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Case Report

A rare case of Erdheim Chester disease ☆

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ABSTRACT

Erdheim-Chester disease (ECD) is a rare form of non-Langerhans cell histiocytosis. There are few documented cases in the medical literature. Here, we present an infrequent case of a 53-year-old patient who presented with cutaneous xanthelasma and a gradual decline in general health characterized by asthenia, anorexia, and chronic dyspnea over the last 5 years. Chest, abdominal, and pelvic CT scans revealed distinct findings suggestive of ECD, including peri-renal fat infiltration resulting in the "hairy kidney" sign, hepatosplenomegaly, renal artery ostial stenosis, pneumopericardium thickening, interstitial lung parenchymal involvement, metaphyseal-diaphyseal osteosclerosis affecting long bones, and sinus osteosclerosis. A biopsy confirmed the diagnosis. This case highlights the importance of radiologists being familiar with the characteristic radiologic signs of ECD to avoid unnecessary repeat examinations, delays in diagnosis, or misdiagnosis.

Key points

- Erdheim-Chester disease has distinct radiologic features that are critical for diagnosis.
- Radiologic imaging plays a unique role in diagnosing, managing, and monitoring Erdheim-Chester disease.
- Recognizable pathognomonic signs include the hairy kidney sign, coated aorta, symmetrical bilateral osteosclerosis of the long bones, intra- and extraconal masses in the orbits with exophthalmos, and masses in the right atrioventricular groove.

Introduction

Erdheim-Chester disease (ECD) is a sporadic form of non-Langerhans histiocytosis with multisystem involvement that is under-recognized and contributes to significant diagnostic delays. It most commonly affects middle-aged individuals. The clinical presentation is highly variable. Imaging plays a central role in the diagnosis. Bone involvement is the most common finding. Retroperitoneal involvement mainly involves perirenal tissue. Pathognomonic imaging findings include symmetric diaphyseal osteosclerosis of long bones,

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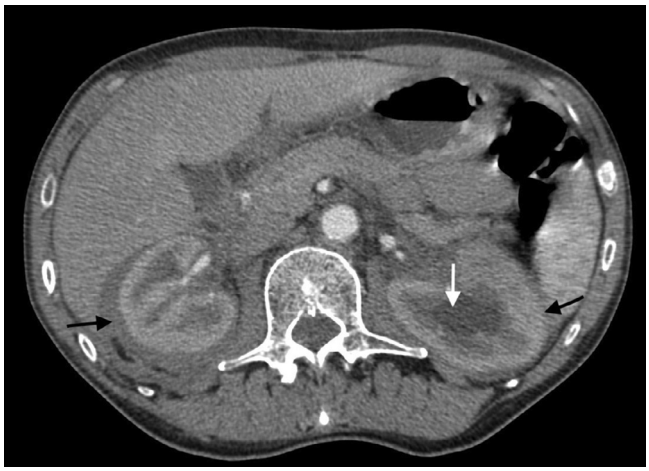

Fig. 1 – A 53-year-old male patient with Erdheim Chester disease. Abdominal CT scan after contrast injection showing thickening and infiltration of peri-renal fat producing the "hairy kidney" sign (black arrow) responsible for the more pronounced bilateral hydronephrosis on the left side (white arrow).

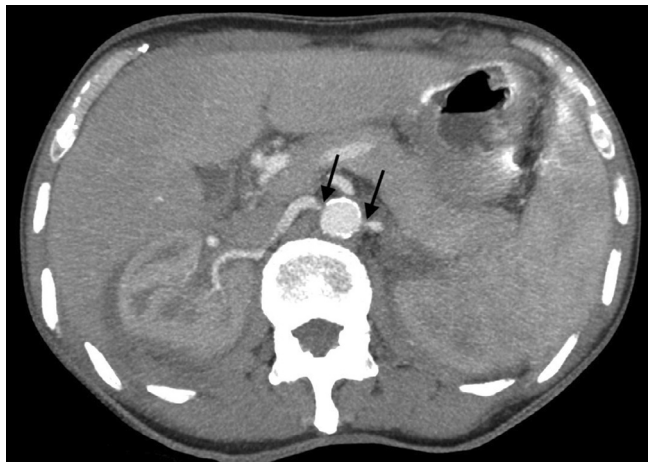

Fig. 2 – A 53-year-old male patient with Erdheim Chester disease. Abdominal CT scan after contrast injection in axial view with maximum intensity projection (MIP) reconstruction showing bilateral renal artery ostial stenosis. (black arrow).

