CASE REPORT

Resolution without treatment of granulomatous pneumonitis due to intravesical BCG for bladder cancer

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SUMMARY

Granulomatous pneumonitis is a well-recognised complication of intravesical BCG therapy. The mechanism is sometimes thought to be 'hypersensitivity' rather than infection as in most cases mycobacteria are not cultured. Despite this it is usually treated with antituberculous chemotherapy with or without corticosteroid. We describe a case of bladder cancer treated with intravesical BCG followed by a febrile illness and malaise lasting for months and the development of miliary pulmonary shadowing, which markedly improved in around 1 year without any treatment. The clinical syndrome was less severe than some others described but this case provides evidence that, at least in some cases, no specific treatment may be necessary.

BACKGROUND

Intravesical instillation of BCG is commonly used to prevent recurrence of superficial bladder tumours following resection. Known, though rare, adverse effects include both local and distant—often pulmonary—granulomatous reactions as well as systemic sepsis. Miliary lung nodules or infiltrates are seen on X-ray and granulomata are usually found if biopsied but mycobacteria have only rarely been cultured from these lesions.¹

BCG is a live attenuated vaccine derived from *Mycobacterium bovis* and has been known to cause human disease. A miliary reaction following administration might naturally be assumed to be the result of infection but some authors consider that it may be a 'hypersensitivity' reaction. This is largely because of (usually) negative cultures and a response in some cases to glucocorticoid: this implies that antimycobacterial treatment may not be necessary. A granulomatous reaction may of course be an appropriate response to the bacilli or antigenic material from them, just as even the more virulent *M bovis* or *Mycobacterium tuberculosis* may be cleared by an immunocompetent host.

Despite the above uncertainties, the usual recommendation is to give antimicrobials appropriate for *M bovis* with the possible addition of corticosteroid. This, of course, has potential adverse effects and a usual course of treatment may be 6–9 months long.

CASE PRESENTATION

A 74-year-old man, otherwise fit, was treated with intravesical BCG for a transitional cell carcinoma of the bladder. Six doses were given without problems

Figure 1 CT scan showing pulmonary nodules in a miliary pattern.

but 6 months later he had further treatment. The next (seventh) dose gave him influenza-like symptoms causing the eighth to be delayed by a week and following that dose the symptoms worsened. Fever, night sweats, shivering, anorexia and weight loss persisted for over a month. Following this, there was a very slow recovery over about 2 months and the duration of symptoms prompted referral back to clinic and a CT (figure 1), which showed multiple small pulmonary nodules and led to his attendance at the chest clinic.

INVESTIGATIONS

The CT showed many small nodules throughout both lungs, also seen on plain film (figure 2). Urinary cultures for mycobacteria were negative. The radiographic findings were assumed to represent a granulomatous pneumonitis caused by infection or hypersensitivity. Bronchoscopy for lavage or biopsy was proposed but, on feeling better, our patient declined further investigation or treatment.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for the X-ray appearance was disseminated infection, a form of hypersensitivity reaction or miliary metastases from the bladder cancer, although the latter was thought far less likely.

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Figure 2 A chest radiograph 4 months following the CT scan.

OUTCOME AND FOLLOW-UP

Our patient came to chest clinic shortly after his illness, already feeling better but with innumerable nodules throughout both lungs. Investigation and treatment were discussed along with the uncertainty of the need for antituberculous medication. This was a difficult decision but it was agreed to withhold treatment and observe, particularly as he had clinically improved so much and did not want to risk further adverse effects from any treatment. Over the next 12 months he remained asymptomatic and the nodular appearance improved greatly (figure 3).

DISCUSSION

There are several reports of granulomatosis affecting the lungs and other organs following intravesical BCG and in a few cases the BCG or *M bovis* has been identified on culture. In a review of cases from Canada and the USA between 1996 and 2002, Gonzalez *et al*¹ classed reactions as 'early' (occurring within 6 months of first treatment, usually earlier) or 'late' (after at least 6 months, more usually after a year). The former group was mainly characterised by pneumonitis, hepatitis or sepsis and

Figure 3 A chest radiograph 1 year after the initial scan and 14 months after the first symptoms.

most cultures were negative while the latter had chiefly vascular (including aneurysm), testicular and bone infections; most of those had positive cultures.

That antimicrobials are not absolutely required is illustrated by one case in the above series with an initial presentation similar to ours who made an initial improvement without treatment. However, by 6 weeks that patient still had dyspnoea, a reduced CO diffusion factor and abnormal radiograph. Steroid was therefore started, followed by a rapid improvement over the next 3 weeks.²

Use of both antimicrobials and steroid is described in a recent report of a patient with a short febrile illness (and a normal chest radiograph) followed by respiratory failure and the development of both pulmonary nodules and ground-glass opacities seen on chest CT. Steroid (prednisolone) and antituberculous treatment (rifampicin, isoniazid and ethambutol) were started with clinical improvement seen within 2 days and radiographic improvement in 5 days.³ We speculate that the speed of improvement in this case may point to hypersensitivity rather than infection as the major problem.

Our patient had a milder illness than the two cited above but his case demonstrates that at least some pulmonary reactions may resolve without any treatment, whether due to 'hypersensitivity' or natural clearance of BCG. We suggest that the timing of the illness, being soon (weeks) after the start of treatment (though not within hours, as in some cases of sepsis) and its evolution suggest an appropriate response to an antigenic challenge with no need for antimicrobials.

Learning points

- ▶ Granulomatous pneumonitis is a recognised side effect of Bacille Calmette-Guérin treatment to the bladder and there is a spectrum of illness and pulmonary involvement.
- ▶ We describe a febrile illness with persisting pulmonary nodules, with significant improvement within 1 year without any treatment. The timing may suggest an immune-mediated response and the rapid clinical resolution that no steroid is needed.
- ▶ Potentially toxic antituberculous therapy is not always required in these patients.

Contributors RMV wrote the initial draft of the paper. NS provided suggestions and treated the patient.

Competing interests None.

Patient consent Obtained.

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