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Case Report

Case Study and Bibliographic Review of Erdheim-Chester Disease

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Abstract

Erdheim-Chester Disease (ECD) is a rare form of non-Langerhans cell histiocytosis, characterized by xanthogranulomatous infiltration of foamy histiocytes surrounded by fibrosis. The disease can manifest asymptomatically or as a potentially severe multisystemic disease, with a predominance of involvement in the skeletal system. Immunohistochemistry reveals cell positivity for CD68, negative CD1a, and negative S100, with an absence of Birbeck granules. We present the case of a 66-year-old man with neurological, cardiac, renal, peritoneal symptoms, and cutaneous signs.

Keywords: *Erdheim-Chester Disease; Histiocytosis; Hairy Kidney Sign; Renal Insufficiency; Enrobed Aorta Sign*

Introduction

Erdheim-Chester Disease (ECD) is a rare form of non-Langerhans cell histiocytosis (LCH), characterized by multisystemic involvement. Although its peak incidence is observed between the 5th and 7th decades of life, it can also affect children. The exact etiopathogenesis of the disease remains to be determined due to its rarity, but it is postulated to be an immune-mediated phenomenon related to excessive proliferation of helper T cells, leading to the release of pro-inflammatory cytokines. The symptomatology of ECD is nonspecific and depends on the site of involvement. It may include constitutional symptoms such as fever, weight loss, and night sweats, often confused with tuberculosis in developing countries. Skeletal involvement is the most frequent, typically causing bone pain. Common extraosseous manifestations include central diabetes insipidus and exophthalmos, forming a classic clinical triad. The prognosis of ECD depends on the sites and extent of extraosseous involvement. Involvement of the central nervous system and the cardiovascular system negatively affects the prognosis due to a poor response to chemotherapy. Although therapeutic advances have reduced morbidity, mortality remains significant, with an overall survival of 96% at 1 year and 68% at 5 years [1,2].

Patient and Observation

The patient, a 66-year-old man, has been suffering from insulin-dependent diabetes for twelve years, had two episodes of stroke in 2013 and 2014, and has been followed since 2009 for stented ischemic heart disease and moderate aortic stenosis. Symptoms began in May 2022 with a rash on the abdomen and extremities, evolving into a deterioration of general condition, accompanied by dizziness, balance disorders, muscle weakness, and progressive gait disturbances. Examinations revealed a sensory-motor axonal polyneuropathy on electromyography, while brain MRI was normal. In September 2023, the patient was admitted due to acute renal failure and altered

general condition. Analyses showed an increase in creatinine to 47 mg/l, a decrease in glomerular filtration rate to 18.03 mg/l, moderate inflammatory syndrome with elevated markers such as CRP (143), elevated IgE, and high values of BNP (4702) and troponin. Transthoracic echocardiography revealed moderate alteration of longitudinal strain, wall thickening with a small pericardial effusion blade. Skin biopsy confirmed subepidermal bullous dermatosis, skull X-ray showed bilateral ethmoidal cell infiltration, and abdominal CT scan revealed significant perineal fat infiltration with the "hairy kidney sign" and slight bilateral hydronephrosis (Figure 1). PET scan indicated pathological cortical and perirenal hypermetabolism, bilateral adrenal hypermetabolism, as well as cardiomegaly with diffuse and heterogeneous cardiac hypermetabolism. Renal biopsy confirmed the presence of histiocytic cells infiltrating the pericapsular renal fibrous tissue with cell positivity for CD68 and CD1. In view of these clinical-biological and radiological results, the patient was initially treated with a solumedrol bolus of 500 mg on the first day, followed by 240 mg on the second and third day, then switched to oral administration at 60 mg/day. Four weeks after the start of treatment, a significant improvement in general condition was observed, accompanied by rapid regression of pruritus and improvement in gait disorders. Biologically, a notable decrease in creatinine to 18 mg/l and CRP to 11 was noted, suggesting a positive response to treatment.

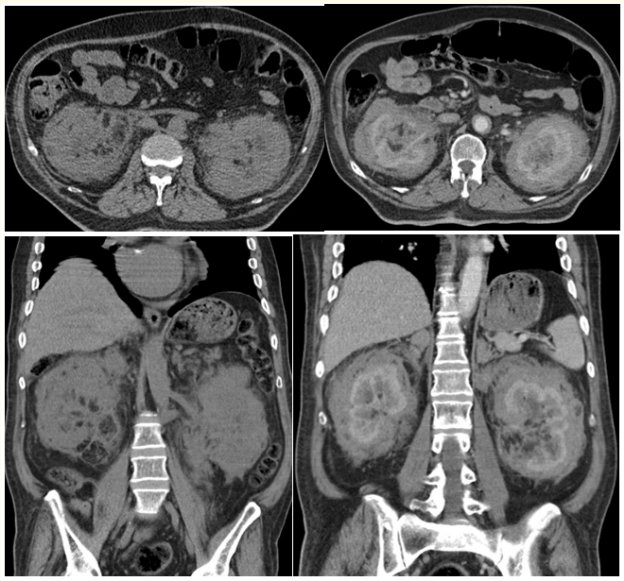

Figure 1: *CT scan in axial and coronal sections before and after injection of contrast agents showing: infiltration of perirenal and peri-pyeloureteral fat bilaterally with hairy kidney appearance, this CT scan appearance is characteristic of Erdheim-Chester disease.*

Discussion

ECD represents a rare xanthogranulomatous form of non-Langerhans cell histiocytosis, characterized by infiltration of foamy histiocytes and surrounding fibrosis. The diagnosis of ECD is established based on specific radiological and histological criteria, as detailed below.

