

Quiz

A 49-year-old man presented with bilateral proptosis of 2 years' duration. He also complained of generalised bone pain, polyuria, and polydipsia. A physical examination was unremarkable except for bilateral proptosis—right eye 28 mm and left eye 26 mm (normal level, ≤ 20 mm) [Fig 1]. His eye movements, both fundi and intra-ocular pressures, were all normal. The thyroid gland was not enlarged and his baseline biochemical evaluation was normal. A water deprivation test confirmed that he had central diabetes insipidus and his bone scan showed multiple areas of increased uptake. What is the likely diagnosis?

Discussion

The patient had Erdheim-Chester disease. Histiocytosis is a group of disorders characterised by the infiltration of monocytes, macrophages and dendritic cells into the affected tissues. It is divided into two varieties: Langerhans' cell histiocytosis and non-Langerhans' cell histiocytosis. Langerhans' cell histiocytosis is further classified into: (1) Letterer-Siwe disease, (2) Hand-Schüller-Christian disease, (3) eosinophilic granuloma, and (4) congenital self-healing reticulohistiocytosis.¹

Hand-Schüller-Christian disease involves the posterior pituitary, causing diabetes insipidus. It can also cause exophthalmos, and osteolytic bone lesions involving the axial skeleton.

Our patient had features suggesting Erdheim-Chester disease. This was first described by Jacob Erdheim and William Chester in 1930.² The clinical presentation, proptosis and diabetes insipidus, is similar to Hand-Schüller-Christian disease but the bone lesions are osteosclerotic, involve the



FIG 1. The patient showing bilateral proptosis

metaphyseal regions of the long bones and it usually occurs in an older age-group. In our patient, 99m Tc-methylene diphosphonate bone scintigraphy showed areas of increased uptake in the left orbit and nasomaxillary region. There was bilateral symmetrical tracer uptake in the diaphyseal regions of both humeri, the metadiaphyseal regions of both femora and foci of increased uptake were also seen in both greater trochanteric regions and in the tibiae, with epiphyseal sparing (Fig 2).³

The points that clinch the diagnosis are the histology and immunohistochemistry of these tumours. Langerhans' cell histiocytosis is characterised by aggregates of pathological Langerhans' cells, macrophages and giant histiocytes with nuclei with irregular margins. They are positive for S-100 + CD-1a on immunohistochemistry and show Birbeck granules on electron microscopy. In our patient, a biopsy of his retro-orbital region revealed sheets and aggregates of foamy macrophages (Fig 3) with occasional 'Touton type' giant cells (Fig 4). These macrophages were

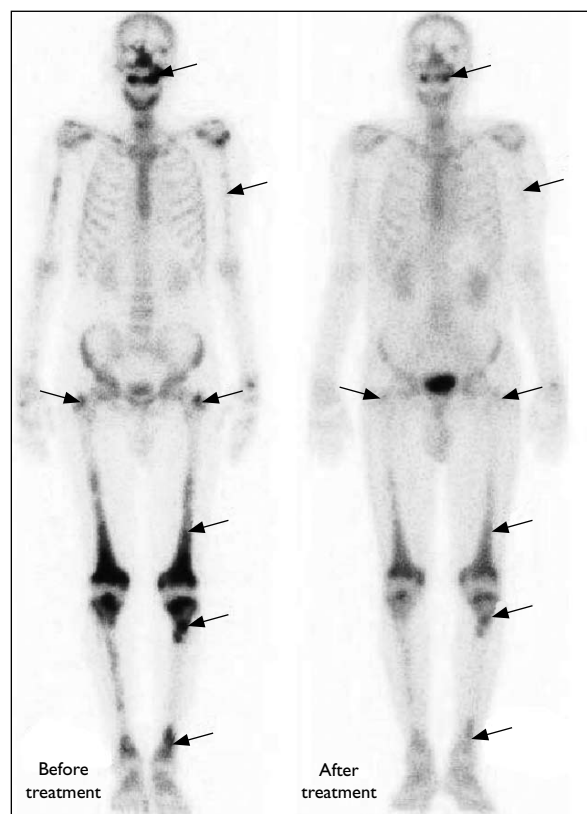


FIG 2. 99m Tc-methylene diphosphonate bone scintigraphy showing increase tracer uptake in highlighted regions (before treatment with interferon) and marked decrease in tracer uptake (after treatment with interferon)

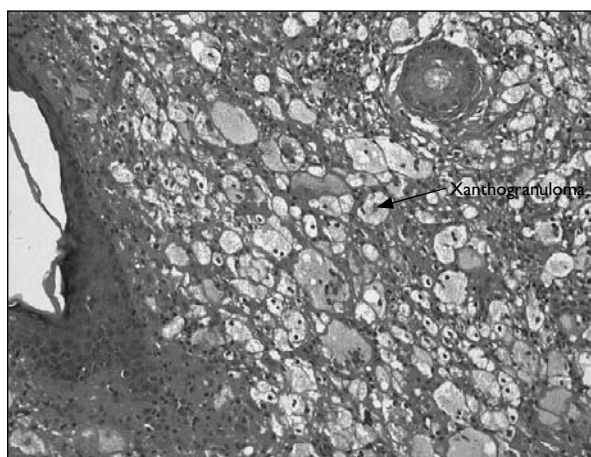


FIG 3. Photomicrograph showing xanthogranuloma (H&E, x 200)

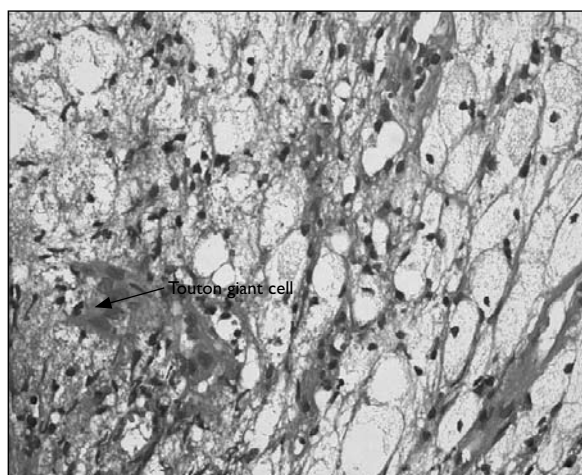


FIG 4. Photomicrograph showing 'Touton type' giant cells (H&E, x 400)

positive for KP1 and negative for S-100 and CD-1a.

This disease is an uncommon disorder and there is no consensus on therapy. Various modalities including steroid therapy, immunomodulatory therapy, and radiotherapy have been unsuccessful. Most of these patients do not survive beyond 32 months from the time of diagnosis. A recent case series has reported promising results with interferon $\alpha 2b$.⁴ Our patient was started on interferon $\alpha 2b$, 3 million units subcutaneously thrice weekly along with prednisolone 20 mg once daily. The prednisolone was tapered off and stopped entirely after 2 months. After 3 months there was an improvement in his proptosis—exophthalmometry of the right eye was 26 mm and the left eye 24 mm. Repeated bone scintigraphy showed a marked decrease in tracer uptake in the previously mentioned areas (Fig 2).

We decided to continue treating him with interferon $\alpha 2b$ at the same dose and review him again after 3 months. We anticipate that he will require this

treatment long-term.

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