Pulmonary complications of intravesicular BCG immunotherapy

A 79-year-old man was admitted to hospital with fever, rigours and malaise 1 week after completing his seventh intravesicular BCG immunotherapy treatment for carcinoma in situ of the bladder. On admission, respiratory examination was normal with a peripheral oxygen saturation of 94% on air and a normal white cell count but raised C reactive protein of 111. His chest radiograph was normal (figure 1). He was treated for presumed urinary sepsis with intravenous antibiotics while awaiting results of microscopy and culture of urine and blood cultures.

By day 5, the patient had become progressively breathless requiring high flow oxygen to maintain his oxygen saturations. Urine and blood cultures taken on admission were negative. A repeat chest radiograph revealed new bilateral pulmonary infiltrates (figure 2). A CT chest was performed which showed bilateral ground glass changes and multiple tiny pulmonary nodules (figure 3). The differential diagnosis was urinary sepsis, miliary tuberculosis or a pulmonary hypersensitivity reaction and due to the severity of his systemic inflammatory response and deterioration in his clinical condition, he was started on rifampicin, isoniazid and ethambutol as well as oral prednisolone at a dose of 60 mg daily. He rapidly improved by day 7 and was discharged on day 10 with repeat chest radiograph showing a significant improvement (figure 4). Multiple urine, blood and sputum cultures taken during the acute phase were negative for mycobacteria.

He continued triple antituberculous medication for 2 months, and then isoniazid and rifampicin for a further 4 months. Steroids were reduced over a 3-month period; this regime was implemented based on his clinical response and information available from previous cases.

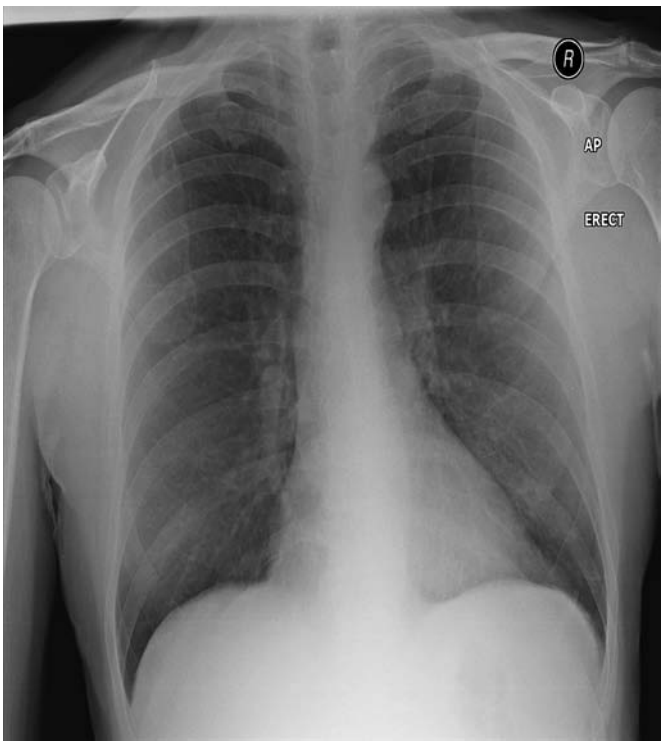

Figure 1 Chest radiograph on admission.

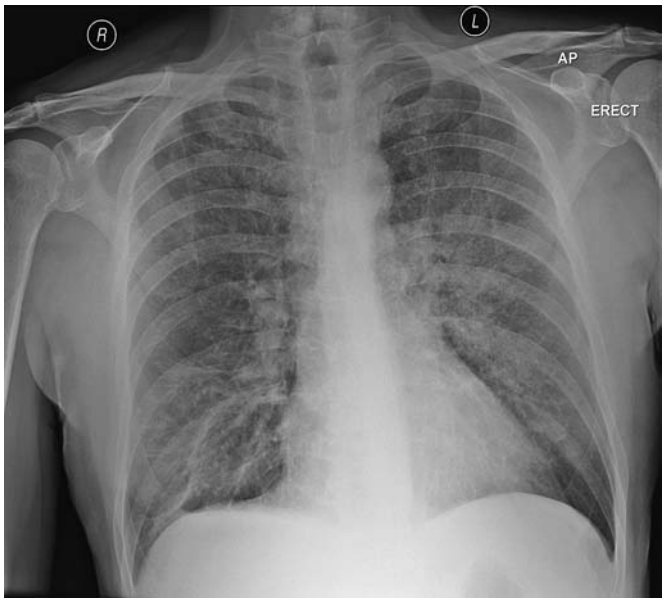

Figure 2 Chest radiograph 48 h after admission showing bilateral pulmonary infiltrates.

