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**Case Report**

# Erdheim-Chester Disease with Involvement of Axial Skeleton: A Rare Presentation of Rare Disease

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**Abstract**
*Erdheim-Chester disease (ECD) is a non-Langerhans cell systemic histiocytosis with an unknown etiology and pathogenesis. In this illness there is generalized sclerosis of the long bones that does not involve the epiphysis and axial skeleton. The extraskeletal sites may also be involved such as the retroperitoneal space, lungs, kidneys, brain, retro-orbital space, and heart .Here we report a case of 45 year old who presented with a chief complaint of back pain for 6 months duration. It was gradually increasing in intensity. On physical examination there was tenderness on palpation of the spinous process of thoracic vertebrae. He was diagnosed as Erdheim-Chester disease (ECD) on the basis of clinical , radiological and histopathological features followed by immunohistochemistry confirmation. Histologically, it shows diffuse inflammatory infiltrate comprising of lymphocytic aggregates with large foamy histiocytes, few Touton-like giant cells along with fibrosis. The histiocytes show positivity for CD68 and negativity for CD1a, S100 protein, langerin which differentiates it from Langerhans cell histiocytosis. Currently there is no effective therapy for this illness.*

**Keywords:** *Non-Langerhans cell systemic histiocytosis , Foamy histiocytes.*

## Introduction

Erdheim-Chester disease (ECD) is a very rare disorder in which there is spumous deposition of foamy histiocytes in various organs. [1] It is a non-Langerhans cell systemic histiocytosis with an unknown etiology and pathogenesis.[2] In this illness there is generalized sclerosis of the long bones that does not involve the epiphysis and axial skeleton.[3] The extra skeletal sites may also be involved such as the retroperitoneal space,

lungs, kidneys, brain, retro-orbital space, and heart.[4] Histologically, it shows diffuse inflammatory infiltrate comprising of lymphocytic aggregates with large foamy histiocytes, few Touton-like giant cells along with fibrosis.[5] The histiocytes show positivity for CD68 and negativity for CD1a, S100 protein, langerin which differentiates it from Langerhans cell histiocytosis. [6] We report a case of ECD in a 45 year old who presented with vertebral collapse. Currently there is no effective therapy for this illness.

**Background**

Our case might contribute to an increased awareness of this rare disease by stressing the involvement of axial skeleton which is extremely rare site of presentation.

**Case Presentation**

A 45 year old male presented with a chief complaint of back pain for 6 months duration. It was gradually increasing in intensity. On physical examination there was tenderness on palpation of the spinous process of thoracic vertebrae.

**Investigations**

MRI spine was performed. T2WI sagittal view revealed diffuse hypointense signal involving body and posterior element of D3 vertebrae. 99mTc bone scintigraph scan also showed increased uptake of thoracic vertebrae. The routine haematological and biochemical investigations like complete blood count, KFT, LFT were normal. Erythrocyte sedimentation rate (ESR) was mildly increased. Serum parathormone and 25-hydroxy vitamin D levels were normal. Later on CT guided biopsy of this lesion was performed which on the histopathology revealed diffuse infiltrates of mononucleated cells, some of which had reniform nuclei. The intervening areas showed foamy histiocytes, numerous Touton giant cells along with fair number of eosinophils. The immunohistochemistry showed CD68 positivity and S-100 protein and Langerin negativity. These results confirmed that the histiocytes in our case were not of LCH. The final diagnosis of ECD was thus rendered.

**Differential Diagnosis:** The histological features bear resemblance with Langerhans cell histiocytosis. However, in contrast to LCH; the histiocytes in ECD are CD68 positive and S-100 protein and Langerin negative which was in accordance to our immunohistochemistry findings. Taken all findings together we gave a final diagnosis of ECD.

