

Mediastinal lymphadenopathy in a patient with previously treated T-cell acute lymphoblastic leukaemia

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Mediastinal lymphadenopathy in a patient with previously treated T-cell acute lymphoblastic leukaemia is a diagnostic problem. The differential diagnosis in an adult is sarcoidosis, metastases, lymphoma or, rarely, tuberculosis. Mediastinal lymph node involvement is uncommon in tuberculosis.

In view of its relative rarity but good prognosis, it is important to distinguish tuberculous mediastinal lymphadenitis in adults from other causes of mediastinal masses. (MJA 2008; 188: 117-118)

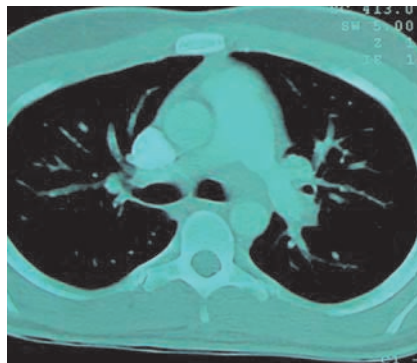
Clinical record

An 11-year-old boy presented in September 1995 with bilateral cervical lymph node enlargement for 2 months and fever for 10 days. There was no significant medical or family history. On examination, he had generalised lymphadenopathy. Systemic examination was normal. He had a high white blood cell count ($60 \times 10^9/L$) and a low platelet count. The diagnosis on bone marrow aspiration was T-cell acute lymphoblastic leukaemia. He was treated with the MCP-841 protocol as induction therapy,¹ after which his bone marrow was reported to be in complete remission. He then underwent consolidation chemotherapy and prophylactic cranial radiotherapy and subsequently received six cycles of maintenance chemotherapy, which were completed by December 1997. He was lost to follow-up.

He presented again in January 2006 with hoarseness of 2 months' duration. His complete blood count was normal. The erythrocyte sedimentation rate was 40 mm/h (reference range, 0–10 mm/h). His chest x-ray appeared normal. The Hopkins test (indirect laryngoscopy) showed a fixed left vocal cord. A subsequent computed tomography (CT) scan of the chest showed lymph nodes in the left para-aortic and aortopulmonary windows (Box 1). CT-guided fine-needle aspiration cytology was reported as inconclusive.

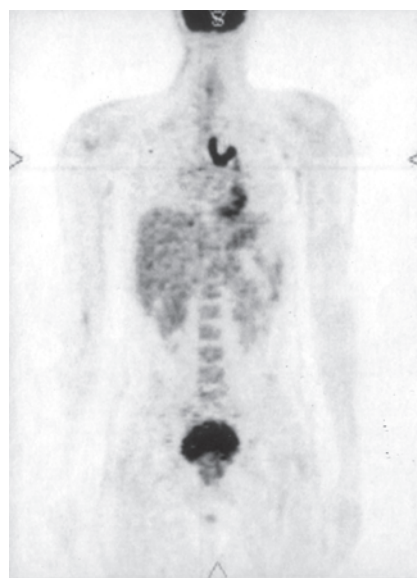
Fluorodeoxyglucose F18 positron emission tomography (PET) scan of the whole body showed active disease foci in lymph nodes in the aortopulmonary window and left axillary regions (Box 2). A bone marrow aspirate appeared normal, and bone marrow biopsy showed mildly hypocellular normal marrow. Video-assisted thoracoscopic surgical biopsy of the aortopulmonary lymph node showed histiocytic collections forming epithelioid granulomas with foreign-body and Langhans giant cells suggestive of necrotising granulomatous inflamma-

1 Computed tomography scan of the thorax



Contrast-enhanced image shows soft tissue density in the region of the aortopulmonary window corresponding with uptake of fluorodeoxyglucose F18.

2 Positron emission tomography (PET) scan



Fluorodeoxyglucose F18 PET scan showing uptake in the aortopulmonary lymph nodes.

tion typical of tuberculosis (Box 3A and Box 3B). Stains for acid-fast bacilli and fungi were negative. Biopsy cultures for mycobacteria and fungi were negative. A Mantoux test was negative.

In April 2006, the patient was started on antituberculosis treatment with the standard four-drug regimen consisting of rifampicin, pyrazinamide, ethambutol and isoniazid. After 2 months of treatment, he was symptom-free and was started on a two-drug regimen of isoniazid and rifampicin for 7 months.

Discussion

Isolated mediastinal lymphadenopathy can be a challenge for the best of clinicians, more so when the patient has a history that might influence the diagnosis. In mediastinal lymphadenopathy, the differential diagnosis has to include both benign and malignant causes, because the therapeutic implications and prognosis of both are broad. Childhood lymphoblastic leukaemia is usually assumed to have been permanently eradicated in patients in long-term remission, but occasionally can recur after many years.² In post-treatment relapses, or even very late relapses (5 to 20 years after diagnosis) in children, the tumour cells are clonally related to the leukaemic cells at diagnosis (shown by immunoglobulin heavy-chain locus or T-cell receptor gene sequencing), and are considered, therefore, to represent a slow re-emergence or escape of the initial cells.³ In a retrospective study of 2169 patients, the cumulative incidence of secondary neoplasm was 4.17% (SE, 0.46%) at 15 years and increased substantially after 20 years, reaching 10.85% (SE, 1.27%) at 30 years.⁴ In our case, the disease-free interval was 9 years. A diagnosis of relapse was initially suspected, but the peripheral smear and bone marrow results were normal.

