Anaplastic large cell lymphoma with axial skeletal lesions portends a poor prognosis

Introduction

Anaplastic large cell lymphoma is unusual and encompasses several lymphomas, usually of T-cell lineage and with different clinical presentations, including primary cutaneous, nodal or skeletal. A primary presentation with skeletal lesions is unusual and appears to portend a particularly poor prognosis.

Discussion

Anaplastic large cell lymphoma is a rare condition, accounting for less than 5% of all cases of non-Hodgkin's lymphoma (Kadin and Morris, 1998). Characterized by the presence of large pleomorphic lymphocytes expressing the cell membrane protein CD30 antigen tumour marker (Lu and Chang, 2011), the peak incidence occurs in childhood and predominantly in males.

Anaplastic large cell lymphomas are usually of T-cell lineage, although reports of B-cell or null cell lineage are described. Anaplastic large cell lymphomas are divided into two subtypes, depending on whether anaplastic lymphoma kinase (ALK) is expressed or not. In a study of 57 patients with anaplastic large cell lymphoma, the 5-year survival rate in ALK-positive patients was 93%, compared with 37% for those who were ALK-negative (Gascoyne et al, 1999). However, when anaplastic large cell lymphoma presents with primary bony involvement, in itself unusual (Ishizawa et al, 1995), the outcome is poor. Nagasaka et al (2000) described six cases of anaplastic large cell lymphoma, three of which were ALK-positive and presented primarily as bone lesions of the axial skeleton. In this series, three of the six patients died of the disease within 2 years of diagnosis, and two who remained alive still had evidence of the disease at follow up (6 months to 2 years).

The treatment of systemic anaplastic large cell lymphoma constitutes intensive chemotherapy, often comprising cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP). Rituximab, a monoclonal antibody targeting CD20 positive B-cells, is often combined with this chemotherapeutic regimen. Autologous stem cell transplantation is usually reserved for patients with relapsed disease. A retrospective study of patients transplanted for relapsed anaplastic large cell lymphoma demonstrated that the 3-year overall survival rate was 86%. Patients who were ALK-positive had an event-free survival rate of 100% at 3 years, compared with 0% in the ALK-negative group (Jagasia et al, 2004). Newer therapies targeting CD30 antigen, such as the chimeric anti-CD30 monoclonal antibody SGN-30 (Bartlett et al, 2008), hold promise in treating relapsed patients.

This case highlights an uncommon form of lymphoma. Despite the patient having a marker for a better prognosis (ALK-positive), the clinical presentation with primary bone lesions of the axial skeleton appears to confer a particularly sinister outcome. **BJHM**

Bartlett NL, Younes A, Carabasi MA et al (2008) Phase I multidose study of SGN-30

Dr Zahra Al-Asaadi *is FY1 in Cardiology in the Department of Cardiology,* **Dr Sammour Fatin** *is Registrar in Haematology and* **Dr Ketan Patel** *is Consultant in Haematology in the Department of Haematology,* **Dr Naren Chetty** *is Consultant in Radiology in the Department of Radiology, and* **Dr Simon Dubrey** *is Consultant in Cardiology in the Department of Cardiology, Hillingdon and Mount Vernon Hospitals NHS Trust, Uxbridge, Middlesex UB8 3NN*

Correspondence to: Dr S Dubrey (simon.dubrey@thh.nhs.uk)

Case Report

A 35-year-old woman presented with right loin pain, malaise and fever. She was pyrexial at 38.5°C, tachycardic (110 beats/min) and tender in both flanks. Blood white cell count and C-reactive protein levels were elevated at 21.7 x10^9/litre and 305 mg/litre. Urine dip was positive for leucocytes. Plain radiographs of the chest and lumbar spine appeared normal, as was an ultrasound scan of the kidneys, ureters and bladder.

The initial management was for suspected pyelonephritis, but the patient had persistent loin pain and, despite antibiotics, spiked daily temperatures of over 38°C. The white cell count and C-reactive protein level remained high, reaching 47.4x10^9/litre and 395 mg/litre respectively. The haemoglobin level dropped from 90 g/litre on admission to 65 g/litre. Hepatitis B, C, human immunodeficiency virus and vasculitic screens were negative, as were tests for tuberculosis and atypical pneumonias. Immunoglobulins and lactate dehydrogenase levels were normal, although serum calcium level was elevated at 2.73 nmol/litre (normal 2.2–2.6 nmol/litre). Both kappa and lambda free light chains were elevated at 32.1 mg/litre (3.3–19.4 mg/litre) and 30.7 mg/litre (5.7–26.3 mg/litre) respectively, with a normal ratio.

Computed tomographic scans of chest, abdomen and pelvis revealed multiple skeletal lytic lesions (*Figure 1*), pulmonary nodules (largest 6 mm) with bilateral pleural effusions, axillary and internal mammary chain lymphadenopathy. Magnetic resonance scans confirmed multiple destructive lesions of the spine (*Figure 2*) and pelvis (*Figure 3*). Lymph node biopsy exhibited no evidence of malignancy and a bone marrow trephine showed no plasma cell infiltration.

Subsequent ultrasound-guided biopsy of a lytic rib lesion suggested a 'metastatic poorly differentiated malignancy'. However, immunohistochemistry staining was positive for leucocyte common antigen and focally for P63, suggestive of a high-grade lymphoma. Further subtyping confirmed an ALK (anaplastic lymphoma kinase) positive anaplastic large cell lymphoma.