Skeletal involvement

Skeletal involvement is observed in up to 96% of patients with Erdheim-Chester Polyostotic Dysplasia (ECD). Bone pain is the most frequent initial manifestation of ECD, occurring in 50% of cases [3]. The presence of bilateral and symmetrical osteosclerosis in the diaphyseal regions of long bones is a distinctive feature of ECD [4]. In contrast, skeletal lesions in LCH are lytic and rarely localized to

long bones [5,6]. Approximately 4% of patients with ECD do not present radiological signs of osteosclerosis in the femurs [7]. The axial skeleton and epiphyseal regions are generally preserved [8]. In a retrospective study of 59 cases of ECD in 1996, Veyssier-Belot., *et al*. reported lytic lesions, either in flat bones such as ribs and skull, or in long bones, in 5 to 8% of cases [9].

Pulmonary involvement

In a multicenter survival study of 53 patients conducted by Arnaud., *et al*. in 2011, pulmonary involvement associated with Erdheim-Chester disease was observed in 43% of cases [10]. Pulmonary manifestations related to ECD present various imaging characteristics. Conventional radiographs may reveal reticular shadows, although often normal. CT scan may show interlobular septal thickening, diffuse and localized centrolobular nodular opacities, ground-glass opacities, and fissural thickening [11]. The differential diagnoses of these radiological characteristics may include lymphangitic spread of carcinoma [12], alveolar proteinosis, sarcoidosis, leukemia, lymphoma, amyloidosis, and some interstitial pneumonias [13,14].

Cardiovascular manifestations

Approximately 75% of patients with ECD present cardiovascular involvement [15], but it is often asymptomatic and incidentally detected on radiological imaging examinations [16], in the same way as other systemic manifestations in these patients. On CT scan, the most frequent abnormality is circumferential sheathing of the soft tissues of the thoracic and abdominal aorta, as well as its branches. This peri-aortic fibrosis, also known as "enrobed aorta" phenomenon, results from periaortic infiltration by histiocytes, being pathognomonic of ECD [17]. The differential diagnosis of this aspect includes retroperitoneal fibrosis and Takayasu arteritis. Venous diseases associated with ECD are much less frequent [18]. Pericardial infiltration is the most common cardiac manifestation of ECD [19] and can occur in up to 45% of patients. It can manifest as pericarditis and pericardial effusion, which can lead to cardiac tamponade [20,21]. Histological analysis of the pericardium may reveal infiltration of foamy histiocytes [17].

Retroperitoneal and renal manifestations

Retroperitoneal involvement is a frequent feature of ECD, affecting 30 to 50% of patients [22]. However, Arnaud., *et al*. reported retroperitoneal space involvement associated with ECD in 68% of patients, most of whom were asymptomatic. When present, symptoms may include abdominal pain and dysuria. The differential diagnosis of retroperitoneal fibrosis associated with ECD includes idiopathic retroperitoneal fibrosis (Ormond's disease) and secondary retroperitoneal fibrosis [23]. The appearance of the kidneys is often described as "hairy" due to infiltration of perirenal fat creating an irregular renal border, which does not enhance after administration of iodinated contrast, thus differentiating it from the kidney itself [24].

Exceptional localizations

Exceptional localizations of involvement have been documented, including cutaneous involvement [25], gastrointestinal tract [26], testes, thyroid, skeletal muscles [27] and breast [28]. These manifestations are reported anecdotally. Cutaneous involvement appears to be the most frequent among these unusual presentations of ECD. In a retrospective study conducted by Veyssier-Belot, 11 out of 59 patients had cutaneous involvement associated with ECD [29]. The most common dermatological manifestations of ECD include xanthoma-like papules [25] and periorbital xanthelasma-like skin lesions [30,31].

Conclusion

Erdheim-Chester Disease presents as a form of non-Langerhans cell histiocytosis, characterized by xanthogranulomatous infiltration of foamy histiocytes surrounded by fibrosis. Due to its rarity and multisystemic nature, diagnosis can be complex, requiring a multidisciplinary approach. Understanding this diagnostic complexity, it is important to note that patients with ECD may remain asymptomatic despite multisystemic involvement. However, recognition of distinctive radiological features, encompassing diagnostic manifestations at skeletal,

pulmonary, cardiac, renal, and retroperitoneal levels, can facilitate the diagnosis of this rare disease, even in the absence of histological confirmation.

Conflicts of Interest

The authors declare no conflicts of interest.

Authors' Contributions

Dr. Ajertil is the lead author, and Professor Cherkaoui contributed to this work by providing his experience in writing.

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