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(CASE REPORT)

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Challenges in diagnosis of Erdheim-chester disease: a case report

Hazem Muhammad ALmasarei [1] and Ashraf ALakkad [2,*]

[1] *Department of diagnostic and Interventional radiology, Madinat Zayed Hospital, AL Dhafra Region, UAE.*
[2] *Department of Internal Medicine, Madinat Zayed Hospital, AL Dhafra Region, UAE.*

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Abstract

Background: Erdheim-Chester disease is a rare non-Langerhans cell histiocytosis characterized by the infiltration of lipid-laden macrophages into various tissues, leading to diverse clinical manifestations.

Case Presentation: A 53-year-old male presented with a history of recurrent flank pain and obstructive uropathy over seven years, which led to multiple imaging studies and treatments for bilateral renal stones. Recent imaging, including a CT scan of the abdomen and pelvis, revealed bilateral perirenal soft tissue thickening extending into the renal sinus and pelvicalyceal systems, moderate hydronephrosis, and bilateral renal stones, suggestive of ECD. A CT-guided biopsy of the perinephric soft tissue confirmed the diagnosis. Histopathological analysis showed fibrofatty tissue with histiocytes exhibiting foamy cytoplasm, lymphocytes, plasma cells, and Touton cells. Immunohistochemistry stains were positive for Factor 13A and CD68 in histiocytes, confirming ECD.

Conclusion: This case underscores the importance of considering ECD in patients with unexplained recurrent flank pain and renal abnormalities. Early recognition and biopsy are crucial for accurate diagnosis and management of this rare disease. The successful identification of ECD in this patient illustrates the critical role of advanced imaging and histopathological evaluation in diagnosing rare conditions.

Keywords: Erdheim-Chester disease; Case Report; CT scan

1. Introduction

Erdheim–Chester disease is a rare medical condition characterized by the presence of foamy non-Langerhans cells and lipid-laden histiocytes in the tissues(1). It is often accompanied by fibrosis and can be identified through distinct radiological features, such as patchy osteosclerosis in the long bones of the extremities. The proximal tibia, fibula, and distal femur are commonly affected(2).

The prevalence of ECD is currently unknown, with approximately 550 cases documented in the literature(3). The disease typically manifests in adulthood, usually between the ages of 40 and 60, with an average onset age of 53 years(4). The cause of this condition is still uncertain, but it is believed to be either a reactive or neoplastic disorder(4). Interestingly, a mutation in the BRAF proto-oncogene has been found in most ECD patients(4). The recent discovery of the clonal nature of the disorder has significantly altered our understanding of how the disease develops(4).

Diagnosing ECD requires a careful evaluation of clinical symptoms, imaging results, and histopathologic findings. There is a significant presence of skeletal involvement in ECD patients, with up to 95% experiencing this. The most frequently reported symptom is bone pain(5).There are several additional areas where the condition can affect the body, such as the eyes, causing symptoms like papilledema, exophthalmos, papulonodular skin lesions, and xanthelasmas (6). It can

* Corresponding author: Ashraf ALakkad

also infiltrate the endocrine system, leading to diabetes insipidus, as well as cause renal failure or severe lung disease, involvement in the retroperitoneal region, disorders of the central nervous system, and cardiomyopathy(7).

The first line of treatment currently available is interferon alfa (IFN-α)(8). There is an alternative to standard IFN-α called pegylated IFN-α. Other agents are often used based on anecdotal case reports(9). Agents like cladribine, a new purine nucleoside analog, can be a valuable treatment option for moderate to severe cases. Vemurafenib (BRAF inhibitors) and Anakinra are currently being recommended as potential second-line treatments for patients who do not respond well to IFN-α(10).

Using corticosteroids can help decrease swelling and improve mild skin symptoms, but they are not a long-term solution when used alone(11). Imatinib is commonly used as a second-line treatment for patients who show high levels of platelet-derived growth factor receptor-beta expression, as this mutation is often associated with a myeloid-origin disease(12). The prognosis for ECD is generally poor, especially for those with central nervous system involvement. However, with the use of IFN-α treatments, there is a significant increase in survival rates, with a 5-year survival rate of 68%(13). This case highlights a challenging diagnostic journey over seven years for a 53-year-old man with recurrent flank pain, obstructive uropathy, and hydronephrosis, ultimately diagnosed with ECD.

