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Case Report

# Erdheim Chester disease: a subtle quiddity; the first case reported from Nepal ☆,☆☆,★

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ABSTRACT

Erdheim-Chester disease (ECD) is a rare entity throughout the world. This is the first case reported in Nepal. ECD is a rare aggressive, non-Langerhan's histocytosis of unknown origin with classical histological features. The patient usually presents with bone pain or skeletal symptoms along with other constitutional syndrome. Although, no definitive therapy has been approved, interferon-alfa (or Pegylated Interferon-alfa) is considered as initial therapy. In this case report, we found a patient with right-sided localized chest pain for which he was evaluated with bone scan and excisional bone biopsy and its findings support the diagnosis of ECD.



## Introduction

Erdheim-Chester disease (ECD) is a rare aggressive, non-Langerhan's histocytosis of unknown origin with classical histological features. It was first reported by Jakob Erdheim and William Chester in 1930. A typical histological findings resembles infiltration with foamy histocytes nested among polymorphic granuloma and fibrosis or xanthogranulomatosis with CD68 positive and CD1a negative immunohistochemical staining [1]. Approximately 550-650 cases have been described in literature since the first publication by the Austrian pathologist Jacob Erdheim and American pathologist William Chester [2,3]. To the best of our available data, this is the first case reported from Nepal. This report best describes a patient with typical clinical presentation and pathological findings in the context of this very uncommon disease.

*Abbreviations:* ECD, Erdheim-Chester Disease; CT, Computed Tomography; SPECT, Single-Photon Emission Computed Tomography; MDP, Methylene Diphosphonate.

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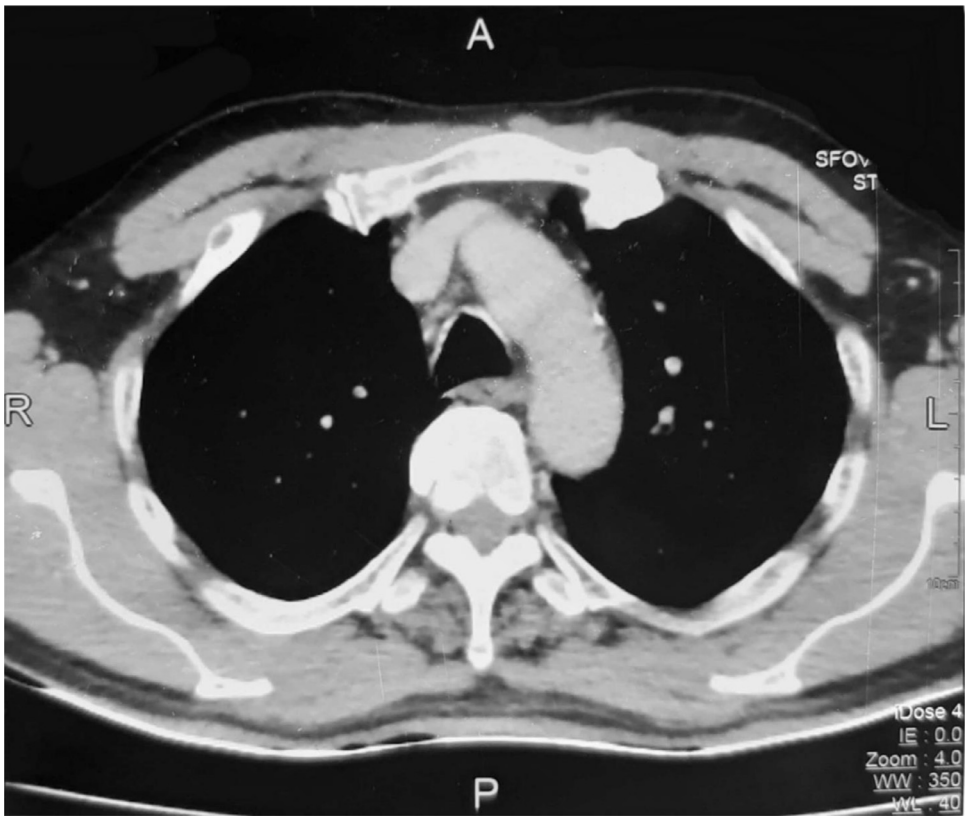


**Fig. 1 – CT-scan of Chest demonstrating expansile lytic lesion in anterior aspect of right second rib.**

## Case report

A 67-year-old male patient presented with right-sided localized chest pain for 6 months that was gradual in onset with low to moderate intensity and sharp in nature.

