

# Erdheim-Chester Disease with Cardiovascular Involvement Evaluated by Multi-Imaging Modalities: A Case Report

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## ***Abstract***

Erdheim-Chester disease (ECD) is a rare multisystemic non-Langerhans cell histiocytosis disease of unknown etiology. Cardiovascular involvement is seen in 40% of patient, and it is usually associated with poor prognosis. We report a 43-year old woman patient who was referred to the Adult Cardiology for further assessment of cardiac arrhythmia. Her ECG showed Left bundle branch block (LBBB) with premature ventricular contractions (PVCs), Mobitz type 1 AV block. Further assessment with cardiac MRI showed irregular and nodular thickening of the walls of the right atrium and interatrial septum, infiltrating the right coronary sulcus. Findings were suggestive of Erdheim-Chester disease (ECD). Tissue biopsy of the soft tissue infiltrating the heart confirmed the diagnosis of Erdheim-Chester disease (ECD).

**Keywords:** Cardiovascular; Case Report; Heart; Heart Neoplasms; right atrium; Erdheim-Chester disease Magnetic Resonance Imaging; Neoplasm.

## **Introduction**

Erdheim-Chester disease (ECD) is a rare, multi-systemic disease, non-Langerhans cell histiocytosis of unknown etiology.<sup>1</sup> It is characterized histopathologically by granulomatosis and fibrosis brought on by foamy histiocyte infiltration of the afflicted organs. Even though awareness and reporting of this unusual pathology are rising, its global incidence is still unclear.<sup>2,3</sup> It is usually affecting middle age group with a slight male predominance, and some studies suggesting an earlier diagnosis in female compared to male patients.<sup>4</sup>

ECD can involve multiple systems including skeletal, central nervous, respiratory, cardiovascular, and renal systems, as well as the retroperitoneum and the skin. The most common and initial presentation is usually bone pain.<sup>5</sup>

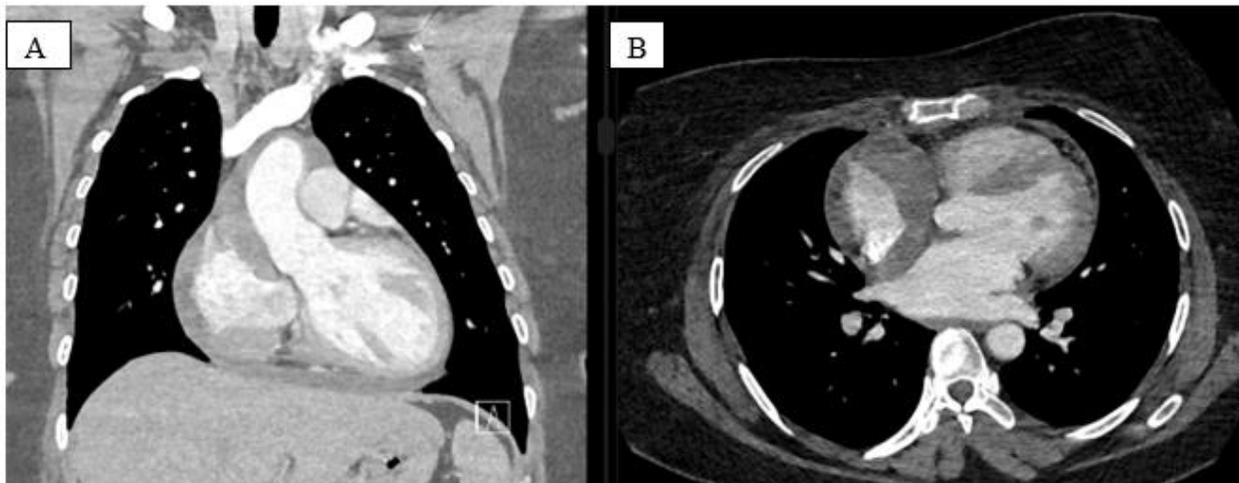
Cardiothoracic involvement is seen in 50-90% of individuals with ECD, and it is indicative of worse prognosis with up to 40% of ECD-related deaths result from cardiorespiratory involvement.<sup>6</sup> Therefore, early detection of cardiothoracic involvement is crucial to initiate appropriate treatment and prevent complications. On imaging ECD has characteristic features, and recognition of these imaging finding allow early diagnosis and prevent the delay in

starting the appropriate treatment. Herein, we present a case of histologically confirmed ECD with characteristic imaging findings on computed tomography (CT), fludeoxyglucose positron emission tomography (FDG PET/CT) and cardiac MRI (CMR). To the best of the authors' knowledge, this is the first case of ECD with cardiac involvement detected by MRI to be reported in Oman