2. Case Presentation

A 53-year-old gentleman presents with a long-standing history of recurrent flank pain, obstructive uropathy, and hydronephrosis spanning over the past seven years. During this period, he underwent multiple imaging studies including a series of X-rays, ultrasounds, and CT scans in different countries. Despite these extensive evaluations, a definitive diagnosis remained elusive until now, except for the identification and treatment of bilateral renal stones by a urologist.

2.1. Clinical Findings and Diagnostic Workup

2.1.1. Abdomen and Pelvis CT Scan(Fig A,B &C)

A recent CT scan of the abdomen and pelvis was conducted using axial images before and after the administration of intravenous contrast media (Omnipaque 350mg/ml, 80 ml). Sagittal and coronal reformatted images were also obtained. The primary reason for this examination was left flank pain.

3. Results

Kidneys: Evidence of bilateral almost symmetrical perirenal enhancing soft tissue thickening extending to the renal pelvis and infiltrating the pelvicalyceal systems, associated with moderate hydronephrosis, giving the appearance of "hairy kidneys." No definite retroperitoneal soft tissue thickening, fibrosis, or adenopathy. Findings are suggestive of Erdheim-Chester disease. Bilateral renal stones with the largest on the right measuring 1.3 x 0.5 cm (600 HU) and the largest on the left measuring 1.5 x 1 cm (200 HU). A cyst in the upper pole of the left kidney. Both kidneys are otherwise normal in size, shape, and cortical thickness with no evidence of masses or back pressure changes. Adrenal Glands: Grossly unremarkable.

- Abdominal Aorta: No focal aneurysmal dilatation or dissection. No vascular encasement.
- Liver: Average in size with homogeneous parenchymal density. No hepatic focal lesions or intra-hepatic biliary tree dilatation. Gall Bladder: Average in size with normal wall thickness. No intra-luminal calculi or masses.
- Spleen and Pancreas: Average in size with homogeneous CT density. No masses or cysts.
- Stomach, Small and Large Bowel: Normal appearance without bowel dilatation, pericolonic fat stranding, free air, free fluid, or inflammatory change. No lymph node enlargement was noted.
- Bony Structures and Muscular Structures: Reflective of the patient's age and intact muscular structures.
- Conclusion: The CT scan findings support the diagnosis of Erdheim-Chester disease, characterized by bilateral perirenal soft tissue thickening and associated hydronephrosis. Additionally, there are bilateral renal stones.