The patient underwent radiological studies, with chest X-ray demonstrating lytic lesion in right second rib. Computed tomography-scan of chest and abdomen was performed which showed expansile lytic lesion in anterior aspect of right second rib with mild-to-moderate peripherally enhancing soft tissue component (Fig. 1).

Bone scan 99M Tc-MDP showed uptake in the right second rib anteriorly. Delayed whole body and static images reveal multiple foci of increased tracer uptake in multiple dorsal/lumbar vertebrae and costovertebral joints. Also, Single-Photon Emission Computerized Tomography (SPECT) study of pelvis shows multiple foci of tracer uptake in bodies of lumbar vertebrae-spondyloartheritis (Fig. 2).

Excisional biopsy of lesion site second rib was taken and sent for microscopic examination which demonstrated tumor composed of sheets of foamy histiocytes intermixed with small lymphoid cells (Fig. 3). Infiltration of bony tissue was identified with surrounding fibrotic proliferation and few multinucleated giant cells. No eosinophils were seen (Fig. 4). A subsequent immunohistochemical study showed lytic lesion of second rib with histiocytic lesion, non-Langerhan's cell type which showed positivity for CD68 immunomarker. Thus, confirming the histiocytic nature of tumor cells and excluding a metastatic carcinoma. Ki-67 proliferation index was low (2%-3%). The immune markers CD1A, S100, SATB2, TLE1, and BCL2 were negative.

On further evaluation, full blood count profile, renal function test, and liver enzymes were found to be normal. His thyroid profile and parathyroid hormone were within normal limits. On examination of eye, his vision was normal (6/6 on both eyes), no other abnormality were detected. Other systemic findings were found to be within the normal limits.

The patient did not have any systemic involvement except skeletal system; patient was kept under observation after surgical excision of the bony lesion and advised for follow-up after 3 months. During follow-up, patient was evaluated clinically which showed stable status and repeat radiological investigations were suggested. However, due to poor financial condition, the requested investigations were refused.

## Discussion

ECD is a rare incurable hematological disorder till date with multifocal involvement, manifested by lesions within the peripheral skeleton [4]. It is slightly more frequent in males (M: F ratio 1.2-1.5:1) and is most often diagnosed during the fourth to seventh decade of life [5,6].