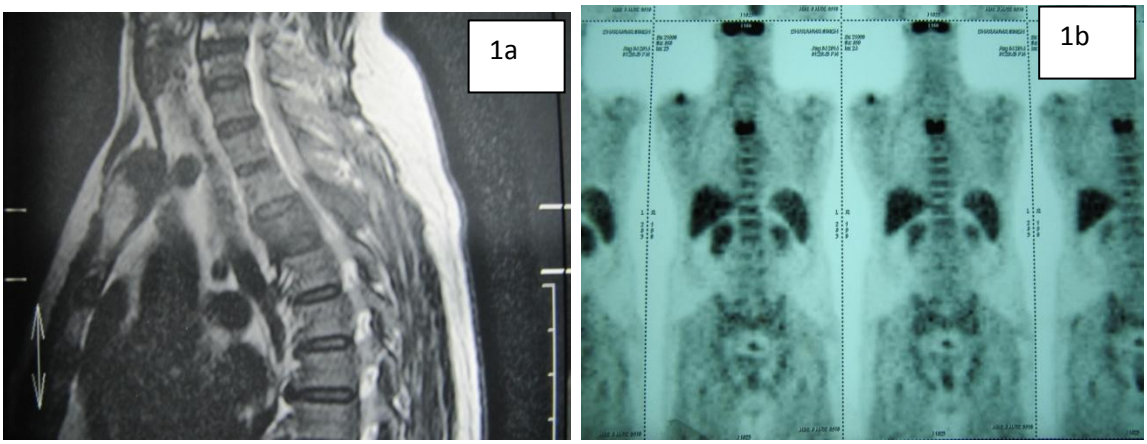


**Figure1a:** MRI cervical spine T2WI sagittal view shows diffuse T2WI hypointense signal involving body and posterior element of D3 vertebrae.**1b:** 99mTc bone scintigraph scan showing increased uptake of thoracic vertebrae

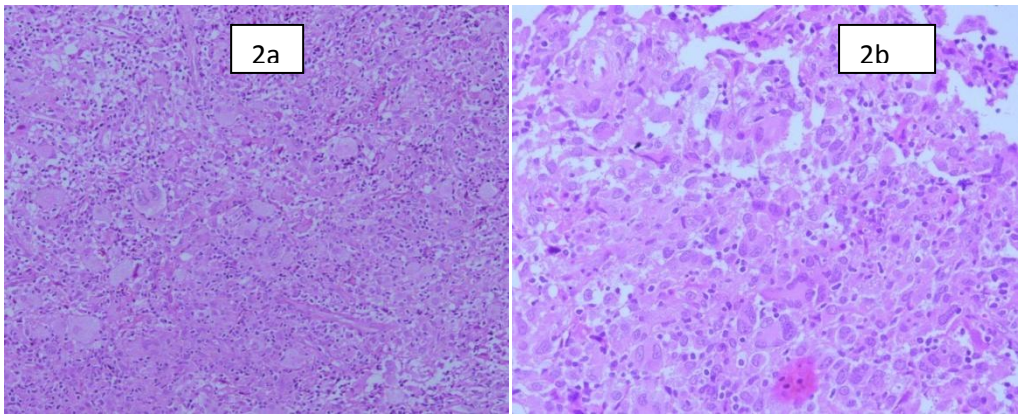


**Figure 2a:** Photomicrograph showing diffuse inflammatory infiltrate comprising of lymphocytes, histiocytes and touton type giant cells. (H&E; 10X) **2b:** Photomicrograph showing histiocytes with abundant pale staining and foamy cytoplasm without granuloma formation. (H&E; 40X)

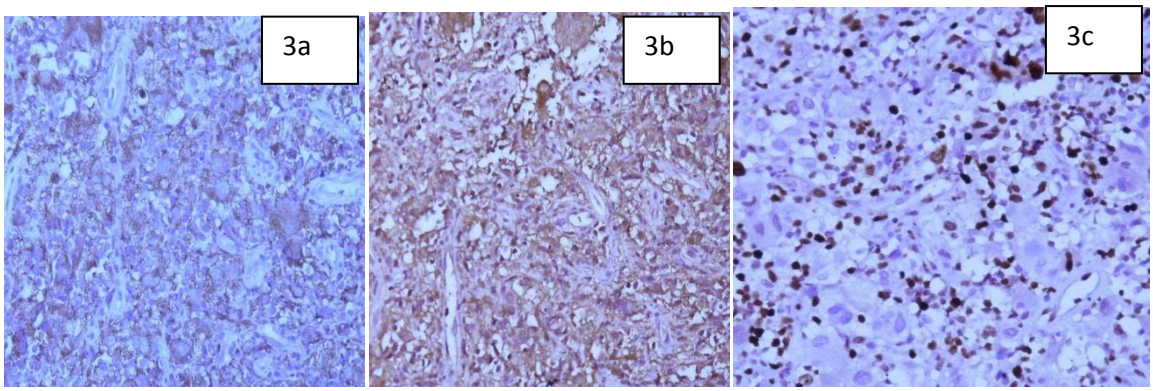


**Figure 3a:** Photomicrograph showing positivity for CD68; **3b:** Osteopontin postivity; **3c:** Ki 67positivity. (Immunohistochemistry; 20 X)

