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Case Report

Disseminated BCG disease: A case report

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ABSTRACT

Disseminated BCG disease is a rare life-threatening complication of BCG administration, characterised by miliary pulmonary nodules. Presentation can mimic tuberculosis, both in symptoms and on radiological imaging. Here we report a case of disseminated BCG disease following intravesical BCG treatment for superficial bladder cancer that responded to anti-tuberculous treatment and corticosteroids, and briefly review the literature on disseminated BCG disease.

1. Educational aims

The educational aims of this manuscript are to

- To raise awareness of disseminated BCG disease as an adverse effect of BCG administration.
- To describe the clinical presentation, including radiological findings, of pulmonary involvement in disseminated BCG disease.
- To describe the treatment of disseminated BCG disease.

2. Introduction

The tuberculosis vaccine Bacillus Calmette–Guérin (BCG) contains live attenuated *Mycobacterium bovis*. In immuno-competent adults, disseminated BCG disease is a rare complication of intravesical BCG treatment for superficial bladder cancer that is often characterised by miliary pulmonary nodules.[1,2] Here we report a case of disseminated BCG disease following intravesical BCG treatment with features mimicking tuberculosis infection.

3. Case report

A seventy-year-old man presented for assessment with a three-week history of fever, lethargy and weight loss of 12 kg. He had undergone transurethral resection of a superficial bladder cancer four months prior to presentation and subsequently received a six-week course of intravesical BCG treatment (one dose per week). Follow-up cystoscopy showed inflammatory changes only. A further course of intravesical BCG was arranged but the patient developed nausea, rigours and suprapubic pain within 24 h of administration. These symptoms progressed into his presenting illness.

Examination revealed normal pulse, blood pressure and respiratory rate. Temperature was initially 36.3 °C, but rose to 39.2 °C later on that day. Oxygen saturations were 93% on room air. Examination of the heart, chest and abdomen was normal. Initial blood tests included a white blood cell count of 4.9×10^9/L and C-reactive protein of 107 mg/L. Chest X-ray showed no focal consolidation with minor bi-basal atelectasis. Urine dip-stick testing was positive for red blood cells, protein, leucocytes and nitrites.

A provisional diagnosis of urinary tract infection was made and treatment with oral ciprofloxacin was commenced. The patient continued to have pyrexial episodes of 39 °C over the next five days. Three sets of blood cultures showed no bacterial growth, and the urine specimen from admission showed sterile pyuria. In view of the ongoing pyrexia, a CT scan of the thorax, abdomen and pelvis was arranged. This revealed extensive nodularity throughout both lungs (Fig. 1).

Three sputum samples showed no acid-fast bacilli or mycobacterial growth. A further set of blood and urine cultures showed no growth. Bronchoscopy was macroscopically normal, but transbronchial biopsy showed scattered epithelioid granulomas, with no evidence of caseation or acid-fast bacilli.

A clinical diagnosis of disseminated BCG disease secondary to intravesical BCG therapy was made. Treatment with rifampicin,

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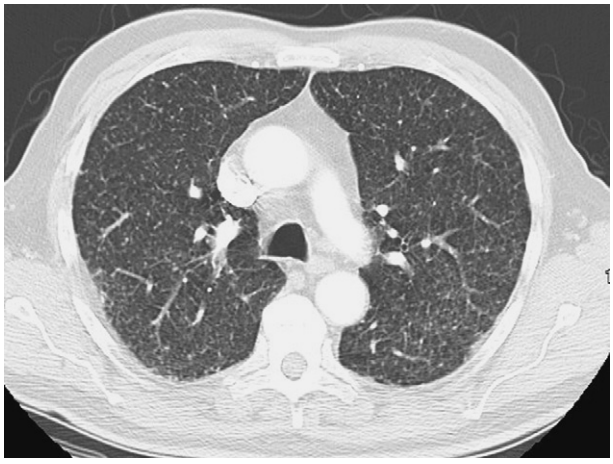

Fig. 1. Thoracic CT showing extensive pulmonary nodularity due to disseminated BCG disease. The differential diagnosis of such an appearance would include miliary tuberculosis.

isoniazid, ethambutol and pyridoxine was commenced. After six days of treatment the pyrexial episodes had not resolved. The addition of prednisolone to his treatment regime resulted in resolution of the persistent pyrexia, and the patient was discharged home.

At follow-up after one month, reduction of the prednisolone dose resulted in recurrence of rigours and weight loss. These symptoms resolved with increasing the prednisolone dose, followed by gradual tapering of steroid treatment.

4. Discussion

Disseminated BCG disease is a rare but life-threatening complication of BCG administration. The spectrum of symptoms may be similar to that of tuberculosis infection, including persistent fever, night sweats and weight loss. The pathogenesis is thought to involve a combination of mycobacteraemia and local inflammatory hypersensitivity at various sites including the lungs. This is supported by the identification of *M. bovis* in some reported cases[3,4] and response to treatment with a combination of antimycobacterial agents and corticosteroids.

There is currently no consensus on the optimum duration of antimycobacterial or corticosteroid therapy in disseminated BCG disease complicating intravesical BCG treatment. Triple-therapy with rifampicin, isoniazid and ethambutol is the first-line combination due to the inherent resistance of *M. bovis* to pyrizinamide. In our patient treatment was continued for nine months, though successful treatment has been described after courses as short as three months.[5] Relapse in symptoms with reduction of corticosteroid dose has been reported previously,[6] suggesting that a prolonged tapering course may be required.

Whilst disseminated BCG disease is rare following intravesical BCG treatment in immuno-competent patients, the incidence amongst children with HIV infection following BCG vaccination has been estimated to be as high as 992 per 100,000.[7] Symptoms include fever and weight loss, and a systematic review reported a mortality rate of 81%.[7] The World Health Organization (WHO) currently recommends that HIV infection in infants is a full contraindication to BCG vaccination. WHO also states that where feasible, infants at risk of HIV infection should be tested for HIV prior to vaccination instead of the previously recommended universal vaccination in countries with a high burden of tuberculosis.[8]

In summary, disseminated BCG disease is a recognised complication of intravesical BCG therapy with symptoms and radiological findings that may mimic tuberculosis infection. Treatment includes corticosteroids in combination with antimycobacterial therapy.

5. Patient consent

Written patient consent obtained.

Conflict of interest

The authors declare no conflict of interest.

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