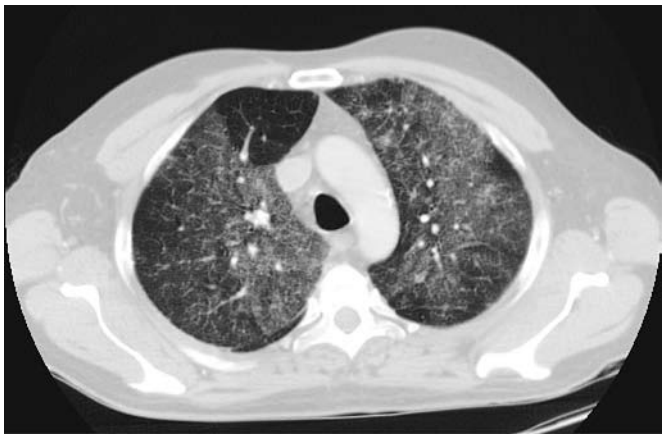

Figure 3 CT chest showing bilateral ground glass changes, most marked in the upper lobes and apices with multiple tiny nodules.

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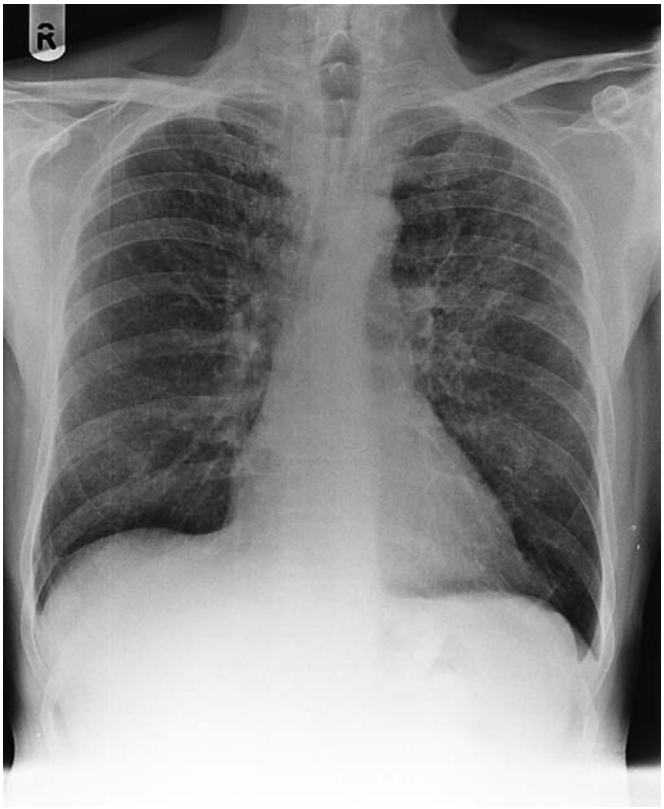

Figure 4 Chest radiograph at day 10 showing resolving pulmonary infiltrates.

Competing interests None.

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Learning points

- Radiological features consistent with interstitial pneumonitis have been reported in 0.7% of patients receiving BCG immunotherapy for carcinoma of the bladder.[1] It is debated as to whether the interstitial pneumonitis associated with intravesical BCG is predominantly a hypersensitivity reaction or is a manifestation of miliary disease caused by BCG, or both.
- Based on case reports, it is suggested that patients should be given antituberculous medication for 6 months;[2–4] pyrazinamide is not included as BCG is resistant to this drug. It should be noted that the National Institute for Clinical Excellence guidance on the management of tuberculosis recommends treatment for a total of 9 months if pyrazinamide is not used in the initial 2 months of therapy.[5] If there appears to be a significant hypersensitivity component, steroids should also be given.[2–4] Although there is no consensus on the optimal duration of steroid therapy, it is recommended that prednisolone be reduced over a period of weeks to months to reduce the risk of recurrence.[6] Microbiological sampling is recommended although our patient was too hypoxaemic to undergo flexible bronchoscopy.
- Bladder carcinoma is the fourth most common cancer in men (11th most common in women) in the UK with an annual incidence of 10 335 in 2008. Within our trust, 45 patients are commenced on BCG immunotherapy each year, with a total of at least 270 instillations. It is important for respiratory physicians to be aware of the pulmonary complications associated with its use.