Histiocytosis X Involving the Skeletal System in a Black Girl

R. J. JACOBSON, M. L. LIFSCHITZ, J. J. JUDELMAN

SUMMARY

A 12-year-old Black girl presented with histiocytosis X diffusely involving her skeletal system. She has been followed for a year, and during this period has been treated with local radiotherapy to three involved skeletal sites, and has received two 6-week courses of vinblastine and prednisolone. Both the absence of extraskeletal involvement and her response to treatment favour a good prognosis.

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Histiocytosis X or idiopathic histiocytosis encompasses a group of diseases, of unknown aetiology, which have in common proliferating histiocytes and bone lesions which may be grossly and radiologically indistinguishable.[1] Depending on the initial extent of the disease and the subsequent course, they have been classified into three categories: Letterer-Siwe disease represents the acute disseminated variety; Hand-Schüller-Christian disease the chronic disseminated variety; and eosinophilic granuloma the variety localised to bone.[2] There is considerable clinical and pathological overlap between these categories.

Idiopathic histiocytosis occurs mainly in Whites. Avery *et al.*,[3] reporting on 40 cases of histiocytosis X from Baltimore, which has a large Negro population, noted only 3 Negro patients. Histiocytosis X in Black patients has rarely been documented. Siew[4] reported a fatal case of Letterer-Siwe disease in a Black male infant. We wish to report a case of histiocytosis X involving multiple bones in a young Black girl.

CASE REPORT

The patient, a 12-year-old prepubertal Black girl, was admitted to hospital in July 1973 because of a one-month history of a painful left thigh and difficulty in walking. For 2 years prior to admission she was aware of a progressively enlarging painless lump on the crown of her head. She had no polyuria or polydypsia and her family history was non-contributory. On examination her height was 131 cm and her weight 30 kg. A soft, fluctuant, non-tender mass, measuring 5 × 7 cm was attached to the top of the skull. She had a thoracic kyphosis. The proximal third of her left femur was tender and swollen and there was decreased movement of the left and right hip joints. There was no organomegaly and no clinical evidence of pituitary or thyroid dysfunction. There was no exophthalmos and her ears, nose and throat were normal. The cardiovascular and chest examinations were within normal limits.

Haematology Clinic, Johannesburg Non-European Hospital and Department of Medicine, University of the Witwatersrand, Johannesburg

R. J. JACOBSON, M.B. B.CH., F.R.C.P.
M. L. LIFSCHITZ, M.B. CH.B.
J. J. JUDELMAN, M.B. B.CH.

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Laboratory Investigations

Haemoglobin was 12,0 g/100 ml, white blood cell count 5 500/mm^3 and platelet count 235 000/mm^3. The blood urea, serum cholesterol, calcium, phosphorus and alkaline phosphatase were all normal. Total serum proteins were 7,3 g/100 ml (albumin 3,7 g/100 ml) and serum immunoglobulins were normal. *In vitro* thyroid function tests and the glucose tolerance test were normal. After adequately induced hypoglycaemia with intravenous insulin (0,1 units/kg), the serum growth hormone (measured by radioimmune assay) increased from a basal value of 0,5 ng/ml to more than 10 ng/ml. There was no evidence of diabetes insipidus as assessed by serial serum and urine osmolalities during water deprivation.

Radiological Findings

Numerous osteolytic lesions were noted throughout the skeletal system (Fig. 1). There was collapse and anterior wedging of the 7th, 10th, and 12th thoracic vertebrae, and there were multicystic osteolytic lesions involving the intertrochanteric region and upper third of the left femur (Fig. 2), and the upper half of the right tibia (Fig. 3A). The right acetabulum protruded inwards as a result of the extensive involvement of the right iliac bone (Fig. 2).

Pathology

A biopsy of the skull tumour demonstrated sheets of clear histiocytic cells surrounded by thin fibrous bands. The histiocytes did not contain lipid.