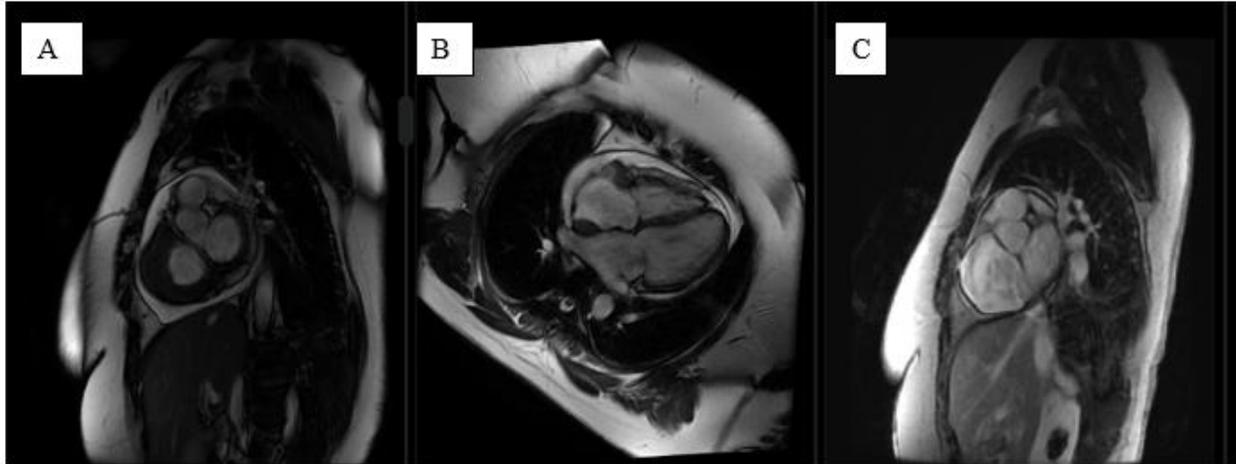
## Case Report

A 43-year-old woman presented to our tertiary hospital emergency department with a history of atypical chest pain and palpitation. Initial physical examination was unremarkable. Her ECG showed Left bundle branch block (LBBB) with premature ventricular contractions (PVCs), Mobitz type 1 AV block. On lab investigations, her blood serum troponin T level was 5 pg/ml (normal <5pg/mL). Other lab investigations showed glomerular filtration rate (GFR > 90 mL/min, hemoglobin 11.6 g/dL and WBC 8.9. Her C- reactive protein (CRP) was elevated reaching up to 48 mg/l. Her initial echocardiogram (ECHO) was normal with and ejection fraction (EF) of 60%.

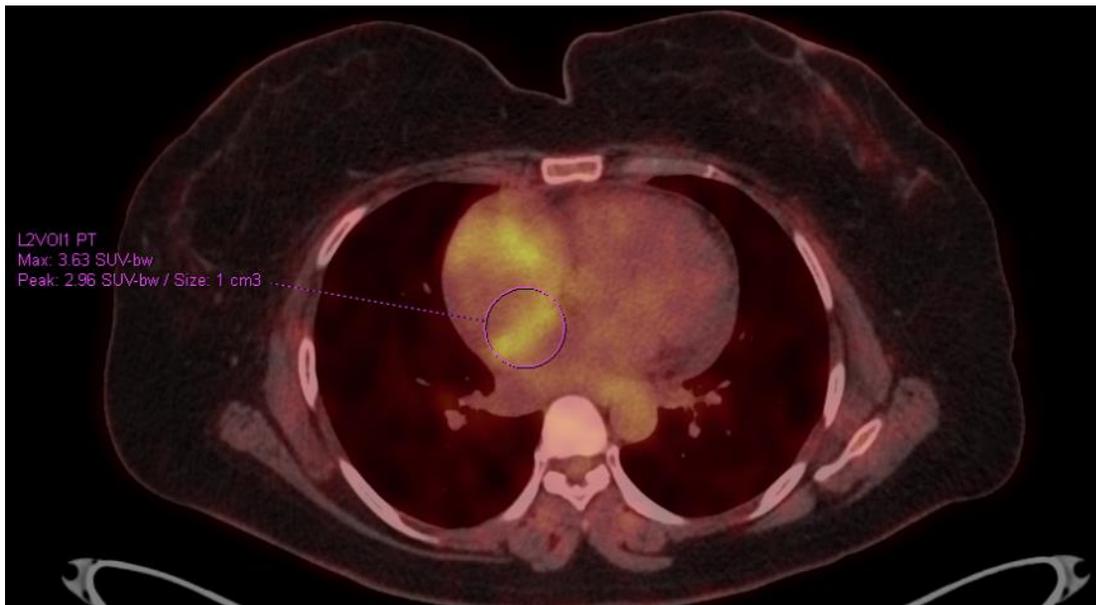
Further work up with a chest CT showed no features of pulmonary sarcoidosis. However, it showed an enhancing soft tissue thickening (Hounsfield unite (HU) 51) involving the wall of the right atrium as well as the interatrial septum and infiltrating the right coronary sulcus. In addition, there are focal areas of abnormal mural thickening of the aortic arch extending to involve the most proximal part of the left subclavian artery, and areas of eccentric mural thickening involving the descending thoracic aorta [Figure 1]. Further assessment with cardiac MRI with IV contrast confirmed the CT findings of a soft tissue thickening involving the right atrial wall and extending to involve the interatrial septum and well as the right coronary sulcus resulting in the appearance of right atrial pseudotumor. This soft tissue was hypointense in steady state precision sequence and showed homogenous enhancement on post contrast examination [Figure 2]. Findings from CT scan and CMR were suggestive of ECD. However, lymphoma could not be excluded. Further evaluation with F18-FDG whole body positron emission tomography with CT scan (F18-FDG PET/CT) was performed and it showed heterogenous increased FDG uptake of the irregular thickening involving the right atrial wall and the interatrial septum [Figure 3]. After multidisciplinary team discussion, the decision was to go for tissue biopsy to conform the diagnosis and to exclude other differential diagnosis. A diagnostic surgical tissue biopsy was performed under general anesthesia and obtained from the thick tissue above the right atrium.



