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CASE REPORT

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Cardiac mass as the primary diagnostic clue of Edheim–Chester disease

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Key Clinical Message

We introduced one of the rare causes of intra-cardiac mass, that is, ECD and a new gene mutation (SLC29A3) that is probably related to this disease, and we noted the importance of using several diagnostic methods to rule out other intra-cardiac causes.

Abstract

Edheim–Chester disease is a rare histiocytosis affecting multiple organs. The infiltration of lipid-laden histiocytes characterizes the disease. Most patients experience bone involvement; over 50% of cases involve the cardiovascular system and other extra-osseous organs. In this case report, we present the case of a 42-year-old man who complained of shortness of breath and bone pain. During echocardiography, a large, homogenous, and fixed mass was found in the right atrium free wall. Computed tomography and cardiac magnetic resonance imaging revealed an infiltrative mass in the RA with atrioventricular groove involvement but coronary sinus encasement, right coronary artery, and superior vena cava encasement. Abdominal CT scans also reported aortic wall involvement and bilateral renal cortical and perirenal involvement. A kidney biopsy confirmed the infiltration of histiocytes and the diagnosis of ECD. The treatment was initiated for him, and his symptoms improved. In this case report, we express the importance of considering the rare causes of cardiac tumors.

KEYWORDS

cardiac, Edheim–Chester disease, histiocytosis, mutation, pseudo-tumor

1 | INTRODUCTION

Edheim Chester disease (ECD) is a rare disease of the non-Langerhans histiocytosis category involving organs such as the long bones, central nervous system (CNS), skin, kidney, heart, arteries, and endocrinopathies.[1,2] The disease is usually more common in the 50–60 years and men. Mutations that disrupt the cellular RAS-RAF-MEK-ERK signaling pathway play an essential role in the pathology of this disease.[3] Also, those diagnosed with the BRAF VR600E- mutation have more cardiac and CNS involvement.[4,5] Cardiac involvement in these patients can

be seen as pseudo-tumor infiltrates of the right atrium (RA) in 36% of patients.[3] Diagnosis of the disease is based on histo-pathological, medical, and radiological findings, among which MRI is a key part of diagnosing the condition.[6,7] In this clinical case, we present a challenging scenario involving a 42-year-old male patient who presented with shortness of breath (SOB) and skeletal pain, in which a multi-disciplinary approach plan led to the diagnosis of ECD.

2 | CASE HISTORY/ EXAMINATION

A 42-year-old man presented with SOB and skeletal pain and was referred to Shahid Rajaei Center. In the physical exam, he had normal sinus rhythm in his electrocardiogram (75 bpm) and normal oxygen saturation in room air (97%), his blood pressure was 110/70 mmHg, and his temperature was 36.9°C. Laboratory results showed elevated erythrocyte sedimentation rate (ESR) and reactive protein (CRP) levels. Echocardiography revealed a large heterogeneous mass-like thickness in the RA measuring 4.8 × 1.6 cm attached to the RA wall (Figure 1). Cardiac magnetic resonance imaging confirmed an infiltrative mass in the RA roof and atrioventricular (AV) groove with the encasement of the right coronary artery and superior vena cava (Figure 2A–D).

3 | METHODS

ECD emerged as the leading differential diagnosis based on MRI tissue characterization criteria. Furthermore, a CT scan (Figure 3) showed mild abdominal aortic wall thickening, bilateral renal cortical and perirenal soft tissue infiltration, mild diffuse osteopenia, and wedge deformity of the thoracolumbar vertebra, all consistent with EDC. Kidney biopsy revealed mixed inflammatory cell infiltration containing some histiocytes, supporting the diagnosis of non-Langerhans cell histiocytosis. The patient, a product of a first-cousin marriage, experienced hearing loss at 7 years old and exhibited flexion contracture of both upper and lower extremity digits soon after. At 33 years old, he underwent a brain and sinus CT scan for a headache, which revealed acute sinusitis. Further investigations, including genetic testing, were performed due to a family history of hearing loss and the presence of a spinal cord mass in the patient's younger brother. The patient had a homozygous pathogenic variant in the SLC29A3 gene, and the patient's younger brother, currently 27 years old, was found to be homozygous for this mutation, too, but both parents were heterozygous. Therefore, the genetic basis of this disease was confirmed, and treatment with corticosteroids and alpha interferon was initiated for him.