Progress

The patient was treated with local radiotherapy (600 rads) to the skull tumour and the involved portion of the left femur. Intravenous vinblastine 6 mg/m^2/week was administered for 6 weeks and daily prednisolone 2 mg/kg

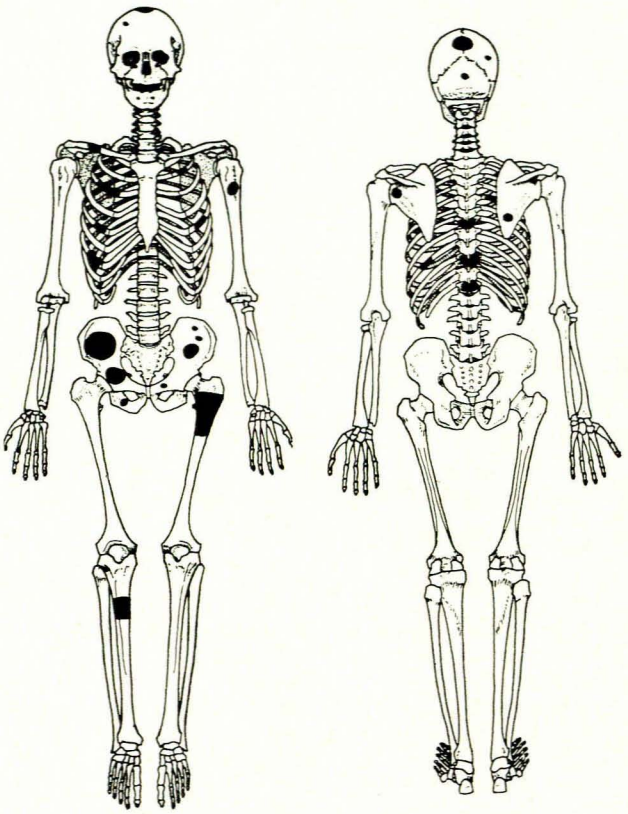

Fig. 1. The blackened areas on the anterior and posterior views of the skeleton represent the anatomical sites of the numerous osteolytic lesions in the patient.

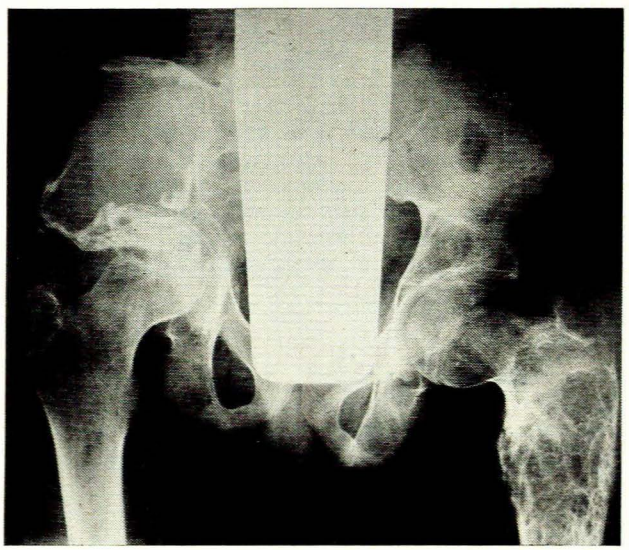

Fig. 2. X-ray film of pelvis showing a large multicystic osteolytic lesion involving the intertrochanteric region and upper third of the left femur. The right iliac bone is severely involved and the right acetabulum protrudes inwards.

