

Erdheim-Chester disease with epiphyseal and systemic disease

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Abstract

A case of Erdheim-Chester disease which affected the epiphysis and showed evidence of systemic disease is presented. Clinical and histopathological similarities with other forms of disseminated Langerhans' cell histiocytosis are noted, particularly reaction of infiltrating histiocytes for S100 and HLA-DR.

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Erdheim-Chester disease is a rare histiocytic disorder of adults characterised by an infiltrate of lipid laden foam cells in the bone marrow and a generalised sclerosis of the long bones that usually spares the epiphysis.^{1,2} Although systemic disease has been reported, this condition is usually separated from disseminated forms of histiocytosis X or Langerhans' cell histiocytosis on the basis of age and the clinical and radiological patterns of bone and systemic disease, as well as the fact that Langerhans' cells have not been positively identified in the lesion.^{2,3}

Case history

A 72 year old Greek farmer was admitted

with a two month history of fever (38.5-39°C), generalised arthralgia predominantly affecting the large joints of legs and arms, and severe pain on pressure over the tibial shaft. Eighteen months earlier, he had sustained weight loss and polydipsia and polyuria. Diabetes insipidus was diagnosed in a German clinic and he was treated with pitressin. A lung biopsy specimen taken at that time showed interstitial fibrosis. He also had a two year history of angina due to ischaemic heart disease. On admission, apart from tenderness over bony tibiae, clinical examination was unremarkable. Investigations showed a haemoglobin concentration of 13.2 g/l, platelet count of $486 \times 10^9/l$, a white cell count of $9.6 \times 10^9/l$, an ESR of 101 mm/first hour; blood urea, electrolytes, blood lipids, liver function tests and plasma proteins (including protein electrophoresis) were all normal. Serological tests for syphilis, antinuclear and rheumatoid factors were negative. A chest x ray picture showed diffuse interstitial shadows in both lungs. x Ray pictures of the tibiae and femora showed a generalised mottled sclerotic coarsening of the medullary bone (fig 1A). A bone scan showed increased uptake in these and both forearm bones (fig 1B). A computed tomogram of the skull showed no abnormality.

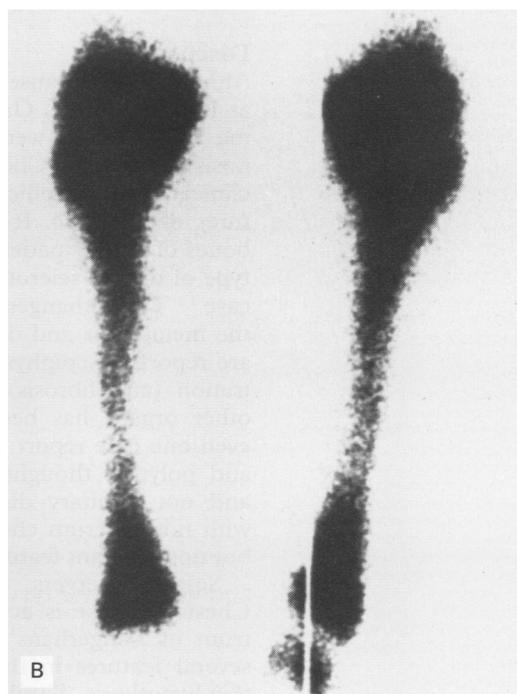
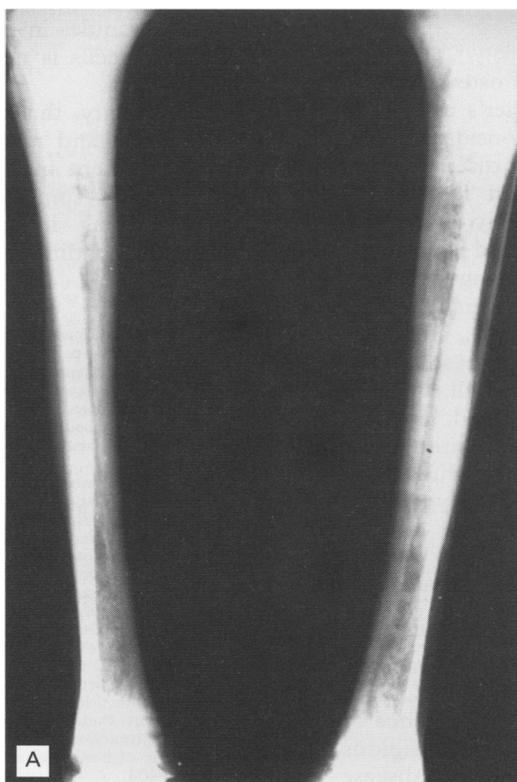


Figure 1 (A) X ray and (B) bone scan of both tibiae showing diffuse osteosclerosis and increased uptake of isotope throughout the entire length of both bones.

