

Erdheim–Chester disease presenting as an intracardiac mass and pericardial effusion confirmed by biopsy: a case report

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Background

Erdheim–Chester disease (ECD) is a rare non-Langerhans cell histiocytosis that can affect the bones, heart, lungs, brain, and other organs. Cardiovascular involvement is common in ECD and is associated with a poor prognosis. Here, we report a case of ECD presenting as an intracardiac mass and pericardial effusion confirmed by biopsy with sternotomy.

Case summary

A 54-year-old man was admitted because of dyspnoea. He was previously diagnosed with bilateral hydronephrosis and retroperitoneal fibrosis. Echocardiography revealed a large amount of pericardial effusion and echogenic mass on the right atrial (RA) side and atrioventricular (AV) groove. Cardiac magnetic resonance imaging and positron emission tomography-computed tomography (CT) revealed infiltrative mass-like lesions in the RA and AV groove. Pericardial window formation and pericardial biopsy were performed, and the pathologic results showed only pericardial fibrosis with no specific findings. Bone scan revealed increased uptake in the long bones. Considering the high probability of ECD based on the patient's manifestations and the imaging findings, we performed a cardiac biopsy with median sternotomy despite initial insufficient pathologic results in the pericardial biopsy. The surgical findings included multiple irregular and firm masses on the cardiac wall and large vessels; after obtaining a large amount of suspicious mass, ECD accompanied with CD68 (+) and BRAF V600E mutation was confirmed.

Discussion

Erdheim–Chester disease can be associated with various forms of cardiovascular involvement. Considering the multi-systemic manifestations and difficulty in identifying this rare disease, a comprehensive and meticulous diagnostic work-up is crucial.

Keywords

Erdheim–Chester disease • Pericardial effusion • Cardiac mass • Open cardiac biopsy • Sternotomy • Case report

Learning points:

- Erdheim–Chester disease (ECD) can present with various cardiovascular manifestations.
- A comprehensive and meticulous diagnostic workup is essential for the diagnosis of ECD, which is characterized by multiorgan involvement.
- Because the yield of a single biopsy is low, obtaining a large number of samples or re-biopsy may be helpful if ECD is clinically highly suspected.

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Introduction

Erdheim–Chester disease (ECD) is a systemic disease and rare form of non-Langerhans cell histiocytosis.¹ The characteristic pathologic finding of ECD is tissue infiltration by foamy non-Langerhans histiocytes surrounded by fibrosis, which leads to systemic xanthogranulomatous infiltration.² This disease was first described by Jakob Erdheim and William Chester in 1930.³ The majority of ECD patients are diagnosed between the ages of 40 and 70 years, with a slight male predominance.¹ Although approximately 550 cases have been reported, the number of case reports of ECD dramatically increased in the last 20 years due to increased recognition of this disease and a wider availability of diagnostic methods.^{1,2}

Erdheim–Chester disease is a multisystem disease affecting the bones, heart, lungs, kidneys, brain, skin, and other organs.⁴ The most common clinical manifestation is bone pain due to bony involvement. Cardiovascular involvement is also common, but not always clinically evident as it is often asymptomatic.^{5,6} However, cardiovascular involvement in ECD is associated with poor prognosis, and cardiac complications are a major cause of death in this disease.^{1,7,8}

Herein, we report a case of ECD presenting as an intracardiac mass and pericardial effusion confirmed by biopsy with sternotomy despite initial negative pathologic findings in the pericardial biopsy.