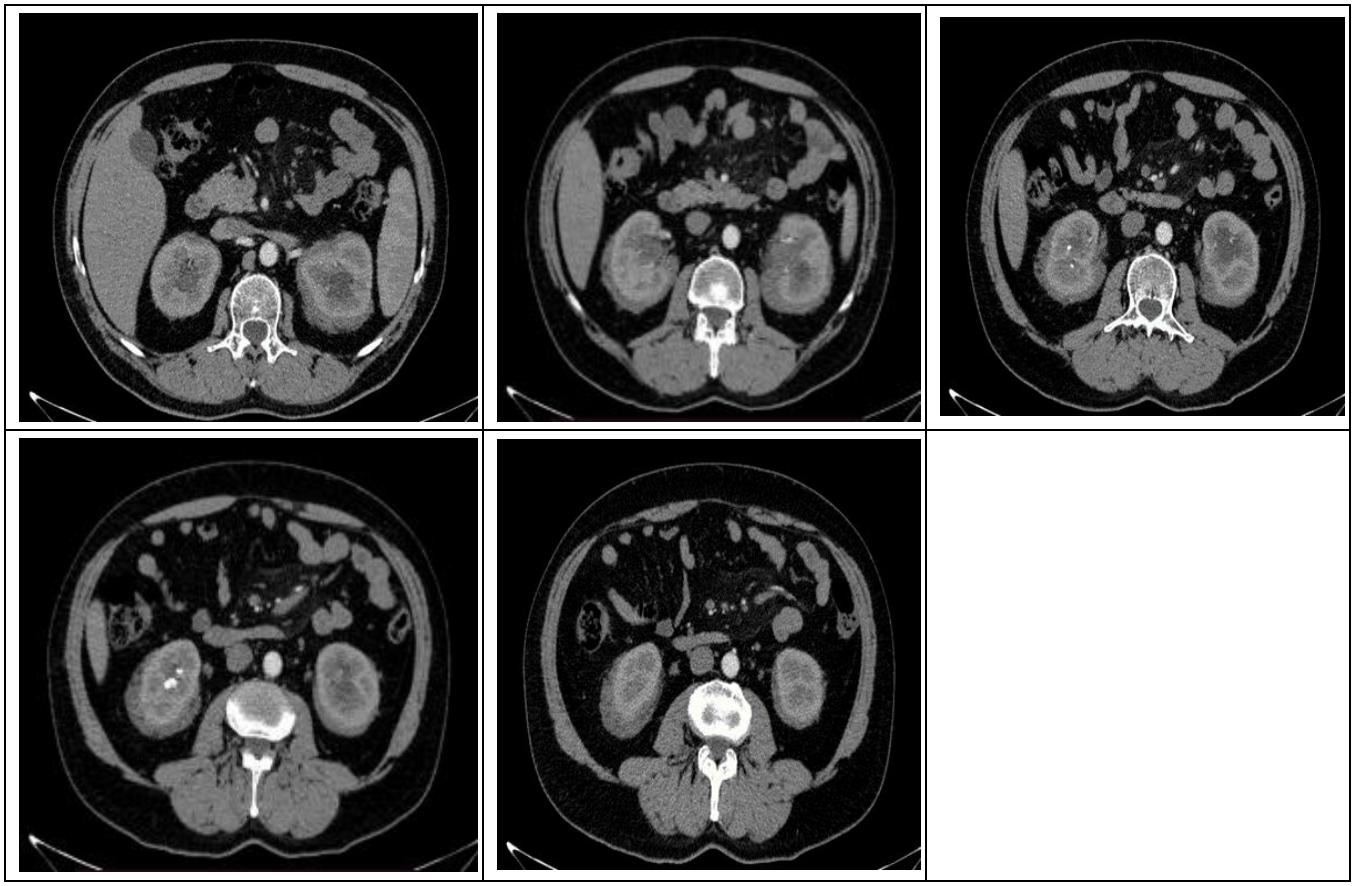

Figure 1 Axial CT scan images showed bilateral almost symmetrical perirenal enhancing soft tissue thickening extending to the renal pelvis and infiltrating the pelvicalyceal systems, associated with moderate hydronephrosis, giving the appearance of "hairy kidneys."