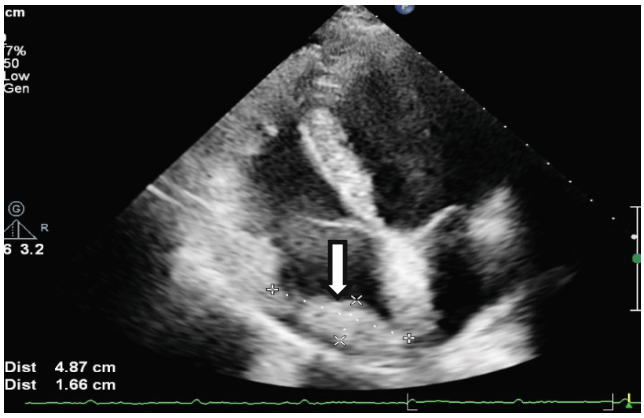

FIGURE 1 A large homogenous mass like thickness in RA (4.87 × 1.66 cm), abnormal thickening post IAS is seem to be infiltrative process.

4 | CONCLUSION AND RESULT

After 2 months of treatment following the confirmation of ECD diagnosis, the patient's symptoms showed improvement, and the treatment continued.

5 | DISCUSSION

Histiocytosis mainly manifests by bone involvement, but extra-osseous manifestations are also present in 50% of cases.[8,9] Kidney involvement pattern, reported in 63% of these patients, was in the form of hairy kidneys with perirenal fat infiltration (also reported in our patient). Moreover, retro-peritoneal fibrosis was also confirmed in 30% of the patients.[4,10] Cardiac manifestations include epicardial fat involvement and soft tissue infiltration in the right AV groove area, causing RCA encasement. In some cases, epicardial involvement causes a mass with a pressure effect on its' underlying cavity (RA and RV free wall).[11] Pericardial involvement manifests as increased thickness, effusion, and tamponade.[7] Other cardiac complications include rhythm disorders, conduction abnormalities, and valve involvement.[12] Extra-cardiac manifestation in the form of peri-aortic infiltration, known as the coated aorta, is reported as soft tissue infiltration at the level of the aortic arch, sometimes affecting the coronary arteries, leading to MI.[8,6] However, cardiac involvement is mainly in the form of an RA pseudo-tumor and infiltration of the right AV sulcus.[11] The cause of cardiac

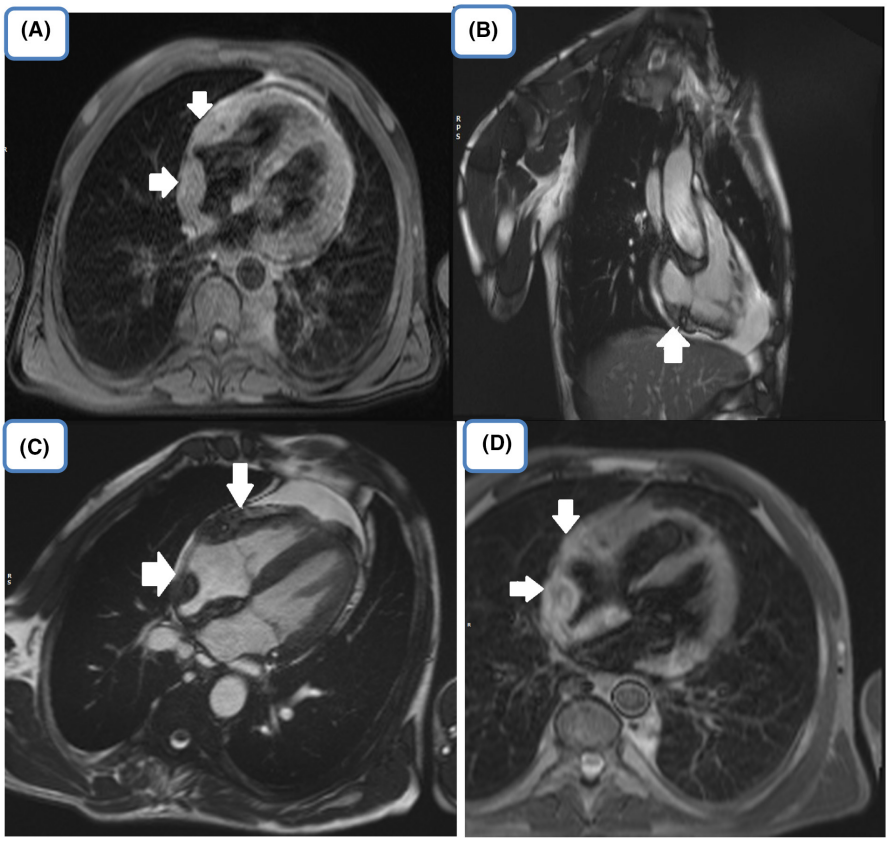

FIGURE 2 (A), Four chamber and RV in and out views in SSFP sequence, there is a large intra-pericardial mass (arrows) that invades into the right atrium (RA) and interatrial septum with intra-cavity portion of the mass in the RA. (B), There is encasement of CS and RCA but No invasion to them. (C), T1 with fs weight (D) T1 without fs and images demonstrate high signal intensity mass (arrows) in T1W without fat suppression.

