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## Case Report

# A case of Erdheim-Chester disease initially mistaken for retroperitoneal lymphoma ☆

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## ABSTRACT

Erdheim-Chester disease (ECD) is an infrequent, autoimmune disorder that is not Langerhans histiocytosis and is characterized by bilateral sclerosis of the diaphyseal medullary regions of the long bones and possible multiorgan involvement. A mononuclear foam histiocyte infiltrate determines the condition's histopathologic form and extensive fibrosis. A case of ECD in a 52-year-old man with retroperitoneal infiltration and bone involvement is described here, in whom the diagnosis was established only after a 3-year course of multiple nonspecific symptoms.

Establishing a diagnosis of ECD is challenging, especially due to vague and nonspecific presenting symptoms. Nonetheless, it is important to recognize both its unique radiographic findings, particularly, symmetric patchy sclerosis of the long bones, and the pathognomonic infiltration of foamy histiocytes with dense fibrosis, as patients can benefit from interferon-alpha therapy if ECD is established.

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## Introduction

Originally described in 1930 by William Chester Tran et al [5] as a "lipoid granulomatosis," Erdheim-Chester disease (ECD) is a very rare xanthogranulomatous non-Langerhans cell histiocytosis of unknown origin [5]. ECD occurs primarily in adults and involves bilateral symmetric sclerosis of the metaphyseal regions of the long bones and infiltrations of several other organs. It is distinguished by spumous histiocyte penetration of xanthomatous and xanthogranulomatous tissues, along with a CD68 positive, CD1a negative, and S100-protein nega-

tive phenotype (in 50% of cases) and the presence of pathognomonic Touton giant cells [5]. Its presentation depends on the organ involved and can variously be exophthalmos, diabetes insipidus, xanthelasma, interstitial lung disease, bilateral adrenal enlargement, retroperitoneal and perirenal fibrosis, and/or ureteral stenosis, renal impairment, infiltration of the testes, and central nervous system and/or cardiovascular involvement [5]. There is no standard treatment and 60% of adult patients die within 32 months of presentation [1]. Treatment options include corticosteroids, chemotherapy, radiotherapy, surgery, and immunotherapy, and interferon-alpha is being increasingly prescribed for ECD in adults [5].

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**Fig. 1 – Plain film abdominal radiograph. Bilateral ureteric stent.**



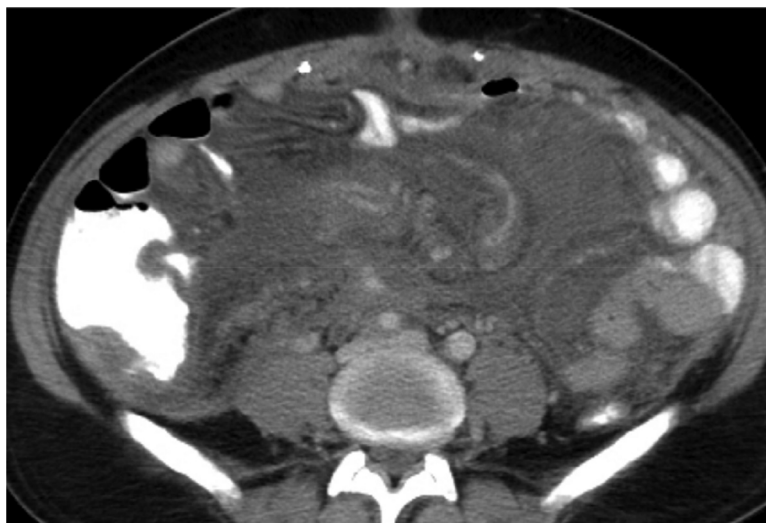
**Fig. 2 – Contrast material-enhanced CT scan coronal image. Extensive retroperitoneal soft tissue density surrounding a small bowel, cecum, and lower abdominal and pelvic vasculature.**

### Case report

A 52-year-old man was referred to our hospital with a history of acute onset obstructive uropathy and was admitted to the urology department for urgent bilateral ureteric stent placement (Figure 1). General physical examination performed and revealed no abnormalities; however, the patient described a 3-

month history of anorexia, generalized weakness, weight loss (> 10 kg), and bilateral loin pain.