retroperitoneal infiltration ("hairy kidney"), and periaortic sheathing ("coated aorta"). Cardiac, neurological, and pulmonary involvement contribute to the severity of the disease. The differential diagnosis depends on the organs involved. The diagnosis is based on histopathologic evidence in a clinically and radiologically suggestive context.

Case report

We present the case of a 53-year-old patient, a carpenter by profession, who presented with a 3-year history of chronic dyspnea at rest, bone pain in both legs and chronic intermittent abdominal pain, all in the context of an altered general condition consisting of asthenia and anorexia.

Physical examination revealed cutaneous xanthelasma and abdominal tenderness of both flanks without other systemic abnormalities.

The patient initially underwent an abdominal CT scan, which showed peri-renal fat infiltration with the pathognomonic "hairy kidney" sign typical of the disease (Fig. 1), hepatosplenomegaly, peri-aortic infiltration, stenosis of the renal artery ostia (Fig. 2), and mesenteric lymphadenopathies.

Chest CT scan showed circumferential and regular bilateral pleural thickening with pericardial thickening (Fig. 3), cardiomegaly, pulmonary interstitial involvement with smooth and regular bilateral septal thickening, bilateral subpleural reticulations, bilateral ground-glass nodules and micronodules with centrolobular distribution and associated subcentimeter air-filled formations (Fig. 4)".

A brain CT scan showed sinus osteosclerosis with diffuse thickening of the diploë (Fig. 5).

Lower limb radiographs showed bilateral symmetric metaphyseal-diaphyseal osteosclerosis with localized periosteal thickening (Fig. 6).

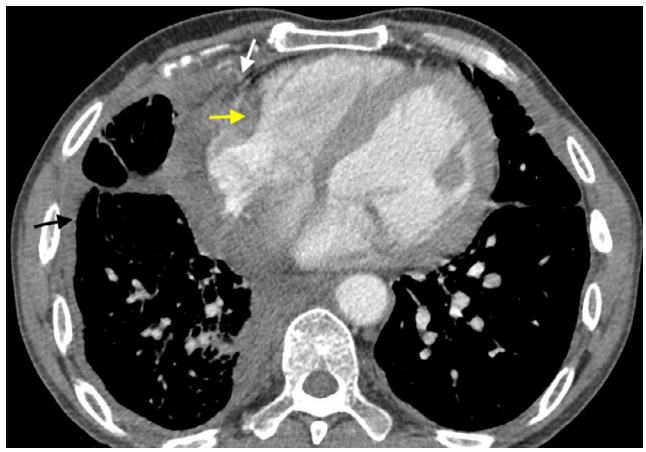

Fig. 3 – A 53-year-old male patient with Erdheim Chester disease. CT scan of the chest in the mediastinal window showing bilateral pleural thickening, more pronounced on the right (black arrow), associated with pericardial thickening (white arrow) and thickening of the right atrial myocardium (yellow arrow).

A mesenteric lymph node biopsy confirmed the diagnosis of Erdheim-Chester disease.

The diagnosis of Erdheim-Chester disease was supported by integrating clinical, radiologic, and histopathologic findings.

Discussion

Erdheim-Chester disease (ECD) is a sporadic form of non-Langerhans histiocytosis first described in 1930 by William Chester and Jakob Erdheim as "lipidic granulomatosis" [1–4]. It

