually thick septation. The patient had undergone two fine-needle aspirations, which yielded purulent material with neutrophils but no observed growth on bacterial, fungal, and acid-fast bacilli cultures. A multidisciplinary review of this case favored additional imaging with computed tomography of the neck and chest (Figure 1). This demonstrated a left lateral neck non-calcified fluid collection with a thick rim and enhancing internal septation. There were no associated calcifications, no surrounding inflammatory changes, and the collection displaced the carotid and jugular vessels anteriorly. Chest CT revealed calcifications within mediastinal lymph nodes and spleen, indicating prior granulomatous infection.

The infectious disease service was consulted for diagnostic workup and management. QuantiFERON-TB Gold Plus returned negative. The patient also tested negative for human immunodeficiency virus, which confers a higher incidence of tuberculous lymphadenitis with co-infection.⁴ Additional antibody and antigen testing for *Histoplasma capsulatum*, *Coccidioides immitis*, *Coxiella burnetii*, *Bartonella* and *Brucella* species was unremarkable. The patient was started empirically on isoniazid, rifampin, and ethambutol given high clinical suspicion for disseminated BCG infection. 16S ribosomal RNA sequencing of FNA specimen ultimately detected *mycobacterium tuberculosis* complex. Specimen was sent to the California State Laboratory for pyrosequencing, which detected DNA of *M. bovis* and confirmed susceptibility to isoniazid and rifampin. On therapy, patient initially experienced paradoxical worsening of the left neck mass before improvement. At most recent follow-up in March 2020, the patient had nearly completed planned six months of antimicrobial therapy with a persistent small area of nodular hyperpigmentation at the neck mass site.

A parapharyngeal space lesion is a rare complication of BCG treatment for urothelial carcinoma. Risk of disseminated mycobacterial infection is increased in individuals with foreshortened time between surgical treatment and intravesical instillation of BCG. Reported onset of symptoms can vary from 3 months to 1 year following BCG treatment.⁵

Disseminated BCG infections may not require surgical intervention, but should be treated with extended courses of medical therapy and undergo surveillance for treatment response. A suggested duration of therapy is three to six months with a multidrug regimen of rifampin, isoniazid, and ethambutol. A close review of the patient's medical history and exposures is needed to raise suspicion for this rare etiology. Molecular diagnostics, such as 16S rRNA sequencing, may be key to diagnosis in cases where serology and culture-based testing is inconclusive.

Author contributions:

KAP performed patient chart review, literature review for prior reported BCG therapy sequelae, and authored the manuscript. PKH and MF were involved in the clinical care for the case patient presented and contributed to the final manuscript. CG reviewed and interpreted imaging studies for the case, identified representative imaging findings, and contributed to the manuscript text.

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Figure Captions:

Figure 1. (A) Axial and (B) sagittal contrast-enhanced computed tomography demonstrating an elongated thick-walled, irregular fluid density collection deep to the sternocleidomastoid muscle, displacing carotid vessels anteriorly. There were no associated calcifications or infiltration of adjacent tissues.