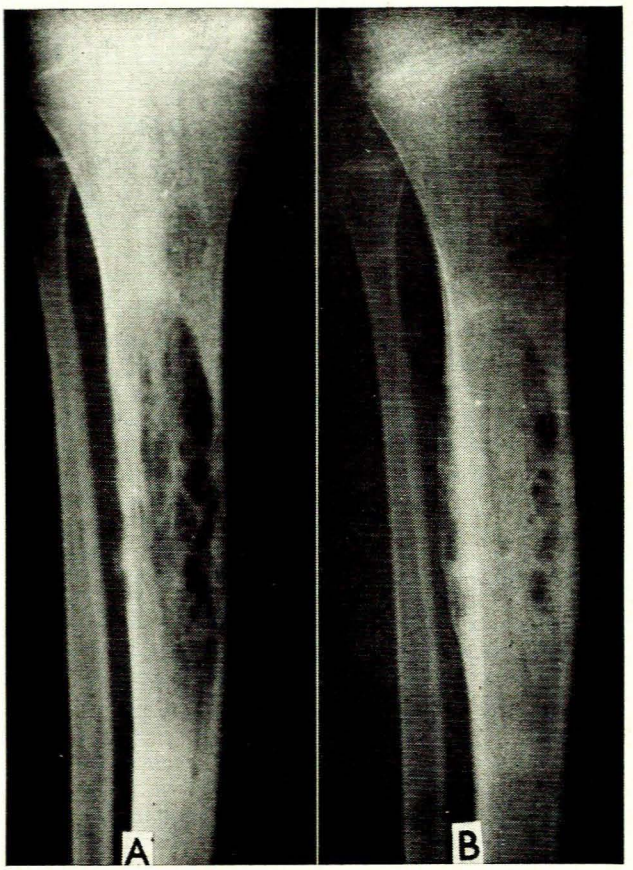

Fig. 3. A — X-ray film of the right tibia showing the multicystic lesion and cortical and periosteal erosion on the lateral aspect of the tibial shaft. B — X-ray film of the right tibia after radiotherapy and chemotherapy showing the healing and subperiosteal new bone formation covering the previously eroded areas.

was taken orally for the same period. The thigh pain and difficulty in walking steadily improved over the next 2 months and the skull tumour decreased in size. In November 1973 the right tibial lesion expanded, causing signs of inflammation and pain. Again local radiotherapy (600 rads) was given, with a beneficial response, and the 6-week course of vinblastine and prednisolone was repeated. The patient has remained well and asymptomatic for the last 6 months, and in June 1974 repeat radiological examination revealed healing of the femoral, pelvic, skull and tibial lesions (Fig. 3B).

DISCUSSION

Our patient had, on pathological examination of a skull biopsy specimen, a predominance of histiocytes, and clinically she had numerous skeletal lesions, with no extraskeletal involvement being demonstrated—these features are consistent with a diagnosis of multiple eosinophilic granuloma of bone. In eosinophilic granuloma, eosinophils and granuloma formation need not be present,

and hyperplastic histiocytic proliferation may be the only histopathological finding.[5]

Eosinophilic granuloma of bone usually presents before the age of 10 years, although cases with onset in adulthood are not uncommon.[6] Males are affected more frequently than females. The skeletal system may be involved unifocally or multifocally, and the lesions occur most commonly in flat bones (skull, ribs, pelvis and scapula) and next commonly in the long bones and dorsilumbar spine.[1] Involved vertebrae may either present as wedge-shaped defects, owing to the collapse of the anterior portion of the vertebra, or may be uniformly flattened. Our patient's short stature was primarily due to vertebral involvement. In the pelvis a common site of involvement is the area in the ileum immediately above the acetabulum (Fig. 2).[7]

Treatment of eosinophilic granuloma usually involves surgical excision or curettage. A tissue irradiation dose in the range 300 - 600 rads is generally sufficient to treat a primary lesion, or to eradicate a recurrence following surgery.[1] Pathological fractures[8] can occur at sites of severe cortical involvement and these may require orthopaedic intervention and radiotherapy. Chemotherapy is recommended for multifocal eosinophilic granuloma and disseminated histiocytosis.[1,6] A variety of chemotherapeutic agents have been used, and the vinca alkaloids and corticosteroids have had the widest usage. The need for maintenance therapy has been stressed by Vogel and Vogel,[1] since original tumours may recur and new lesions develop if therapy is discontinued. The duration of therapy is weighed against unpleasant side-effects, and the continuous use of corticosteroids, particularly in growing children, may create numerous problems.

The factors which appear to limit the prognosis in histiocytosis X are an onset before 3 years of age, extraskeletal involvement (particularly of the skin) and pancytopenia due to bone marrow infiltration.[1,8] Lieberman *et al.*[6] reported no deaths in a group of 74 patients with unifocal or multifocal eosinophilic granuloma, but noted considerable morbidity associated with the multifocal lesions.

Our patient has none of the features which severely limit the prognosis in histiocytosis X, and appears to have responded well to her treatment. Since she is prepubertal, and a growing child, it was felt best to limit the use of corticosteroids to episodes of acute exacerbation of her disease.

ADDENDUM

Since submitting this case report, a second case of histiocytosis X in a young Coloured girl has been assessed by us. The patient, 7 years old, presented with a solitary tumour of her left parietal bone. Histological examination of a biopsy specimen revealed eosinophilic granuloma. The skull lesion has responded well to radiotherapy.

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