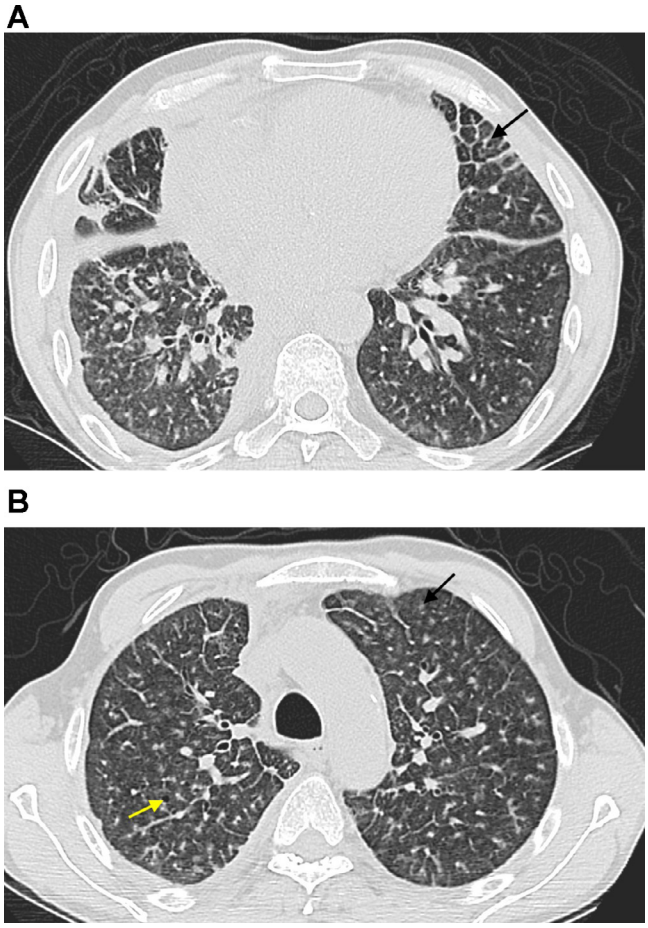

Fig. 4 – A 53-year-old male patient with Erdheim Chester disease. Thoracic CT scan in parenchymal window showing: (A) smooth and regular septal thickening (yellow arrow). (B) Centrolobular micronodules (black arrow) and small air-filled cystic formations (yellow arrow).

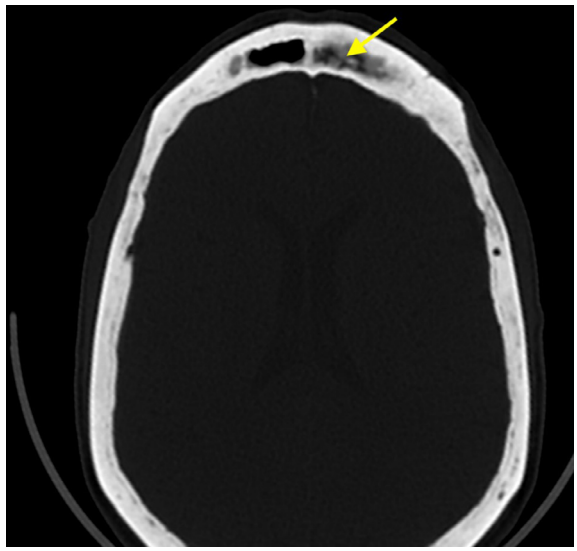

Fig. 5 – A 53-year-old male patient with Erdheim Chester disease. CT scan of the brain in the bone window showing sinus osteosclerosis (yellow arrow).

includes xanthogranulomatous infiltration involving multiple systems, including the skin, heart, breast, bone marrow, kidneys, lungs, abdomen, eyes, brain, pituitary, and bones. [4,5].

ECD typically manifests between the fifth and seventh decade of life, mainly in males [1,6]. The diagnosis relies on clinical, laboratory, radiological, and histopathological findings [6]. Although nonmalignant, ECD can lead to life-threatening organ dysfunction [6].

According to the 2016 classification of histiocytoses by the Histiocyte Society, ECD falls into group L, which includes Langerhans cell histiocytosis (LCH) [7,8].

Patients may present with a variety of symptoms ranging from focal neurological deficits to multiple organ failure, with bone pain being the most common symptom. Diagnosis is often delayed [8].