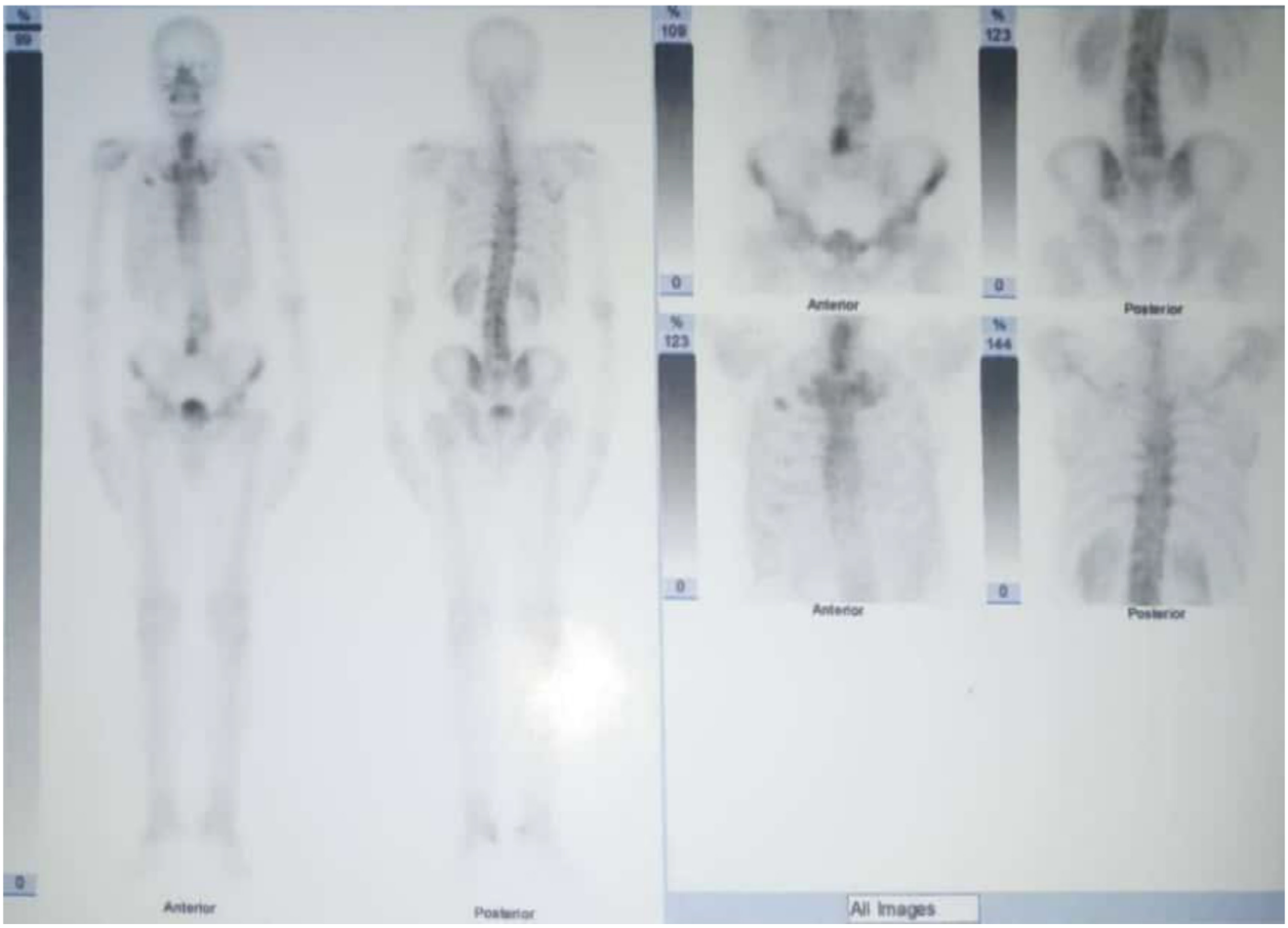


**Fig. 2 – 99mTc-MDP three phase bone scan showing uptake noted in right 2nd rib.**

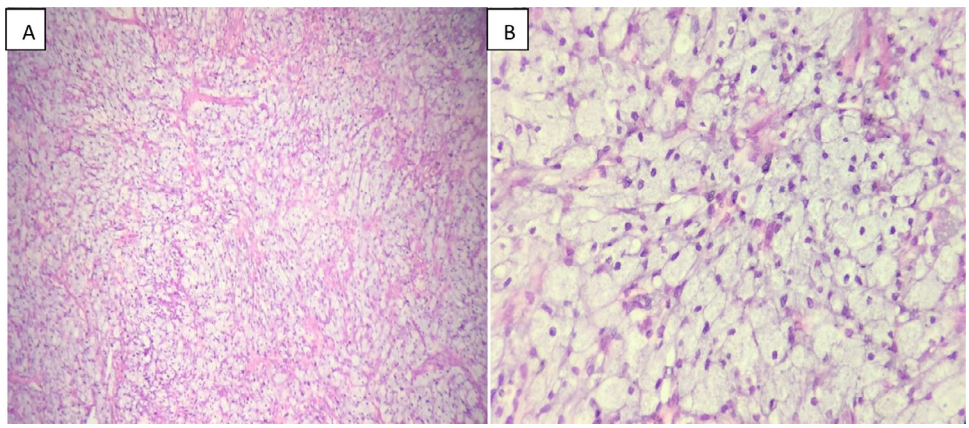


**Fig. 3 – (A, B) Section showing tumor composed of foamy histiocytes intermixed with small lymphoid cells.**

The etiopathogenesis of ECD is unknown; however, it is believed to be a reactive or neoplastic disorder. Recent findings of mutation in the BRAF proto-oncogene in >50% of ECD cases clearly add future complexity to the pathophysiology [2,7].