As the CT-guided fine-needle aspiration cytology, done to clinch the diagnosis of relapse, had inconclusive results, a PET scan was planned to avoid an invasive procedure. PET is more efficacious than CT in differentiating benign from malignant focal lesions. However, fluorodeoxyglucose is not a cancer-specific agent, and false-positive findings have been reported. Infectious diseases (mycobacterial, fungal and bacterial), sarcoidosis, radiation pneumonitis and postoperative surgical conditions are reflected by intense uptake of fluorodeoxyglucose on PET scan.⁵

The results of bone marrow aspiration to rule out relapse were normal. Hence, it was decided to go ahead with a video-assisted thoracoscopic surgical biopsy of the active focus in the aortopulmonary window, which led finally to the diagnosis of tuberculosis. Although mediastinal lymphadenopathy is not a common manifestation of tuberculosis in an adult, the possibility should be considered in the differential diagnosis.⁶

In a study of 1161 patients admitted to hospital for tuberculosis, the incidence of lymph node tuberculosis without pulmonary involvement was reported to be about 5.1% (60 patients). Of these, 1.3% (16) had isolated mediastinal lymphadenopathy.⁷ Mediastinal lymphadenopathy may occur as a complication of pulmonary tuberculosis or as a primary disease without pulmonary involvement. Tuberculous adenitis of the mediastinum manifests itself as dysphagia, stridor, acute respiratory distress, chest pain or perforation of the oesophagus or tracheobronchial tree.⁸

Paralysis of the recurrent laryngeal nerve caused by mediastinal lymphadenopathy due to tuberculosis is an extremely rare condition. We have come across just two published cases.^{9,10} Awareness of the occurrence of mediastinal tuberculous lymphadenopathy could lead to early diagnosis by bronchoscopy or thoracoscopy and early implementation of antitubercular chemotherapy. This would help to reduce the significant morbidity associated with mediastinal complications.

In our case, the diagnostic dilemma was compounded by the fact that the patient had previously been treated for T-cell acute lymphoblastic leukaemia.

Competing interests

None identified.

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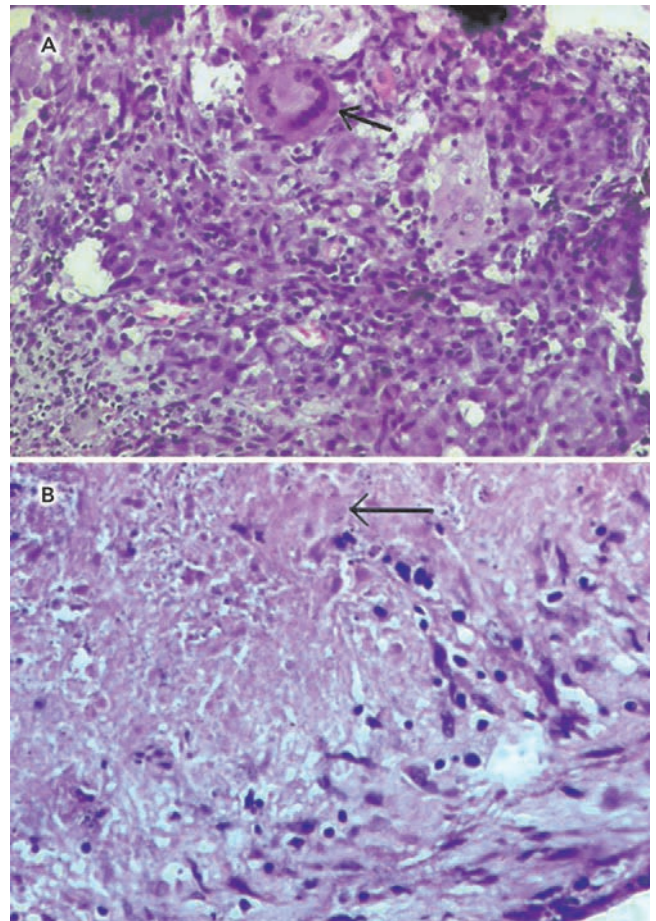
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3 Biopsy specimen of aortopulmonary lymph node



A: Histological view of a biopsy specimen showing a Langhans giant cell (arrow) and epithelioid histiocytes (magnification $\times 20$). **B:** View of the same specimen, showing central caseation necrosis (arrow) surrounded by palisading epithelioid histiocytes. Haematoxylin and eosin stain, magnification $\times 40$. ◆

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