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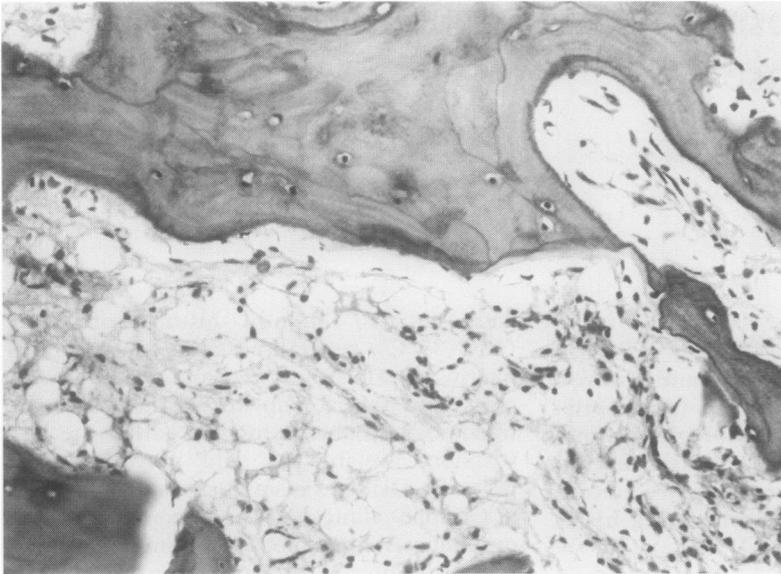


Figure 2 Marrow infiltrate of numerous foamy histiocytes and scattered chronic inflammatory cells between woven bone trabeculae containing prominent cement lines (haematoxylin and eosin).

Pathology

A biopsy specimen taken from the anterior surface of the upper end of the tibia showed that the marrow spaces were filled with numerous foamy histiocytes (fig 2); there was patchy cellular fibrous tissue and scattered inflammatory cells, mostly lymphocytes with a few neutrophil polymorphs and no plasma cells. Trabecular bone was largely woven in type with irregular margins and a prominent mosaic cement line pattern. Infiltrating cells were positive for leucocyte common antigen, HLA-DR, CD68 (macrophage associated antigen) and S100, with monoclonal antibodies, PD7/26, CR3/43, KP1 and S161, respectively. Ziehl Nielsen and periodic acid Schiff stains were negative.

Discussion

Although other causes of osteosclerosis, such as Paget's disease, Gaucher's disease, myeloma and fluorosis were considered, the diagnosis of Erdheim-Chester disease best fits the clinical, radiographic, and histological features of this case. It mostly affects the long bones of elderly patients and is a cause of the type of diffuse sclerotic changes noted in this case.^{1,2} These changes are usually restricted to the metaphysis and diaphysis, although there are reports of epiphyseal disease.¹ Lung infiltration (and fibrosis), as well as disease of other organs has been noted, and there is even one case report documenting polydipsia and polyuria thought to be due to hysteria and not pituitary disease.³ Hyperlipidaemia with raised serum cholesterol is a recognised but not constant feature.

Some observers believe that Erdheim-Chester disease is actually part of the spectrum of Langerhans' cell histiocytosis,⁴ and several features in the present case support this hypothesis. Similarities with Langerhans' cell histiocytosis include the presence of lung infiltrates and fibrosis, diabetes insipidus, and bone disease. Erdheim-Chester disease was

called lipoid granulomatosis by Jaffe,³ who like others² regarded this condition as distinct from disseminated forms of Langerhans' cell histiocytosis, in particular Hand-Schüller-Christian disease. The latter mostly affects children and is rare in the elderly; it produces infiltrates in the lungs and other organs, commonly affects the pituitary gland, and produces well defined osteolytic lesions in bone.² Exceptions to the typical clinical and radiological pattern of tissue disease by Hand-Schüller-Christian disease are well recognised, and Erdheim-Chester disease itself shows some heterogeneity of bone and systemic pathology. In the late phase of Hand-Schüller-Christian disease foamy histiocytes and fibrosis are the main features^{2,3}; these pathological features are also seen in Erdheim-Chester disease. Immunohistochemical staining of cases of classic Erdheim-Chester disease with antibodies directed against S100 protein, which is known to be present on Langerhans' cells,⁵ has not identified S100 on infiltrating histiocytes before.^{6,7} It has been noted on a case of bilateral, symmetrical eosinophilic granulomas of both tibiae, however, which showed some similarities with Erdheim-Chester disease.⁸ In the present case, infiltrating histiocytic cells stained strongly for S100, as well as HLA-DR and CD68, antigens known to be present on cells in eosinophilic granuloma.⁹ In addition to these immunophenotypic similarities, the previously noted clinical, radiological, and histopathological overlap with localised and disseminated forms of Langerhans' cell histiocytosis, and its predominance in the elderly, suggest that Erdheim-Chester disease may represent one of a spectrum of changes occurring in old lesions of disseminated Langerhans' cell histiocytosis. Ultrastructural identification of Birbeck granules in Erdheim-Chester disease infiltrating cells is necessary to confirm this possibility.

In summary, this case highlights the variable clinical and radiological features which may be present in Erdheim-Chester disease and provides some immunophenotypic evidence arguing in favour of its inclusion among the conditions of Langerhans' cell histiocytosis.

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