Timeline

Time	Event
2010	Diagnosed with dilated cardiomyopathy.
2012	Abdominal pelvic computed tomography (CT) and diagnostic ureteroscopy were performed. He was diagnosed with idiopathic retroperitoneal fibrosis and bilateral hydronephrosis.
Day 1 (30 December 2020)	Admission due to dyspnoea. Transthoracic echocardiography revealed a large amount of pericardial effusion and an echogenic mass on the right atrial side and atrioventricular groove.
Day 4	Heart magnetic resonance image showed infiltrative mass-like lesions in the right atrial (RA) wall and atrioventricular (AV) groove.
Day 8	Cardiac positron emission tomography–CT showed fluorodeoxyglucose uptake in the RA and AV groove.
Day 9	Pericardial window formation and pericardial biopsy were performed. Pathologic results showed only pericardial fibrosis with no specific findings.
Day 14	Whole-body bone scan revealed increased uptake in both distal femurs and proximal tibiae.
Day 16	Cardiac biopsy following median sternotomy.
Day 23	Pathologic report revealed chronic inflammation and fibrosis and CD68 positivity on

Continued

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Time	Event
	immunohistochemical staining. In addition, <i>BRAF</i> V600E mutation was detected.
1 month later	Finally diagnosed with Erdheim–Chester disease. Referral to the haematology department; chemotherapy with etoposide and dexamethasone started.



Figure 1 Contrast-enhanced axial abdominal pelvis computed tomography image showing bilateral hydronephrosis and bilateral fat infiltration in the perirenal space (thick arrows).

Case presentation

A 54-year-old man was admitted to our hospital because of dyspnoea. He had a past medical history of diabetes mellitus and Stage 3 chronic kidney disease. He was diagnosed with heart failure with reduced ejection fraction (HFrEF) in 2010. The aetiology of HFrEF was suspected to be idiopathic dilated cardiomyopathy with comprehensive evaluation, including transthoracic echocardiography (TTE), coronary angiography, and cardiac magnetic resonance imaging (MRI). He was followed up in a cardiology outpatient clinic with guideline-directed medical therapy for 10 years. In 2012, he was diagnosed with a ureter stone, and abdominal pelvic computed tomography (CT) revealed bilateral hydronephrosis and bilateral fat infiltration in the perirenal and periureteric spaces (*Figure 1*). Diagnostic ureteroscopy and biopsy were performed, and the pathology results showed chronic non-specific inflammation. He was referred to a rheumatologic clinic, and the diagnosis was suspected to be idiopathic retroperitoneal fibrosis. Oral steroids and azathioprine for immunosuppression were started and followed up in the outpatient clinic.

On admission, his vital signs were: blood pressure 119/63 mmHg, pulse rate of 60 beats/min, respiratory rate of 16 breaths/min, and body temperature of 37.0°C. He had a little dehydrated tongue, but

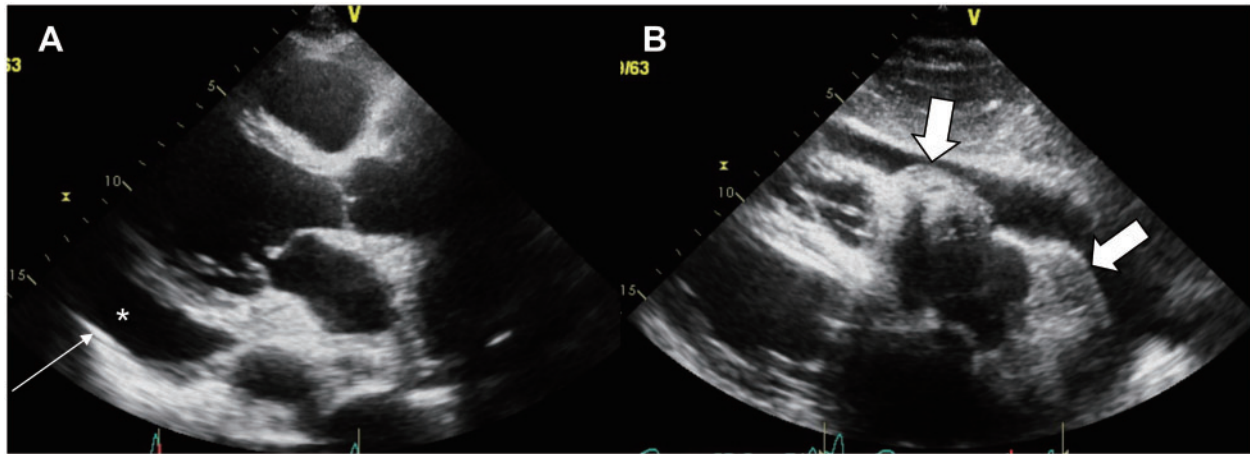
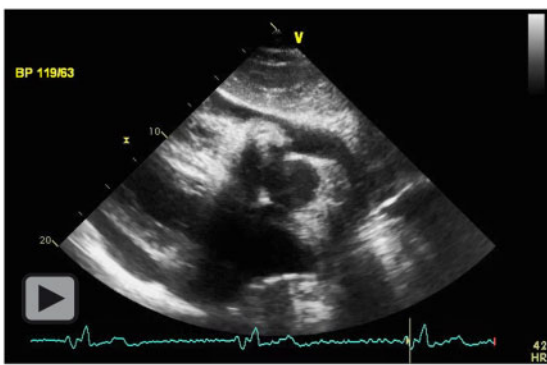