**Figure 1:** Coronal (A) and axial (B) image of contrast enhanced CT scan showing an enhancing soft tissue thickening involving the walls of the right atrium as well as the interatrial septum and infiltrating the right coronary sulcus.

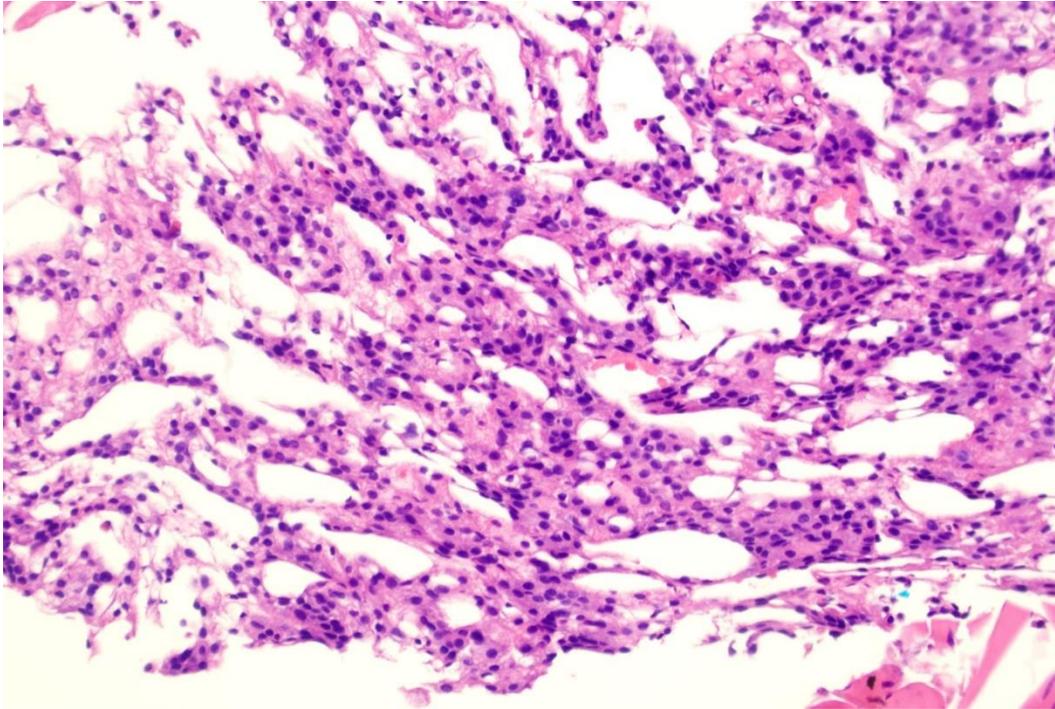


**Figure 2:** Steady state free precision short axis oblique (A) and 4-chamber view (B) showing soft tissue thickening of the right atrium extending to involve the intraarterial septum resulting in the appearance of a pseudotumor. Post contrast image showing homogenous enhancement of the soft tissue.