An abdominal CT performed next day showed aggressive peritoneal and mesenteric infiltration encasing the bowels, particularly the cecum and the ascending colon, that also reached retroperitoneal structures including the kidneys, the



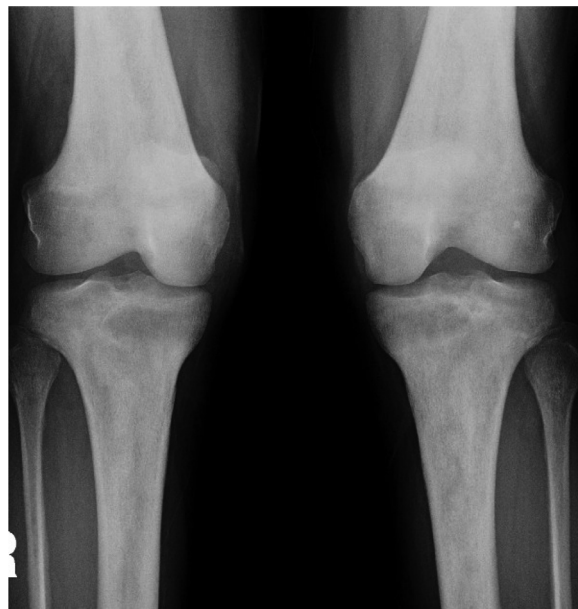
**Fig. 3 – Contrast material-enhanced CT scan axial image. Extensive retroperitoneal soft tissue density surrounding small bowel, cecum, and lower abdominal and pelvic vasculature.**



**Fig. 4 – Contrast material-enhanced CT scan coronal image. Extensive retroperitoneal soft tissue density surrounding adrenals, kidneys, ureters, bladder, small bowel, cecum, and lower abdominal and pelvic vasculature.**

second part of the duodenum, and the distal abdominal aorta (Figure 2–5).

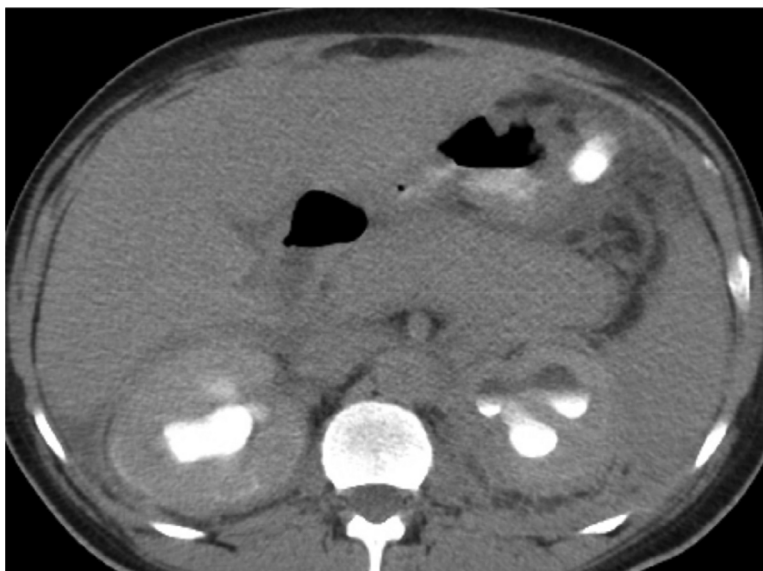
Further evaluation, including a radiographic skeletal survey, showed patchy sclerotic lesions in the diametaphyseal re-



