We describe the case of a 45-year-old man presenting with chest pain and pleural effusions. These symptoms were progressive over a period of three years, with pericardial involvement and respiratory insufficiency finally resulting in death. Despite repeated diagnostic procedures, a final diagnosis could only be made at autopsy. Multisystem foamy histiocyte infiltration suggested the diagnosis of Erdheim-Chester disease.

**Keywords**
Chest pain, Erdheim-Chester disease, pleural effusion

**Introduction**

Erdheim-Chester disease (ECD) is a rare, life-threatening multisystem disease that is characterised by infiltration of foamy histiocytes. This disease was described for the first time by Chester and his tutor Erdheim in 1930. The aetiology is unknown. Bone pain is the most common presenting symptom and characteristic radiographic changes are bilateral sclerosis of the long bones, predominantly in the diaphyses and metaphyses. Approximately 50% of the patients have involvement of other tissues, such as periorbital, heart, skeletal muscles, skin and lung. Allen found 176 cases, among them 41 cases with pulmonary involvement. We describe the case of a middle-aged man with pulmonary involvement of ECD, but without skeletal pain.

**Case Report**

In January 2000, a man aged 45 years first experienced chest pain and a nonproductive cough on a skiing trip. Treatment with a macrolide resulted in substantial improvement. Six months later, these symptoms recurred with increased intensity. He noticed chills and night sweats, but no fever. The symptoms worsened and he developed increasing shortness of breath on exertion. In June 2000 he could only walk about 100 meters. Apart from a slightly raised erythrocyte sedimentation rate, there were no abnormalities in the blood biochemistry. In September 2000, chest X-rays showed bilateral pleural thickening and a decreased volume of the right lung. CT scan showed pleural thickening and subpleural fibrotic deformity, but no lymphadenopathy. Pulmonary function tests showed mild restriction and decreased static lung volumes (table 1). A tru-cut pleural biopsy showed fibrous tissue and chronic inflammation. He was treated for several months with ibuprofen 600 mg three to four times daily with little effect.

In October 2001 he was seen for the first time in our outpatient department. His only medical history was a nonsymptomatic diaphragmatic hernia and knee surgery. He had never smoked and had never been in contact with tuberculosis patients. He was unaware of any asbestos exposure in his job as a construction worker. On physical examination, tachypnoea was noted but no further abnormalities. A repeated CT scan showed stable disease.

**Table 1. Pulmonary function tests**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>November 2000</th>
<th>November 2002</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vital capacity litres (%)</td>
<td>3.0 (62)</td>
<td>1.5 (40)</td>
</tr>
<tr>
<td>FEV1 litres (%)</td>
<td>2.5 (63)</td>
<td>1.3 (30)</td>
</tr>
<tr>
<td>TLC litres (%)</td>
<td>4.5 (61)</td>
<td>2.9 (40)</td>
</tr>
<tr>
<td>RV litres (%)</td>
<td>1.3 (63)</td>
<td>1.1 (50)</td>
</tr>
</tbody>
</table>

FEV1 = forced expiratory volume in one second; TLC = total lung capacity; RV = residual volume.
There was no sign of pleural effusions and his pulmonary function tests showed a further reduction in lung volumes (table 1). Repeated blood biochemistry and haematology were normal. A tuberculin skin test was negative. The histology of a second tru-cut biopsy was identical to the previous one. Moreover, no infectious organisms were seen and cultures for tuberculosis, aspergillosis and actinomyces were negative.

Despite empirical therapy with up to 40 mg of prednisolone his symptoms and pulmonary function worsened. In June 2002 an open lung biopsy was performed. The pleurae were thickened to about 3 cm with a yellow discoloration and several adhesions. Biopsies showed extensive fibrosis, with infiltration of lymphocytes, plasma cells and histiocytes. A few clusters of histiocytes with foamy cytoplasm were present. No micro-organisms were identified, and there was no evidence of a malignant tumour. Six months after the open lung biopsy, there was further clinical deterioration, and signs and symptoms of right-sided heart failure and respiratory insufficiency developed. He was admitted to the ICU for mechanical ventilation. CT scan showed extensive pleural and pericardial thickening and effusions, diffuse smooth interlobular septal thickening and patchy areas of ground-glass attenuation (figure 1). There were no centrilobular abnormalities. The extent of the abnormalities prohibited decortication. High-dose corticosteroids were started as well as cyclophosphamide and broad-spectrum antibiotics.