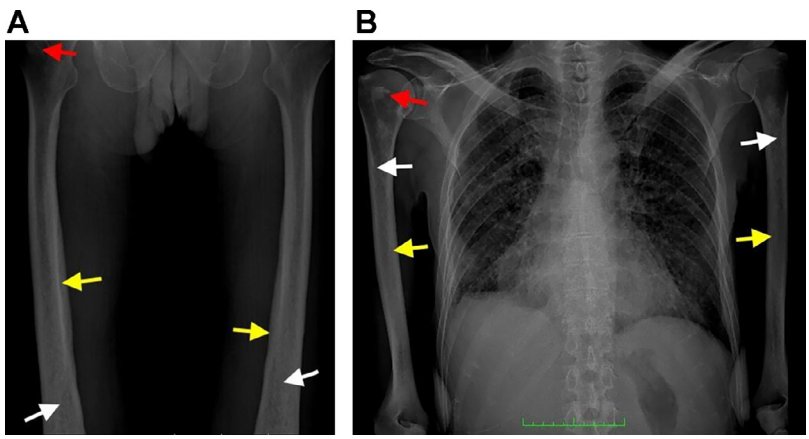

Fig. 6 – A53-year-old male patient with Erdheim Chester disease. Frontal radiographs of both femurs (A) and both humeri (B) show bilateral and symmetrical metaphyseal-diaphyseal patchy medullary sclerosis (white arrow) with resultant mild loss of corticomedullary differentiation. There is cortical thickening of the femur (yellow arrow) and an osteocondensing lesion at the neck of the right femur and humerus (red arrow).

Cardiovascular, pulmonary, and central nervous system involvement significantly affect the prognosis of this disease.

Imaging modalities such as CT scan, PET-CT, brain MRI, and cardiac MRI show different manifestations that aid the diagnosis. These modalities are usually sufficient to confirm the disease [9].

Bone manifestations

Bone involvement occurs in 96% of cases [1,10]. It presents with a typical imaging appearance characterized by bilateral and symmetric diaphyseal-metaphyseal involvement primarily of the long bones of the lower limbs around the knee, known as the "hot knees sign" [2].

Upper limb involvement is also possible. In contrast to Langerhans cell histiocytosis, there is no involvement of the mandible or axial skeleton [1,6].

Radiologic features may include heterogeneous osteosclerosis of cancellous bone, lytic or mixed lesions, endosteal cortical thickening, or loss of corticomedullary differentiation [7]. Bone infarcts may also be present.

These abnormalities are seen on standard radiographs or CT, which allow a more detailed analysis of cortical bone changes, including periosteal and endosteal bone apposition and trabecular changes (thickened trabeculae contributing to bone condensation in diaphyseal-metaphyseal regions) [7,10].

Although not essential, bone MRI can sometimes show bone marrow replacement with hypointensity on T1-weighted images and hyperintensity on T2-weighted images, heterogeneous enhancement depending on fibrous or edematous areas, clear boundaries between healthy and pathological zones, and subchondral sparing. Periostitis may also appear as hyperintense T2-weighted images or linear pericortical enhancement.

Symmetrical metaphyseal-diaphyseal uptake on nuclear scintigraphy is specific to this pathology. However, PET-CT is increasingly replacing bone scintigraphy [6].

The differential diagnosis of bone involvement includes other osteosclerotic diseases such as Paget's disease, lymphoma, metastasis, and chronic osteomyelitis [1,10].

Retroperitoneal involvement

Retroperitoneal involvement, including the kidneys, is observed in 68% of cases [1]. Renal involvement in Erdheim-Chester disease presents with a typical and pathognomonic imaging appearance characterized by bilateral, symmetric, and irregular infiltration of the renal fascia and peri-renal fat, resulting in the "hairy kidney sign" with the risk of bilateral hydronephrosis [2,6,9,11].

The infiltration may also involve the adrenal gland, rarely leading to adrenal insufficiency [9].

This presentation may mimic retroperitoneal fibrosis; however, retroperitoneal fibrosis typically originates from the proximal aorta and progresses upward, whereas Erdheim-Chester disease primarily involves the renal hilum [1]. In addition, Erdheim-Chester disease does not extend to the inferior vena cava [6].

It is also important to note that hematologic pathologies such as lymphoma and extramedullary plasmacytoma may infiltrate perirenal fat [12].

Cardiovascular involvement

The vascular involvement in Erdheim-Chester disease predominantly involves the aorta and presents as the 'coated aorta sign', this manifestation appears circumferential, homogeneous, and regular. It primarily includes the periadventitial layer rather than the vessel wall itself. It typically does not result in arterial diameter abnormalities [1].