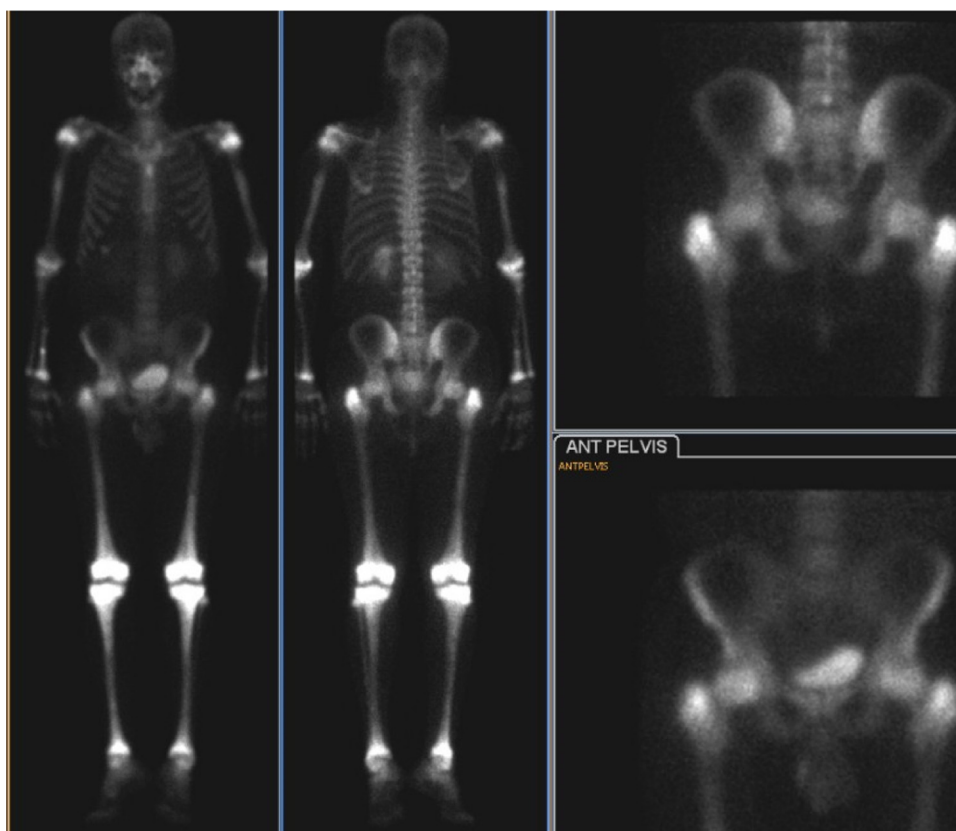
**Fig. 6 – Standing knee x-ray. Appearance of symmetrical metaphyseal sclerosis.**

gions of the distal and proximal upper and lower limbs (Figure 6). Tc-99m bone scintigraphy showed diffuse but intense radiotracer uptake in almost all epiphysis of the long bones, and particularly in the humeri, radii, ulnas, greater trochanters, the distal end of both femurs, and the proximal and distal ends of both tibiae (Figure 7).

Fat-suppressed T2-weighted images of skeletal magnetic resonance imaging (MRI) showed hyperintensity of the skeletal bone marrow, and the metadiaphyses displayed diffuse low-intensity signal in coronal T1-weighted MR images. Fur-



**Fig. 5 – Excretory phase CT scan axial image shows bilateral dilated collecting system with delayed excretion represent bilateral renal obstruction.**



**Fig. 7 – Technetium -methyl diphosphonate (Tc-MDP) bone scan uptake almost in all epiphysis of the long bones in particular hummers, radii, ulnas, greater trochanters, distal end of both femurs, proximal, and distal ends of both tibias.**

ther, all T1- and T2-weighted images showed heterogeneous signal intensity in the epiphyses (Figure 8–9).

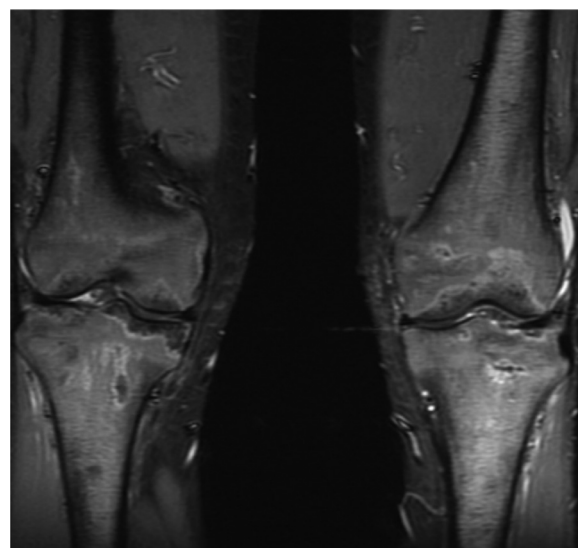
In contrast to the above, MRI of the brain and the sella turcica appeared unremarkable, and a biopsy of the omental and peritoneal tissue revealed the presence of numerous fibrohistiocytic cells. These cells displayed variable amounts of amphophilic foamy cytoplasm with oval vesicular nuclei and occasional mitoses, and Touton-type giant cells were seen along with a small number of lymphocytes.

Fibrosis was present without evidence of granuloma. Immunohistochemistry revealed these cells to be positive for vimentin, CD68, CD163, fascin, and Factor XIIIa but negative for CD1a, S100-protein, cytokeratin, CD21, desmin, Alk1, and CD30 (Figure 10–13.).

