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Rare Presentation of a Rare Disease (Erdheim-Chester disease): A Case Report

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ABSTRACT

Erdheim-Chester disease (ECD) was first reported by J. Erdheim and W. Chester, in 1930. There are less than 250 reported cases till date. We report a case of ECD in a 16-year-old Malay male, who initially presented with elusive anemic symptoms with more specific symptoms of bony pain, cardiorespiratory and hepatic involvement evolving as the disease progressed.

Key Words:
Erdheim-Chester disease

CASE REPORT

16-year-old Malay male, with no known past medical illness, presented one year ago with complaints of generalized malaise, palpitation, giddiness, headaches, anemia and fever. He was suspected to have leptospirosis with IgM being positive on blood investigations and was treated accordingly.

Over the last one year he had multiple admissions to the hospital for similar symptoms. During this period, he developed multiple cervical lymph nodes and complained of bleeding per rectum. A complete blood picture showed unspecific moderate microcytic anemia secondary to blood loss, with vacuolated neutrophils which suggested infection. There were no blast cells noted.

Four months ago, patient was readmitted with severe anemic symptoms and bony pain in the limbs. He also had a distended painful abdomen. On general examination, patient was cachexic and abdominal examination revealed presence of ascites. There was no evidence of central nervous system involvement.

On investigation, plain chest X-ray showed cardiomegaly and Echo studies of the heart revealed poor left ventricular systolic function with ejection fraction of 26%. In addition to the global hypokinesia, there was a dilated left ventricle and a mild tricuspid regurgitation with EPASP of 30mmHg.

The results of laboratory tests showed low haemoglobin levels, markedly raised C-reactive protein and ESR levels and low serum albumin levels. Urine for Bence-Jones protein was negative. Plasma protein electrophoresis was normal. (Table I)

Peripheral blood smear was suggestive of iron deficiency anemia with no lymphoma/ leukemic cells seen.

Plain X-ray of upper and lower limbs showed multiple sclerotic and lytic lesions over the metaphyseal regions of both humeri, femur and tibia (Fig 1). The radiologist considered the lesions to be more likely suggestive of leukemia, with infiltrative metastasis to be ruled out. Ultrasound of the abdomen shows features suggestive of leukemic infiltration of liver and kidney.

An endoscopic liver biopsy was inconclusive. A trephine biopsy of the right tibial metaphysis was reported as sheets of foamy histiocytes between bony trabculae that were CD68 negative with S-100 protein with markedly reduced normal haemopoeitic marrow precursor cells and no obvious malignant cells (Fig 2).

Patient was then referred to Hematology unit for further management. A course of intravenous corticosteroid showed some improvement in the bony pain and liver size. However chemotherapy/interferon-α could not be initiated as planned due to recurrent septicemia and respiratory failure and he succumbed after four months of diagnosis.

DISCUSSION

Erdheim-Chester disease (ECD) or polyostotic sclerosing histiocytosis is a non familial xanthogranulomatous, systemic histocytosis with unknown aetiology and pathogenesis that predominantly affects the bone and viscera[1]. The age of presentation ranges from 7 - 84 years with a male-to-female ratio of 1:3. The varied presentation of the disease adds to the delay in diagnosis.

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Table I: Laboratory investigation results

Test	Result	Normal
Hemoglobin level (Hb)	5.1g/dL	13.3-16.2 g/dL –adult male
Platelet count	173 x 10^9/L	165-415 x 109/L
Total white blood cell count (TWBC)	4.3 x 10^9/L	3.54-9.06 x 109/L
Serum calcium	2.42 mmol/L	2.2-2.6 mmol/L
Albumin	19g/L	40-50 g/L –male
Free thryoxine level(T4)	11.23pmol/L	5.4–11.7 µg/dL
Thyroid stimulating hormone (TSH)	4.94mIU/L	0.34–4.25 µIU/mL
Erythrocyte sedimentation rate (ESR)	62mm/Hr	Adult male: 0–15 mm/h
C – reactive protein (CRP)	104mg/d	0.2–3.0 mg/L
Serum intact parathyroid hormone (iPTH)	2.1pmol/L	8–51 ng/L
Growth hormone level	23ug/L	
Urine for Bence Jones protein	Negative	
Plasma electrophoresis	Negative	

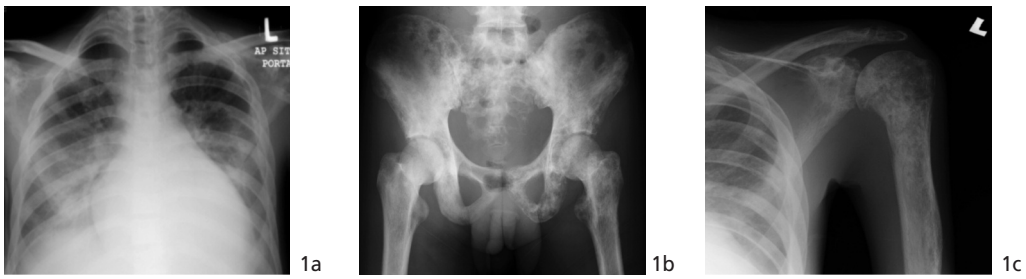

Fig. 1: Chest X-ray showing cardiac involvement (1a), pelvic X-ray (1b) and shoulder X-ray (1c) showing multiple lytic/sclerotic lesions.