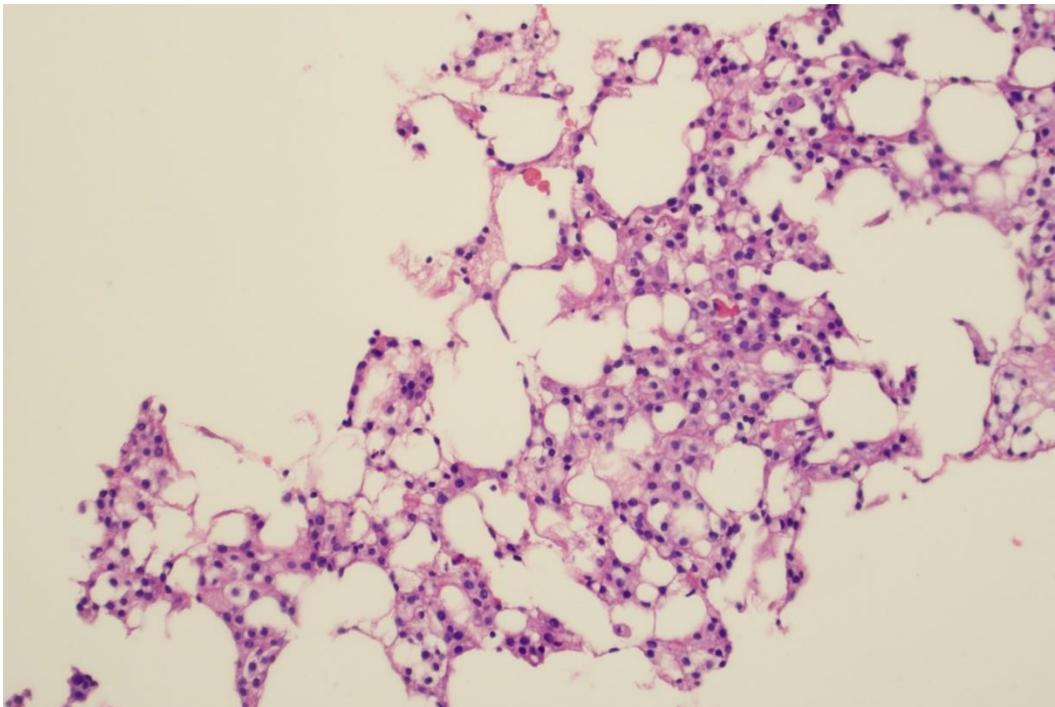


**Figure 3:** PET/CT showing increased uptake in the soft tissue thickening involving the wall of the right atrium and extending to involve the intraarterial septum.

The histopathologic findings revealed variable infiltration by aggregates of histiocytes with central nuclei and pale eosinophilic or vacuolated cytoplasm. Admixed few lymphocytes and rare plasma cells are noted. By immunohistochemistry, these histiocytes are positive for CD68 and negative for S100, CD1a, calretinin, CK5/6 and BerEp4. This immunoprofile was that of xanthogranulomatous histiocytes and compatible with ECD. Negative S100 and CD1a excludes Langerhans histiocytosis [Figure 4, 5, and 6]. The patient was then referred to a different institute for treatment and follow up.



**Figure 4:** Pleural biopsy, sheets of histiocytes with central round nuclei and pale to eosinophilic cytoplasm. (Hematoxylin and eosin, magnification = 20 $\times$ ).



**Figure 5:** Cardiac biopsy, aggregates of histiocytes with central nuclei and vacuolated cytoplasm (Hematoxylin and eosin, magnification = 20 $\times$ ).



**Figure 6:** The histiocytes are positive for CD68 immunostain.

## Discussion

ECD is a rare multisystemic non-Langerhans cell histiocytosis of unknown etiology. It was described for the first time by William Chester and Jakob Erdheim as uncontrolled chronic inflammatory disorder.<sup>7</sup> The median age of presentation is usually 52.8 years with a slight male predominance (62.3%).<sup>8</sup>

The clinical presentation is usually variable and depended on the affected organs. Different systems in the body can be affected by ECD including skeletal system, central nervous system, cardiovascular system, lungs, and retroperitoneum. Skeletal system is the most affected system (96%), and most of the patients present with bone pain.<sup>8</sup>