After a few days he was successfully extubated, but his right-sided heart failure recurred the next day. A cardiac ultrasound showed pericardial effusion without inflow disruption. A pericardectomy was considered but rejected on account of the lack of a diagnosis and treatment options. Shortly thereafter, the patient died and autopsy was performed. At autopsy, the pleura were fibrotic with abundant infiltration of foamy histiocytes. Multinucleated cells were also present (figure 2). The fibrosis and histiocytic infiltration extended into the lung. Foamy histiocytes were found in the retroperitoneum, mesentery, spleen and bone marrow. These findings are consistent with ECD.

**DISCUSSION**

ECD primarily affects middle-aged and older adults. Since the histiocytic infiltration is mainly found in the large bones of the extremities, the most common presentation is with bone pain. Radiographic examination of the long bones shows characteristic changes: a symmetric pattern of diffuse or patchy sclerosis in the diaphyses and metaphyses of the long bones, a coarsened trabecular pattern and cortical thickening. These skeletal abnormalities often result in only mild symptoms. Extraskeletal manifestations are present in half of patients and are the main determinants of survival. With pulmonary involvement, the morbidity and mortality increase substantially. Pulmonary ECD typically presents with dyspnoea and a nonproductive cough. Pulmonary function tests show a mild restrictive defect and a decrease in carbon monoxide transfer. Gas exchange stays normal until the very final stages of the disease. On chest CT scan, the most common findings are smooth interlobular septal thickening and centriflobular nodular opacities, visceral thickening and pleural effusions. The pericardium is frequently involved with thickening and fluid effusions. Histopathologically, lung involvement is characterised by accumulation of foamy or clear histiocytes, variable amounts of associated fibrosis, and variable lymphoplasmacytic inflammatory infiltrates arranged in a lymphangitic pattern.

There is no evidence-based treatment for ECD. Recently, disease stabilisation was reported by using prednisolone 40 mg in combination with cyclophosphamide 100 mg once daily. Treatments with various other agents have been reported, such as vinblastine, vincristine, adriamycin,
colchicine and radiotherapy, in various combinations, but with only minor effects.\textsuperscript{2,3,9} Braiteh et al. reported successful treatment with interferon-α.\textsuperscript{16}

Our patient presented with only pulmonary symptoms. Since he did not complain of bone pain, the diagnosis of ECD was not considered. Rather, a presumptive diagnosis of mesothelioma was made based on the combination of extensive pleural thickening, a restrictive pulmonary function defect and the fact that our patient was a construction worker. Unfortunately, a clear diagnosis could not be made on the tissue samples obtained during surgery. Because the histological findings of fibrosis, chronic inflammation and some foamy histiocytes are nonspecific, a tentative diagnosis of ECD can only be made if clinical data, radiological findings and pathological findings are considered together. The most reliable diagnostic procedure is reported to be radiological investigation of the tubular long bones.

In our patient, the disease took a much more aggressive course after surgery, with extensive pulmonary involvement on top of the pre-existent pleural abnormalities. An infectious contribution was excluded by microbiological bronchoalveolar lavage. Repeated tissue sampling was refused by the patient. Empirical treatment with steroids and cyclophosphamide was followed by a very short improvement but might have been more successful if instituted at an earlier stage.

In conclusion, ECD should be included in the differential diagnosis of bilateral pleural thickening and a restrictive pulmonary impairment. The disease has a poor prognosis and limited treatment results have been reported with prednisolone and cyclophosphamide.

\textbf{REFERENCES}


Suboerali, et al. Pleural thickening is not always mesothelioma.