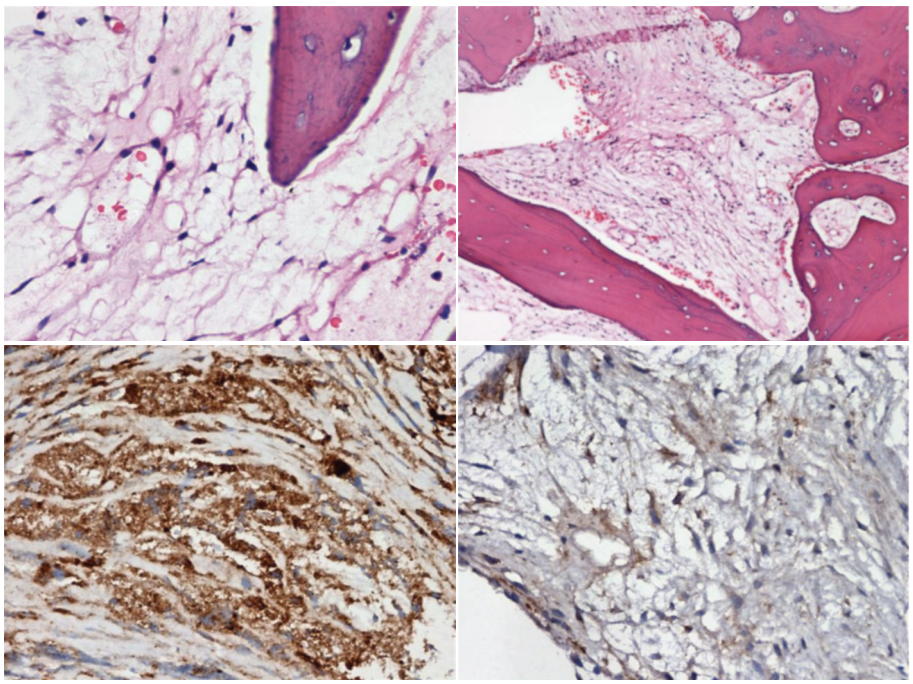

Fig. 2: Sheets of foamy histiocytes (CD68 positive with S -100 protein negative) seen in between the bony trabecules.

Bone pain often localized to metaphysis and diaphysis was the most common symptom. Pain abdomen and backache are commonly caused by retroperitoneal fibrosis. Patients present with diabetes insipidus due to histiocytic granulomatous infiltration of the pituitary stalk while dyspnea is due to interlobular septal and pleural thickening. Retroconal fat and optic nerve sheath involvement presents with exopthalmos and disturbances in vision (fluttering of peripheral vision and diplopia [3]) while neurological signs may include ataxia. Valvular lesions (mitral and aortic) are seen leading to atrial enlargement [3] and infiltration of the skin leads to Xanthomas. Involvement of the liver and lymph nodes has not been consistently quoted in literature.

Several differential diagnoses become possible based on presenting feature, necessitating a battery of investigations. Metabolic and endocrinal disorders, malignancies, multiple sclerosis, thyroid abnormalities are some of the differential diagnoses that are considered.

Radiological features have been consistent and useful in diagnosis. Bilateral patchy or diffuse increase in density of the involved areas with coarsened trabecular pattern and minor changes, or sparing of the epiphysis is commonly seen. MRI is useful with involvement of the brain and bone where typical changes are noted [2].

Elisa Dion *et al.* noted bilateral and symmetric osteosclerosis of the diaphysis of the long bones present in 98% of the visible lesion in the bone [4].

Organ biopsies have been frequently inconclusive [2]. Bone biopsy is the gold standard in diagnosis. The typical histology of such bone lesions is described to be showing infiltration by clusters of lipid laden or foamy histocytes with chronic infiltration and Touton-type giant cells, usually surrounded by fibrosis and possibly fat necrosis [3]. Further, the histiocytes are typically, CD68 positive, CD1a negative and have variable expression for S-100 protein [3] with absent Birbeck granules. The histiocytes are also said to be Factor XIIIa positive [5].

ECD as a reactive or neoplastic process has been debated. Vencio EF *et al.*[1] supported some cases of ECD to be clonal neoplastic disorders of putative histiocytic differentiation.

The treatment of ECD consists of surgical debulking, high dose corticosteroid therapy, cyclosporine, and radiation therapy and interferon-α therapy. However more research is necessary to prove the efficacy of the therapy.

In the present case, the infrequent age of presentation, involvement of organs (liver and lymph nodes), interpretation of the X-rays and ultrasound of abdomen (reported to be more suggestive of leukemia or metastasis), inconclusive liver biopsy, uncommon tricuspid valve involvement and ventricular hypertrophy were some of the parameters that led to the delay in diagnosis that is often associated with this condition.

Prognosis of the disease is poor and mortality is high due to associated complications.

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