The patient was commenced on rituximab (a monoclonal antibody) with cyclophosphamide, doxorubicin, vincristine and prednisolone (R-CHOP chemotherapy regimen). Three months later, after four cycles of chemotherapy, she was admitted with a multi-antibiotic resistant staphylococcal pneumonia. Despite inotropes and continued antibiotics, ventilatory support was eventually withdrawn. The patient died 15 weeks after the initial diagnosis.

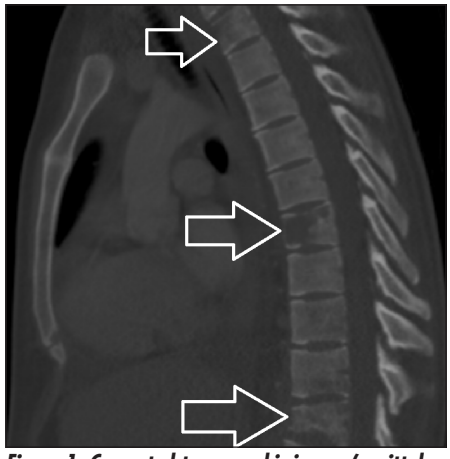

Figure 1. Computed tomographic image (sagittal section) of the chest showing a destructive lesion (open arrow) occupying a large part of the T8 vertebra and to a lesser extent T3.

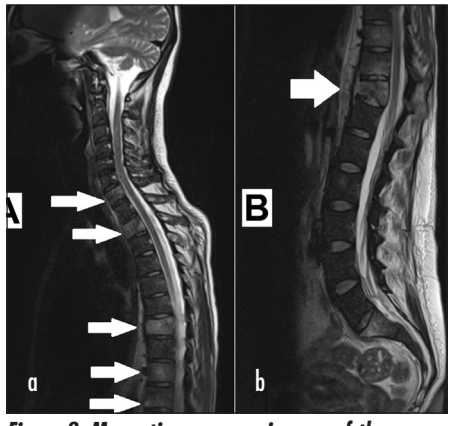

Figure 2. Magnetic resonance images of the (a) cervical and (b) thoracic spine showing lytic lesions (solid arrows) in a number of vertebrae.

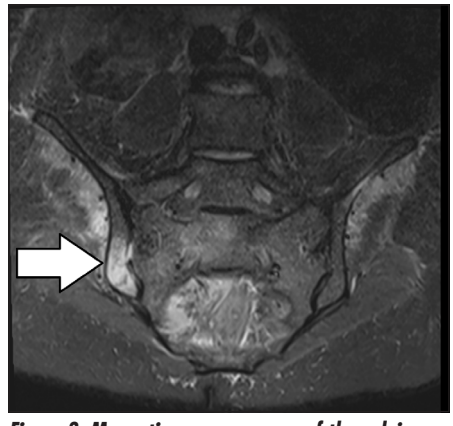

Figure 3. Magnetic resonance scan of the pelvis showing an abnormality in the iliac bone (arrow) on the right side of the pelvis. This STIR (short TI inversion recovery) image suppresses the fat signal and shows up marrow oedema as a bright signal.

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LEARNING POINTS

- Anaplastic large cell lymphoma is a rare (<5%) type of non-Hodgkin's lymphoma.
- Axial skeletal lytic lesions are associated with a poor prognosis.
- Anaplastic large cell lymphoma typically (although not uniquely) displays the cell membrane protein antigen CD30.

Obscure intra-abdominal bleeding

A 73-year-old frail woman attended accident and emergency with lower abdominal pain and nausea in hypovolaemic shock. She was on chemotherapy for recurrent right parotid adenocarcinoma and on therapeutic low molecular weight heparin for atrial fibrillation. Clinical examination revealed tachycardia with atrial fibrillation, hypotension and a soft but tender abdomen with bruising along her flanks. Prompt resuscitative measures were instituted; a clinical diagnosis of intra-abdominal bleed was established and contrast-enhanced computed tomography showed a 10 x 8 cm retroperitoneal haematoma with evidence of recent active bleeding (*Figure 1*).

Since she responded well to initial resuscitative measures, a conservative approach was taken to manage her retroperitoneal bleed, with in-hospital monitoring, discontinuing the heparin and keeping a close eye on her coagulation profile. Her recovery was uneventful and a serial computed tomography scan showed ongoing resolution of the bleed (*Figure 2*). BJHM

Mr Diwakar R Sarma *is Surgical Registrar and* **Dr Greta Mclachlan** *is Surgical House Officer in the Department of General Surgery, Darent Valley Hospital, Dartford & Gravesham NHS Trust, Dartford DA2 8DA*

Correspondence to: Mr DR Sarma (dsarma@nhs.net)

Figure 1. Initial computed tomography scan showing retroperitoneal haematoma.

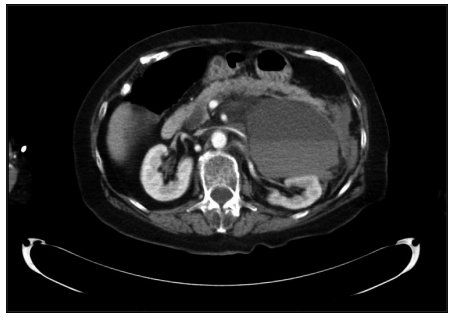

Figure 2. Interval computed tomography scan (6 weeks) showing partial resolution of haematoma.