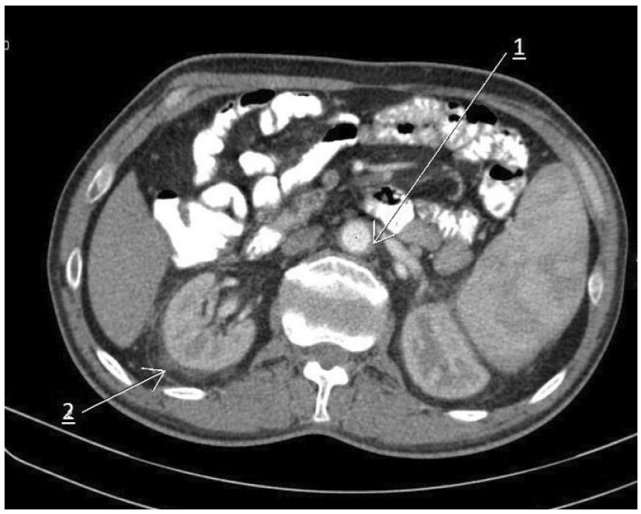

FIGURE 3 Abdominal CT scan findings of the patient showed: 1. Abdominal aortic wall thickening 2. Perirenal soft tissue infiltration and mild splenomegal.

pseudo-tumor, mainly associated with BRAF mutation, is still unclear. However, RA includes cardiac appendage stem cells that originate from medullary progenitors, so the stages of somatic mutation can occur during their evolution.[4] By examining the BRAF gene in these patients, those with this mutation had more cardiac and CNS involvement.[4,13] Our patient had SLC29A3 mutation, which was previously seen in histiocyte-lymphadenopathy plus syndrome, including Faisalabad histiocytosis, H-syndrome, pigmented hypertrichotic dermatosis and insulin-dependent diabetes and in a recent study that examined four cases, SLC29A3 was introduced as an inherited monogenic mutation associated with atypical ECD-like hystiocytosis.[14,15] ECD patients' pathology shows bland xanthogranulomatous inflammation with different degrees of fibrosis and foamy, lipid-laden histiocytes.[16] Cardiac MRI of the patients shows soft tissue mass density appearing Hypo-intense in the balanced steady-state free precession (B-SSFP) and T2W sequences. In addition, slight diffuse hyper-intensity is seen in fat signal suppression. In the T1W sequence, late enhancement of soft tissue lesions is seen in favor of disease activity and inflammation, as with our patient's MRI.[7]

Treatment with vemurafenib for ECD patients with the BRAF V600F mutation is recommended, but in other mutations, as in our patient, treatment with Interferon-alpha and corticosteroids and non-specific therapies are used, and localized treatments such as radiotherapy treatment also have a limited role in treating the disease and its local complications.[17–19]

This case highlights the diagnostic challenges encountered in infiltrative cardiac masses and the importance

of considering rare diseases, such as Erdheim-Chester, in the differential diagnosis. Multimodal imaging, genetic testing, and histo-pathological examination were instrumental in reaching an accurate diagnosis. A multidisciplinary approach involving multiple specialties and tailored treatment strategies is also necessary for optimal management. In addition, further research and collaboration are needed to enhance our understanding of Erdheim–Chester disease and to improve patient outcomes.

AUTHOR CONTRIBUTIONS

Azin Alizadehasl: Investigation; supervision. **Maryam Mohseni Salehi:** Conceptualization; data curation; validation; writing – original draft. **Zeinab Soltani:** Investigation; methodology; validation; visualization. **Soudeh Roudbari:** Data curation; formal analysis; validation; writing – original draft. **Mahsa Akbarian:** Formal analysis; investigation; visualization; writing – original draft. **Somaye Mohebbi:** Data curation; formal analysis; writing – review and editing. **Pegah Salehi:** Formal analysis; investigation; methodology; writing – original draft; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflict of interest to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author (Pegah Salehi) on request and this case report had been preprinted on Authorea and its link is: https://doi.org/10.22541/au.169899222.28959802/v1

CONSENT STATEMENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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