Figure 2 Transthoracic echocardiography. (A) Parasternal long axis view, large amount of pericardial effusion (thin arrow) (B) Subcostal view, echogenic mass on the right atrial side, and atrioventricular groove (thick arrows).



Video 1 Transthoracic echocardiography, subcostal view showing pericardial effusion and echogenic mass on the right atrial side and atrioventricular groove.

his chest and abdomen physical examination showed no abnormalities. Chest radiography revealed cardiomegaly, and TTE revealed a large amount of pericardial effusion and an echogenic mass on the right atrial (RA) side and atrioventricular (AV) groove (Figure 2, Video 1). Cardiac MRI revealed infiltrative mass-like lesions in the RA wall and AV groove, indicating the likely cardiac involvement of a systemic disease, such as ECD, IgG4-related disease, or lymphoma (Figure 3A). Cardiac MRI showed normal systolic function (left ventricular ejection fraction: 68%) and increased native T1 (1468 ms) value, and normal T2 (44.4 ms) value on the mass-like lesion. Cardiac positron emission tomography (PET)–CT was performed to evaluate the disease activity, and it revealed fluorodeoxyglucose uptake in the RA wall and AV groove (Figure 3B and C).

He underwent subxiphoid pericardial window formation and pericardial biopsy to drain the pericardial effusion and obtain a sample of suspicious tissue. In the operating room, there was a large amount of serous pericardial effusion. In addition, firm and irregular cardiac

masses were observed in the pericardial space and on the right ventricle (RV) surface. We could only obtain some pericardial tissue due to the limitations of the surgical field; pathological examination revealed only pericardial fibrosis with no specific findings. Immunohistochemical staining with IgG and IgG4 showed negative results, and *BRAF* mutation analysis revealed the patient had the wild-type.

However, bone radiography revealed suspicious heterogeneous radiolucency in the distal femur and proximal tibia, and a whole-body bone scan revealed increased uptake in both distal femurs and proximal tibiae (Figure 4). Considering the pericardial effusion, cardiac masses, hydronephrosis, retroperitoneal fibrosis, and multifocal bone lesion, we believed that the patient likely had ECD despite initial insufficient pathologic results (Supplementary material online, Figure S1). After a multidisciplinary team approach, we performed a cardiac biopsy with median sternotomy; multiple irregular and firm masses were found on the surface of RA, RV, AV groove, inferior vena cava, superior vena cava, and aorta (Figure 5). We obtained a large amount of suspicious mass, and pathological examination found chronic inflammation, fibrosis, and CD68 positivity on immunohistochemical staining (Supplementary material online, Figure S2). In addition, the *BRAF* V600E mutation was detected. Finally, the patient was diagnosed with ECD.

He was referred to the haematology department and started chemotherapy with etoposide and dexamethasone. After the 2 months of initial chemotherapy, he was started with vemurafenib, an inhibitor of *BRAF* harbouring the V600E mutation. Treatment response will be assessed after 2 or 3 months of vemurafenib treatment.