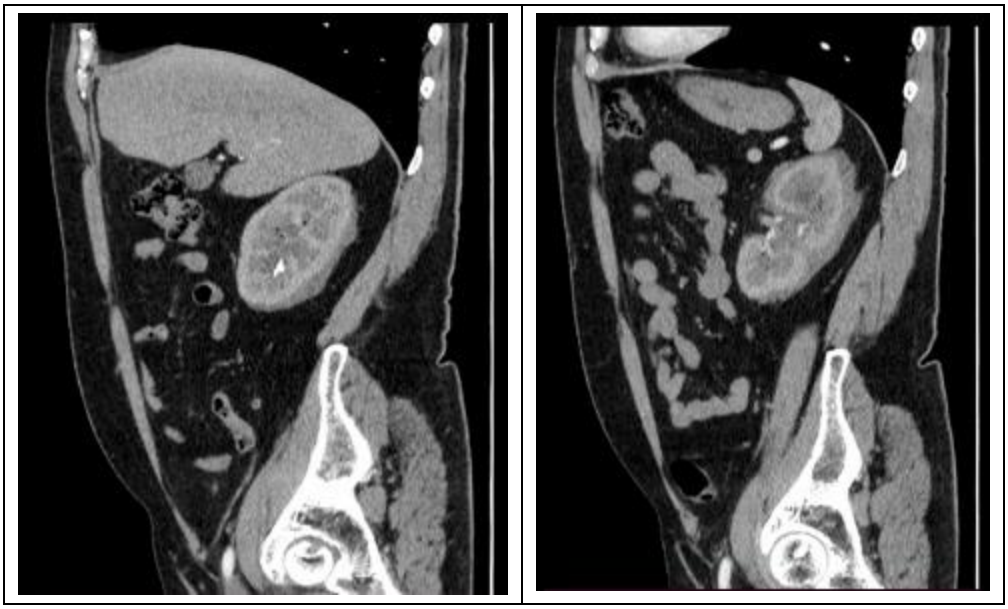

Figure 2 Sagittal CT scan images showed perirenal soft tissue thickening extending to the renal pelvis and infiltrating the pelvicalyceal systems, associated with moderate hydronephrosis, giving the appearance of "hairy kidneys."

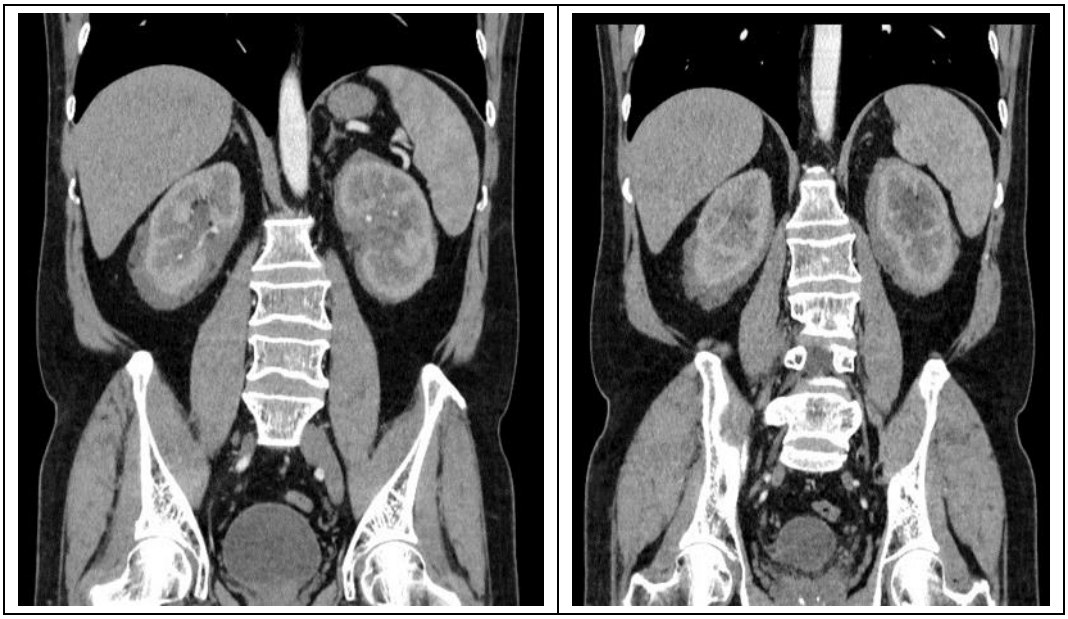

Figure 3 Coronal CT scan images showed perirenal soft tissue thickening extending to the renal pelvis and infiltrating the pelvicalyceal systems, associated with moderate hydronephrosis, giving the appearance of "hairy kidneys."