## Discussion

ECD is a very rare xanthogranulomatous condition, and it is a non-Langerhans cell systemic histiocytosis with unknown etiology and pathogenesis. Histologically, it is characterized by diffuse infiltrates of large, foamy histiocytes, fibrosis, and bilateral symmetrical sclerosis of the long appendicular bones [1,5].

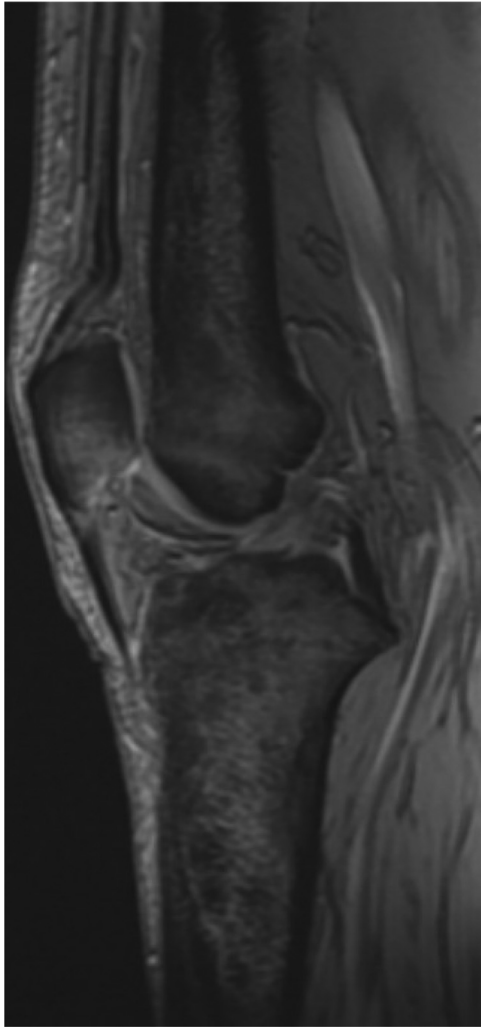
This condition usually affects people above 40 years predominance in males. Usually patient presented with nonspe-



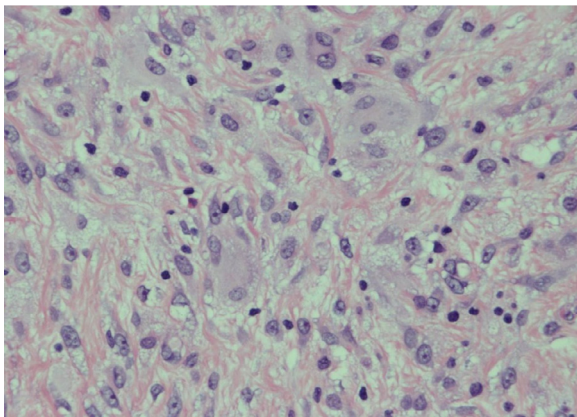
**Fig. 8 – Coronal T2 weighted image (WI) knee MRI. Appearance of heterogeneous signal intensity alteration along epiphyseal metaphyseal aspect.**

cific symptom; however, it is well known with long history of generalized bone pain [6]. Many medical indications can contribute to a misdiagnosis in ECD, and in our case, the initial

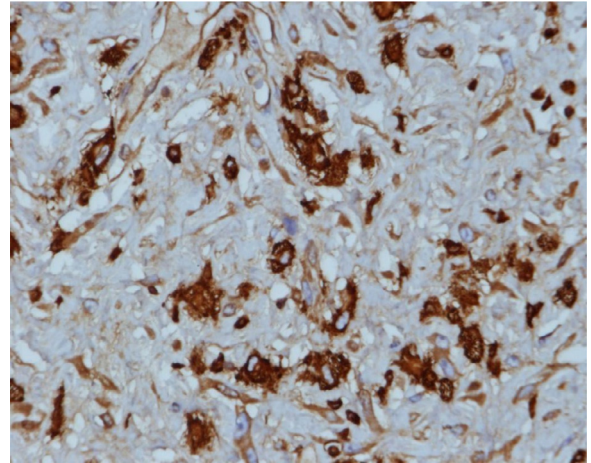




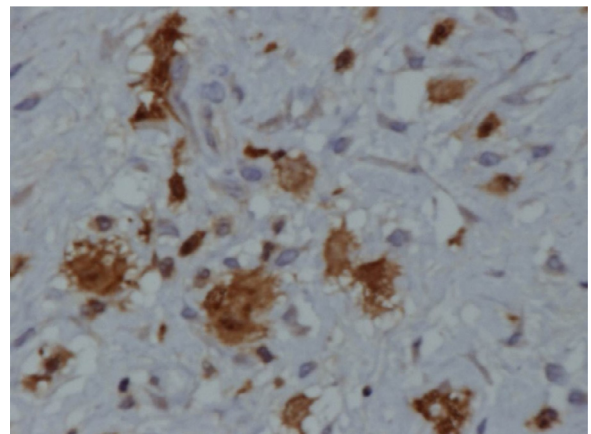
**Fig. 9** – Sagittal T2\* demonstrate heterogeneous predominant high signal intensity at the metadiaphyses of proximal tibia.