Discussion

Erdheim–Chester disease can affect any organ; therefore, its manifestations vary among patients, making it difficult to diagnose. Cardiovascular involvement is important because it is common and

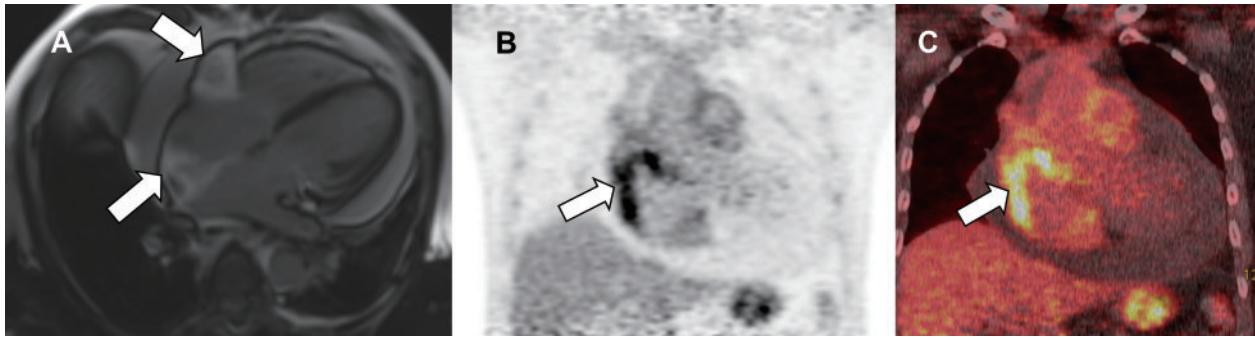


Figure 3 (A) Axial late gadolinium enhanced cardiac magnetic resonance image showing infiltrative mass-like lesions in the right atrial wall and atrio-ventricular groove (thick arrows). Cardiac magnetic resonance image showed normal systolic function (left ventricular ejection fraction: 68%) and increased native T1 (1468 ms) value, and normal T2 (44.4 ms) value on mass-like lesion. (B, C) Coronal cardiac positron emission tomography-computed tomography images showing increased fluorodeoxyglucose uptake in the right atrial wall and atrioventricular groove (thick arrow).

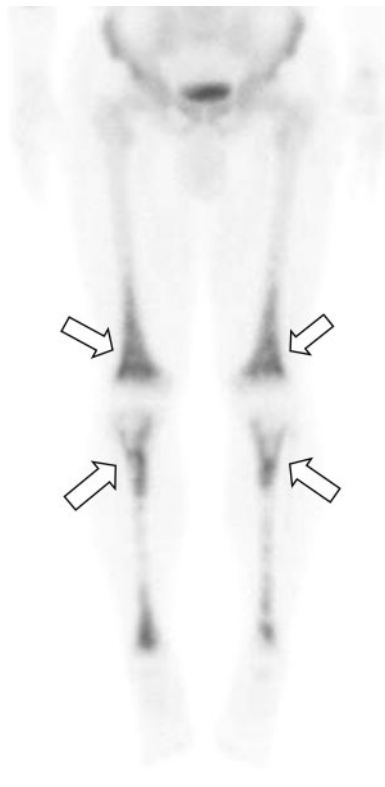


Figure 4 Whole-body bone scan by Technetium-99m showing increased uptake in both distal femurs and proximal tibiae in the anterior whole-body view (thick arrows).

associated with a poor prognosis.^{4,7,8} Cardiovascular manifestations are the major cause of death in ECD since 60% of patients with ECD die due to cardiovascular complications including heart failure and myocardial infarction.^{8,9} The prognosis of ECD was reported as poor, with 57% of patients dead after an average follow-up of 32 months.¹ Erdheim–Chester disease may affect the myocardium,