Cardiothoracic involvement is seen in 50-90% of patients affected by ECD, and include periaortitis, pericardial, myocardial, and coronary arteries as well as the aorta and its branches.<sup>6</sup> 75% of patients with cardiovascular involvement will have their heart affected by ECD. Clinically, patients with cardiovascular ECD can be asymptomatic, or presented with arrhythmias, valvular heart disease, ischemia, or cardiac failure. Our patient presented with history of supraventricular tachycardia (SVT) with right bundle branch block morphology (RBBB), and bradycardia with evidence of atrioventricular dissociation and left bundle branch block (LBBB).<sup>7</sup>

Imaging play an important role in the assessment of ECD. Cardiac MRI is now advised for all patients with ECD to identify cardiac involvement and define the extent of the disease according to published consensus recommendations for baseline evaluation of ECD.<sup>9</sup> MRI with IV contrast is optimal for assessment of pericardial and myocardial infiltration as well as characterization of the infiltrative soft tissue and assessment of cardiac function. Pericardial involvement can be seen in 13-24% of patients with cardiac involvement and manifest as generalized pericardial thickening and/or pericardial effusion. This can infrequently cause cardiac tamponade. Pericardial calcification is rarely seen, and it has been reported in 4% of the cases.<sup>6</sup> Myocardial infiltration by ECD is usually seen in 25-31% of patients and commonly involve the right atrium and right atrioventricular groove, resulting in right atrial "pseudotumor" in up to 30% of cases.<sup>6</sup> Primary cardiac lymphoma and angiosarcoma are two main differential diagnosis for cardiac ECD. On cardiac MRI, ECD appears as hypointense infiltration on T1 and balanced steady state free precession (b-SSFP) images, which demonstrates intense enhancement on post-contrast sequence. Although

primary cardiac lymphoma appears hypointense infiltration on T1 weighted images, it shows less intense enhancement.<sup>10</sup> Primary cardiac angiosarcoma appears more aggressive on imaging with irregular and ill-define infiltrative soft tissue that is heterogenous on post contrast sequence due internal hemorrhage and tumor necrosis.<sup>8</sup>

Our patient has small pericardial effusion along with an enhancing irregular and nodular thickening of the right atrium wall and the interatrial septum resulting in right atrial "pseudotumor." The thickening was also extending to infiltrate the right atrioventricular groove.

Involvement of the heart and pericardium on PET/CT may show aberrant FDG uptake with a maximum standardized uptake value (SUVmax) ranging from 3.6 to 8.1 in individuals with ECD. Because physiologic cardiac FDG uptake occurs to varying degrees primarily in the left ventricular wall, it might be difficult to identify pathological FDG uptake in the heart. While ECD frequently shows a patchy heterogeneous uptake pattern, most frequently in atrial walls or in the interatrial septum, physiological cardiac uptake typically exhibits a uniform uptake pattern with smooth edges. Before PET imaging, a high-fat, low-carb diet can be suggested to lessen physiologic heart uptake.<sup>6</sup>

To achieve a conclusive diagnosis of cardiothoracic ECD and formulate a treatment strategy, close multidisciplinary cooperation and collaboration are necessary given the rarity, complexity, and multisystemic clinical presentation of ECD. Additional imaging advised by the radiologist may be helpful in assessing for other implicated sites, in particular the lower limbs/femoral, the retroperitoneum, and the brain, if ECD is included in the differential diagnosis based on distinctive cardiothoracic involvement. Consensus recommendations for the initial evaluation of patients when a pathology diagnosis has been made include brain and cardiac MRIs, whole-body PET/CT, chest, abdomen, and pelvic CT, and whole-body PET/CT.<sup>11</sup> Patients with ECD have historically 3–5-year survival rates between 43 and 68%. Baseline imaging to define the extent of disease, biopsy confirming characteristic histopathology, are vital prior to commencing therapy.

ECD treatment is still not entirely established. Interferon was the most frequently prescribed therapy according to the literature, and according to consensus guidelines, treatment should be started for all patients except those who are minimally symptomatic.<sup>11</sup> In a prospective multicenter study included 53 patients with ECD, they found interferon significantly increased overall survival. Vemurafenib, a mutated BRAF inhibitor, was successful in treating BRAF-positive patients, as evidenced by the significantly improved clinical and radiographic outcomes.<sup>11</sup>

## Conclusion

Erdheim-Chester disease (ECD) is a rare, multi-systemic disease. Cardiac involving by ECD is usually associated with poor prognosis. Knowing the imaging and clinical characteristics of ECD is crucial for the early and accurate diagnosis and treatment of this condition. In this case report we reviewed the features of ECD in different imaging modalities.

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