The diagnosis is usually challenging due to the rarity of the disease and clinical overlap with many other conditions. In the presented case, clinical presentation, morphologic features pathognomic radiographic findings, bone biopsy with immunohistochemical profile are all consistent with ECD. The definite diagnosis was confirmed by histological findings of positivity for CD68 immunomarker, thus confirming the histocytic nature of the cells and excluding a

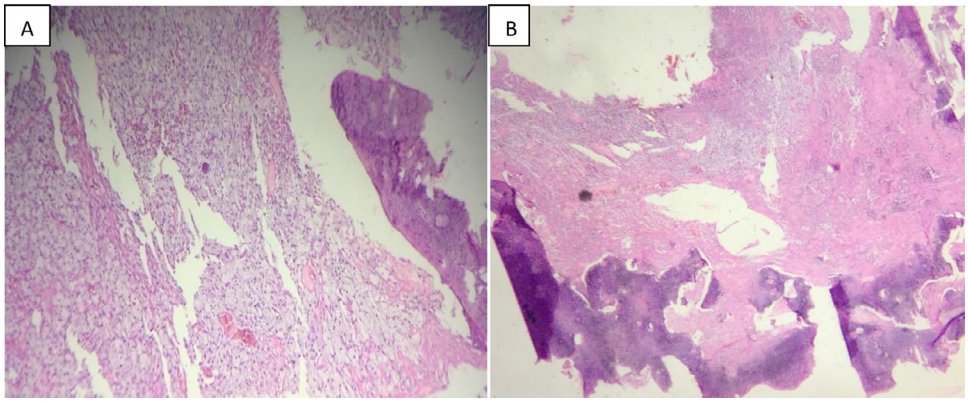


**Fig. 4 – (A, B) Section showing infiltration of bony tissue with surrounding fibroblastic proliferation and few multinucleated giant cells.**

metastatic carcinoma. Ki-67, S100, SATB2, TCE, and Bcl-2 were negative.

There is no definite first-line therapeutic regimen for ECD, however initial therapy seems to be administration of interferon-alfa (or Pegylated Interferon-alfa), and prolonged treatment significantly improves survival. The vinca alkaloids and anthracyclines also have been used most commonly [2,3]. Vemurafenib, an oral FDA approved agent targated to the BRAF protein for melanoma, shows drastic activity in patients with ECD whose tumor contains the same mutation [8]. In 2017, the US FDA approved Vemurafenib for this indication [9]. Furthermore, other reported treatment regimens includes corticosteroids, chemotherapy, anticytokine-directed therapy (Anakinra, Infliximab, and Tocilizummab), serine/threonine kinase inhibitors (Vemurafenib and Imatinib), bisphosphonates, autologous hematopoietic stem-cell transplantation, surgery, and radiation therapy [2,3,5].

Skeletal findings is one of the most common manifestations described both at presentation and during the course of disease that is, bilateral and symmetrical cortical osteosclerosis of diaphyseal and metaphyseal regions along with symmetrical and abnormally increased labeling of distal ends of long bones of lower limbs and sometimes the upper limbs, on 99tc bone scintigraphy [1].

A part from bony symptoms, central nervous system involvement (diabetic insipidus) is quite frequent in ECD low level of IGF-1 have also been reported in some cases. Additionally, very few literature have also mentioned the involvement of testes and adrenal glands in this rare disease [2,3,5].

The overall prognosis of ECD is variable and depends mainly on the extent and distribution of the disease and is mainly associated with high mortality rates [10,11]. It varies from asymptomatic bone lesions to multisystemic life-threatening forms. Some of the researches published before 2000, often report a very poor prognosis but treatment has improved since. In 2005, the survival rate was below 50% at 3 years of diagnosis which eventually changed to 5 years survival of 68% with interferon therapy [2].

Moreover, our patient had the classical presentation with skeletal pain and bony infiltration site without any systemic manifestation. After excision of the lesion, patient was asymptomatic; hence, patient was kept under surveillance and advised to follow-up after 3 months.

## Disclosure

The authors have no multiplicity of interest to disclosure. The patient consented to the publication of his data.

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