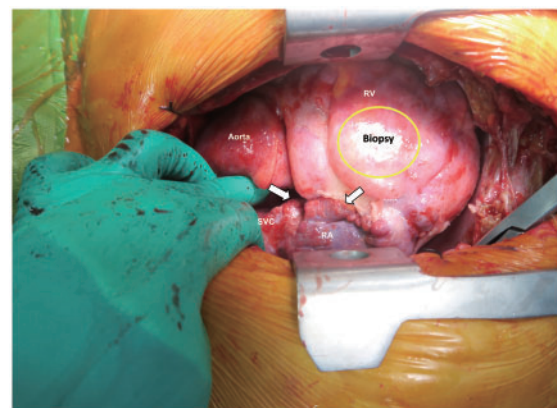


Figure 5 Cardiac biopsy with median sternotomy was performed. Multiple irregular and firm masses were found on the right atrium, right ventricle, atrioventricular groove, superior vena cava, inferior vena cava, and aorta (thick arrows). Biopsy was performed in suspicious lesion on right ventricle and right atrium. AV, atrio-ventricular; IVC, inferior vena cava; RA, right atrium; RV, right ventricle; SVC, superior vena cava.

pericardium, cardiac valves, aorta, coronary arteries, and conduction system.¹⁰ Pericardial involvement is frequent, occurring in 40–45% of patients when evaluated using TTE, and it can be totally asymptomatic or can lead to pericarditis, effusion, and even tamponade.¹¹ Pathological histiocytes can also infiltrate the heart wall, thus producing a pseudotumour typically localized to the RA or AV groove.⁸ Erdheim–Chester disease can also affect the aorta, causing circumferential infiltration, which can be detectable in a CT scan.⁸ This radiologic finding in the aorta is referred to as a ‘coated aorta’.¹² In this case, pericardial effusion and cardiac mass were cardiac manifestations of ECD.

Diagnosing ECD is very challenging because the most common clinical manifestations (e.g. bone pain) usually lack adequate specificity. In this multi-systemic disease, various multi-modal imaging

approaches, including CT, brain MRI, cardiac MRI, PET–CT, and bone scan, can be helpful in the diagnosis.¹³ For this rare and complex disease, it is essential that clinicians know the main features of the disease so that they can perform an early and comprehensive diagnostic investigation.¹⁴

An accurate diagnosis of ECD is made by identifying the pathological histiocytes in the tissue. Nonetheless, selection of the biopsy site and histopathologic confirmation of ECD remains challenging.¹ Because the yield of a single biopsy is low due to histologic changes from field to field, efforts should be made to obtain several samples, regardless of the biopsy site.¹⁵

In this case, the patient presented with pericardial effusion and cardiac masses. Multi-modal imaging, including CT, MRI, PET–CT, and bone scan, was beneficial for diagnosis. Although the initial pathologic results from the pericardial biopsy showed non-specific findings, the cardiac biopsy with sternotomy allowed a large amount of suspicious masses to be obtained, which confirmed ECD.

Conclusion

We report a patient with ECD presenting as an intracardiac mass, pericardial effusion, retroperitoneal fibrosis, and multifocal bone lesions. He was diagnosed with ECD after performing a cardiac biopsy with median sternotomy despite initial insufficient pathologic results from pericardial biopsy. Because the yield of a single biopsy is low, obtaining a large amount of samples or re-biopsy may be helpful if ECD is clinically highly suspected. Considering the various clinical manifestations and the difficulty in identifying this rare disease, a comprehensive and meticulous diagnostic work-up is crucial.

Lead author biography



Minjae Yoon was born in 1989 in Seoul, Republic of Korea. He received the MD degree from Yonsei University in 2013. He completed one year of internship and four years of resident program at Severance Hospital (2013–18). Currently, he is working as a cardiologist in Severance Cardiovascular Hospital. His research interest is focused on heart failure and heart transplantation.

Supplementary data

Supplementary material is available at *European Heart Journal—Case Reports* online.

Slide sets: A fully edited slide set detailing these cases and suitable for local presentation is available online as [Supplementary data](#).

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: None declared.

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