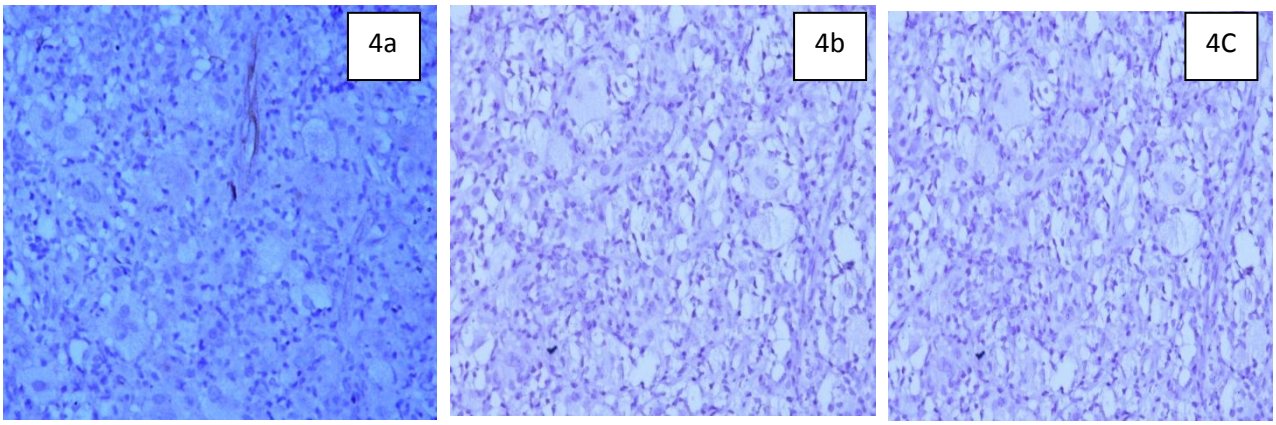


**Figure 4a:** Photomicrograph showing negativity for CD23; **4b:** Langerin negativity;
**4c:** S100 negativity. (Immunohistochemistry; 20X)

**Discussion**

ECD is a rare disease which was originally described as "Lipid Granulomatosis" in 1930 by Jakob Erdheim and William Chester.[7] The disease has unknown etiology and pathogenesis. The clinical presentation may vary from an indolent focal disease to a life threatening complications. The most common presenting symptom of this disease is bone pain. Veyssier-Belot et al stated that besides bone pain patients can present with diabetes inspidus and exopthalmos. [9] It primarily affects adults between 5th to 7th decades of life. However a very few cases in younger age group have also been

reported.[10,11] There is slight male preponderance. [12] Our patient was 45 years old male. The diagnosis of this disease is based on well established histological plus radiological criteria. None of the common imaging modalities that are used in ECD (i.e., radiography, 99mTc bone scintigraphy, computed tomography (CT) and MRI) are able to completely assess of lesions. However PET CT is the most ideal imaging modality among all. [12] 99mTc bone scintigraphs also aid in the diagnosis which exhibit abnormally strong labeling of involved bones. These patients show characteristic lytic or sclerotic changes in the long bones chiefly involving the diaphyseal & metaphyseal regions. The axial skeleton is usually spared. Our case was unusual in this respect that there was involvement of axial skeleton. Our patient presented with a sclerotic lesion at D3 vertebrae which was detected on MRI. 99mTc bone scintigraphs showed increased tracer uptake by D3 vertebrae. PET CT was not performed in our case. Dion et al in their study reported partial epiphyseal involvement of long bones with periostitis rimming on 99mTc bone scintigraphs in 11 cases of ECD.[13] Similarly Breuil et al reported a case of 58 years old man with diametaphyseal involvement of femoral tibial, radius and tarsal bones. [14]The histological diagnostic criterion is the presence of typical histiocytes in the lesion. These histiocytes are non langerhans foamy histiocytes as theses are CD 68 positive, CD1a and Langerin negative. Moreover, ultra structurally these histiocytes lack Birbeck granules. In our case histiocytes showed CD68 positivity whereas CD1a and Langerin negative. Electron microscopy was not performed. Although diagnosis wise ECD is less changeling due to well established clear cut diagnostic criteria but still a very high clinical suspicion and imaging characteristics will lead to a presumptive diagnosis that will help in triage of patients. However, since no definite cure exists, the goals of treatment should be prolonging life and maximizing their quality.

**Learning points**

1. Bilateral symmetric diametaphyseal osteosclerosis of long bones is common presentation. The axial skeleton is usually spared.
2. The presence of foamy histiocytes in biopsies taken from involved tissues or organs.
3. These histiocytes are show positivity for CD68 and negativity for CD1a, S100 protein, langerin which differentiates it from Langerhans cell histiocytosis.
4. Currently no therapy is available.
5. Though rare, awareness of this illness along with careful clinical and histopathological examination is warranted.

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**Conflict of Interest:** All authors have no conflicts of interest.

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