3.1.1. Interventional Radiology Note (Fig D)

CT scan guided perinephric soft tissue biopsy

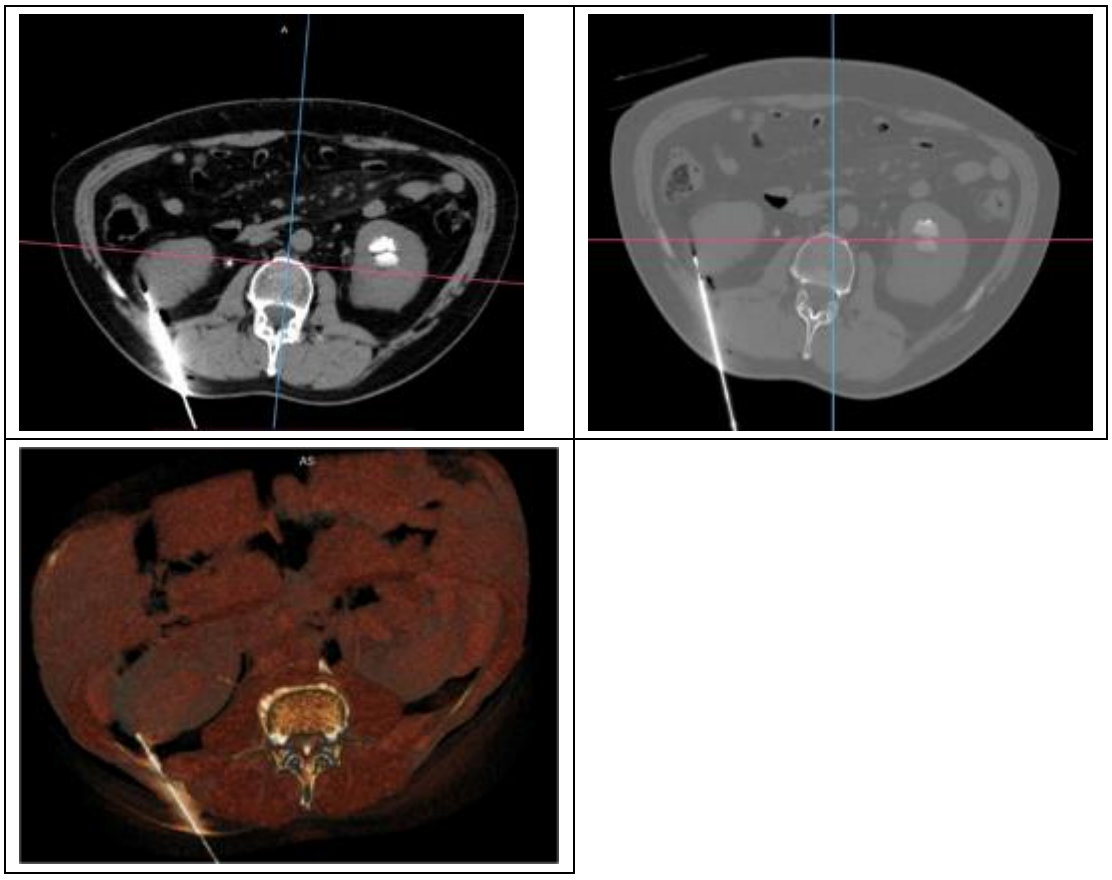

Figure 4 CT scan guided perinephric soft tissue biopsy, under local anesthesia (8 cc Lidocaine 2%), a 20 G x 15 cm, biopsy device was used to obtain tissue samples from the right kidney

CT scan guided perinephric soft tissue biopsy was performed due to perirenal enhancing soft tissue thickening extending to the renal pelvis and infiltrating the pelvicalyceal systems. Prior to the procedure, informed consent detailing risks, benefits, and alternatives was obtained after a thorough discussion. A time-out procedure was performed to verify patient identity, procedure type, and correct site. Under local anesthesia (8 cc Lidocaine 2%), a 20 G x 15 cm biopsy device was used to obtain four tissue samples from the right kidney. The procedure was conducted under sterile conditions following standard protocols. Post-procedure, the patient experienced no complications and was discharged in stable condition. Tissue samples were appropriately preserved in formalin for further analysis. The successful biopsy aims to provide definitive histopathological insights into the underlying etiology, guiding subsequent management decisions.

3.2. Histopathology

The histopathology report provided crucial insights into the tissue samples obtained from the patient's right perinephric area, confirming a suspected diagnosis of Erdheim-Chester disease (ECD). The clinical context included symmetrical perirenal enhancing soft tissue thickening with associated moderate hydronephrosis, prompting a CT-guided biopsy. The specimen, comprising four fragments of pale to gray-brown soft tissue ranging from 0.1 to 0.3 cm in size, was received in formalin and meticulously examined under microscopy.