Any vascular structure may be affected [11].

Ostial stenoses may develop, particularly in the renal arteries, leading to a risk of renovascular hypertension [6].

Affection of arteries supplying the brain may lead to ischemic strokes [1].

The differential diagnosis for vascular involvement includes Takayasu's arteritis, characterized by transmural vascular inflammation, unlike the predominantly periadventitial involvement in Erdheim-Chester disease.

Cardiac involvement in Erdheim-Chester disease manifests as pericardial infiltration, myocardial and endocardial infiltration [6], myocardial infarction due to coronary infiltration, valvular disease, presence of effusion, cardiomegaly and right atrioventricular groove involvement which should be systematically assessed.

Pericardial infiltration is the most common cardiac manifestation. It occurs in 42% of cases [4,6].

Pulmonary involvement

Lung parenchymal involvement is seen in 25% to 50% of cases [11]. Manifestations include interstitial, alveolar, or combined involvement characterized by smooth septal and fissural thickening, ground-glass and centrolobular nodules or micronodular infiltrates, ground-glass opacities, and cysts. Pleural involvement with effusion or thickening may also occur. Consolidations have also been reported [13,14].

Pulmonary involvement may progress to fibrosis [15].

Isolated pulmonary parenchymal involvement is difficult to differentiate from other pathologies with similar features. Therefore, combining with other pathognomonic features is essential to help make the diagnosis [1].

Neurological involvement

Central nervous system manifestations are seen in 50% of cases [2]. MRI is more sensitive than CT in detecting lesions [8].

Craniocerebral manifestations may include:

- Involvement of the hypothalamus-hypophysis axis, often with loss of spontaneous T1 hypersignal in the posterior pituitary due to vasopressin depletion or presence of

enhanced infundibular nodules, single or multiple, with thickening of the pituitary stalk after gadolinium injection.
- Meningeal involvement is characterized by multiple focal thickenings and diffuse thickening of the falx, which enhances contrast and may mimic meningiomas.
- Parenchymal involvement often occurs in the subtentorial region, with frequent T2 hyperintensities in the dentate and peri-dentate nuclei and middle cerebellar peduncles [1], with variable enhancement, sometimes accompanied by atrophy of the affected organs [8]. Supratentorial structures and spinal lesions may also be involved [11,15].
- Orbital involvement presents as intraconal or extraconal masses due to histiocyte accumulation, which may cause exophthalmos [1,2].
- Osseous involvement manifests as sclerosing lesions in the sinus walls and cranial vault without osteolysis, in contrast to Wegener's disease [1,2].

Other sites

Skin involvement occurs in 27% of cases [4] and manifests as xanthelasma on the eyelids or periorbital regions. Other less common sites include the visceral organs, thyroid, breast, testes, lymph nodes, and pancreas [1,6,16,17].

Histologic confirmation is essential for the diagnosis, based on a biopsy of peri-renal fat or other relevant site.

Characteristic findings include histiocytic infiltration, fibrosis, and multinucleated Touton giant cells. Immunohistochemistry shows positivity for CD163, CD68, and factor XIIIa and negativity for CD1a and langerin, essential for differentiation from Langerhans cell histiocytosis. The S100 protein is absent in 80% of cases [6,8]. In addition, detection of the BRAF V600 mutation is critical for tailoring treatment.

Approximately 20% of Erdheim-Chester disease cases are associated with Langerhans cell histiocytosis.

Treatment strategies vary according to disease extent and often include interferon-alpha as initial therapy, supplemented by corticosteroids and BRAF inhibitors [6]. Despite therapeutic advances, the prognosis remains poor, with a high mortality rate due primarily to extra-skeletal manifestations. Overall survival rates are 96% at 1 year and 68% at 5 years [1,4,10].

Conclusion

Erdheim-Chester disease is a rare disorder characterized by several pathognomonic signs. Recognition of these signs and increased awareness of the condition are essential to prevent diagnostic delays and improve patient management and prognosis.

Patient consent

Written informed consent was obtained from the patient for publication of his case.

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