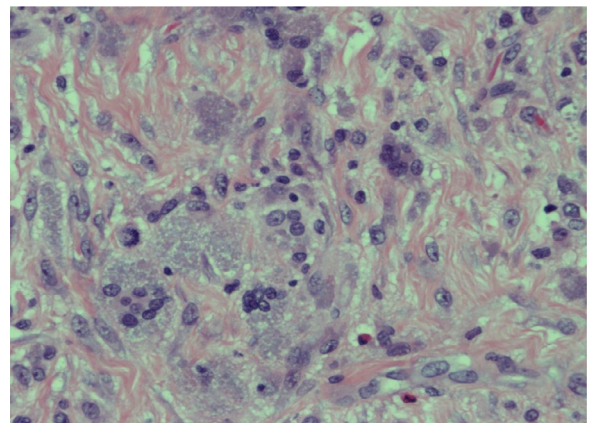
**Fig. 10** – Infiltration by numerous fibrohistiocytic cells with variable amount of amphophilic foamy cytoplasm (Hemotoxylin-eosin x 400 magnification).



**Fig. 11** – Infiltration by numerous fibrohistiocytic cells with variable amount of Touton-type giant cells (Hemotoxylin-eosin x 400 magnification).



**Fig. 12** – Fibrohistiocytic cells stained positive with CD163 (immunohistochemistry x 400 magnification).



**Fig. 13** – Fibrohistiocytic cells stained positive with Factor XIIIa (immunohistochemistry x 400 magnification).

suspected diagnosis was a rare type of peritoneal lymphoma. This is probably due to the fact that the only pathognomonic signs for diagnosing ECD are radiological findings of symmetrical long bone osteosclerosis along with histological results [1,5]. Significantly, such widespread appendicular osteosclerotic skeletal lesions of the long bone are very rarely associated with lytic lesions and spare both epiphyses and axial flat bones. Differential diagnoses include the following mastocytosis, lymphoma, myeloid metaplasia, and metastasis [6]. As such bone signs may be insignificant or missing on skeletal x-ray survey, bone scintigraphy is useful because it reveals all the affected bone areas in one diagnostic technique.

Extraskelletal manifestations are present in more than 50% of the patients and these may occur in multiple organs, including kidneys, pericardium, skin, orbit, and retroperitoneum. These retroperitoneal deposits tend to be mainly in the upper retroperitoneum in the perirenal fat, may also sometimes encase the adrenal glands, and even extend throughout the length of the aorta (up to the heart) and mediastinum, with potentially life-threatening complications, such as heart failure, tamponade, and renal failure, as seen in the case described here. In contrast, involvement of the liver, the pancreas, and the mesentery is extremely rare [1,2,5]. It is important to note that a retroperitoneal xanthogranuloma alone is radiologically indistinguishable from similar conditions such as inflammatory fibrosarcoma, retroperitoneal fibrosis (Ormond's disease) [4], or retroperitoneal lymphoma.

Due to its clinical nonspecificity, an ECD diagnosis relies exclusively on the correlation between radiological and pathological findings. Histologically, xanthogranulomatous lesions in ECD indicate medullary fibrosis and accumulated lipid-laden. In our patient, the clinical presentation, radiographic findings, and histologic characteristics were all consistent with a diagnosis of ECD. Among reported cases, treatment usually included oral steroids and, in more severe cases, chemotherapy or external radiation therapy, but with variable outcomes [3]. However, clinical trials for the treatment of ECD

have not been reported. The most common causes of death include pulmonary and heart failure and it is thought that prognosis depends on the extent and distribution of extraskelletal disease.

## Conclusions

ECD is a rare non-Langerhans histiocytosis with pathognomonic radiological and histological characteristics that involve almost all tissues. Extraskelletal presentations also occur and predict a poor prognosis.

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