Microscopic examination revealed loose fibrofatty tissue containing histiocytes with foamy cytoplasm, interspersed with lymphocytes, plasma cells, and occasional Touton cells—a hallmark of ECD. Immunohistochemistry stains further supported the diagnosis, with Factor 13A positive in spindle cells and CD68 positive in all histiocytes, corroborating the histomorphological findings. CD13 was positive in a few histiocytes as well. These findings collectively confirm the presence of Erdheim-Chester disease in the patient, aligning with the initial clinical suspicions derived from imaging and biopsy results.

4. Discussion

The diagnosis of ECD typically occurs around the age of 52, with a slightly higher occurrence in males(14). It is a rare condition characterized by the infiltration of xanthomatous cells that are not Langerhans cells(14). The cause of ECD is still unknown. Recent research indicates that ECD is a relatively uncommon clonal disorder(14). It is caused by mutations in the mitogen-activated protein kinase/extracellular signal-regulated kinase pathway, with a significant number of cases (over 50%) showing the BRAFV600E mutation(15). The presence of chronic inflammation is believed to play a crucial role in the development of ECD(15).

Diagnosing ECD involves analyzing histopathological findings alongside radiographic context and clinical manifestations. The clinical manifestations primarily relied on the organs that were affected. In a case report, their patient primarily showed symptoms of cardiac tamponade or right heart failure, such as pitting edema in the lower legs, fatigue, and exertional dyspnea(16). The patient also experienced sick sinus syndrome, with episodes of dizziness, palpitations, and syncope, and had kidneys of hairy shape. Additionally, the patient also showed symptoms of diabetes insipidus, including excessive urination, which was caused by the involvement of the heart (pericardium and myocardium) and pituitary gland. In this case, they observed not only renovascular involvement but also other vascular infiltration and periaortic involvement. These findings could potentially contribute to the development of hypertension(16). In our case, there was renal involvement as the patient suffered from recurrent flank pain, obstructive uropathy, and moderate hydronephrosis over the past seven years. He also had renal stones, cysts, and atelectasis. Hairy kidney appearance was also noted in our case.

Understanding radiology is crucial in the diagnosis and management of ECD(6, 17). Thus, in order to arrive at an accurate diagnosis, it is recommended by consensus guidelines that patients who are suspected to have ECD undergo a series of imaging tests including CT scans of the pelvis, abdomen, and chest as well as positron emission tomography or computed tomography scans, brain MRI, and cardiac MRI(6, 17).

Furthermore, additional radiological examinations may be chosen based on clinical symptoms or signs(6, 17). Cardiovascular complications are frequently observed in individuals with ECD and have been linked to a more unfavorable outlook (18). An optimal way to evaluate the extent of myocardial and pericardial infiltration, tissue characterization of the lesion, and ventricular dysfunction is through a contrast-enhanced cardiac MRI(18). However, no cardiovascular involvement was noted in our patient.

The treatment of ECD is still being researched and developed(19). According to the literature, it is generally recommended that therapy be started for all patients, except for those who do not show any symptoms. Interferon is

the therapy that is most commonly prescribed, as per consensus guidelines(19). A study involving 53 patients with ECD found that interferon had a significant positive impact on overall survival(19). For BRAF-positive patients, vemurafenib showed promising results as it effectively inhibited mutated BRAF, leading to significant clinical and radiographic improvement(20). Our report highlights the importance of providing targeted treatment for the underlying causes of ECD, rather than relying solely on observation or symptomatic relief. This is crucial due to the progressive nature of the disease in our patients.

5. Conclusion

This case underscores the complexity and diagnostic challenges associated with Erdheim-Chester disease (ECD), a rare and often elusive condition. The patient's prolonged history of recurrent flank pain, obstructive uropathy, and hydronephrosis, coupled with extensive but inconclusive imaging studies, highlights the difficulty in diagnosing ECD. The eventual identification of bilateral perirenal soft tissue thickening and characteristic imaging findings, followed by a confirmatory CT-guided biopsy and histopathological analysis, emphasizes the importance of considering ECD in similar clinical scenarios. Early and accurate diagnosis through comprehensive imaging and tissue biopsy is essential for guiding appropriate management and improving patient outcomes in this rare disease.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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