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CASE REPORT

ADVANCED

CLINICAL CASE: SURGERY AND INTERVENTIONS

Pericardiectomy for Constrictive Pericarditis in a Young Patient With Erdheim-Chester Disease

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ABSTRACT

Erdheim-Chester Disease (ECD) is an extremely rare non-Langerhans histiocytosis that most often presents in the fifth to seventh decades of life. In this case report, we present a 34-year-old woman who underwent successful pericardiectomy for constrictive pericarditis secondary to ECD, which is the youngest reported patient with ECD to undergo pericardiectomy. (**Level of Difficulty: Advanced.**) (J Am Coll Cardiol Case Rep 2022;4:862–867) © 2022 Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 34-year-old woman presented with shortness of breath (SOB) on exertion, reduced exercise capacity, and fluid overload. Heart rate was 103 beats/min, blood pressure 119/77 mm Hg, temperature 36.3°C, respiratory rate 20, and SPo_2 98% on room air. She was found to have constrictive pericarditis and referred for pericardiectomy.

Ten years prior, at 25 years of age, the patient developed symptoms of polyuria and polydipsia secondary to diabetes insipidus, tenosynovitis, joint effusions, and skin lesions. Lymph node and skin biopsies suggested histiocytosis with $S100^+$ and $CD1A^+$. Based on these findings, the patient was diagnosed with Langerhans histiocytosis 4 years after symptom onset. Treatment included methotrexate, which was discontinued for side effects, and prednisone during flares of tenosynovitis and joint effusions. Five years later, the patient presented with SOB, decreased exercise tolerance, peripheral edema, ascites, 20 lb weight gain, and joint effusions. Physical examination revealed a jugular venous pressure 6 cm above sternal angle, muffled heart sounds, and peripheral edema.

LEARNING OBJECTIVES

- To learn about potential presentations of ECD and be able to recognize it, especially with atypical presentations.
- To understand the role of pericardiectomy in patients with ECD presenting with constrictive pericarditis.

PAST MEDICAL HISTORY

Past medical history included iron deficiency anemia, diabetes insipidus, and presumptive diagnosis of Langerhans histiocytosis.

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DIFFERENTIAL DIAGNOSIS

The patient's symptoms were initially attributed to Langerhans histiocytosis, although Erdheim-Chester disease (ECD) was added to the differential diagnosis based on further workup.

INVESTIGATIONS

Histologic skin samples revealed foamy histiocytic cells in loose clusters throughout the dermal collagen fascicles. Immunohistochemical studies confirmed histiocytic cells as $CD68K^{+}$, $CD68P^{+}$, and mostly $S100^{-}$. Magnetic resonance imaging (MRI) revealed moderate bilateral pleural effusions, loculated pericardial effusion, pericardium thickened up to 18 mm, left ventricular ejection fraction 69%, and septal shift with inspiration (**Figure 1A**). Transthoracic echocardiogram revealed signs of constrictive pericarditis, including hepatic vein flow reversal, septal bounce, and increased pericardial echogenicity (**Figure 1B,** Video 1). Computed tomography (CT) scan identified thickened pericardium, moderate pericardial effusion, and bilateral pleural effusions (**Figure 1C**). A fluorodeoxyglucose (FDG) positron emission tomography (PET) CT demonstrated moderate pericardial effusion, diffuse pericardial, pleural, peritoneal, and tibial FDG uptake (**Figures 1D and 1E**). An endomyocardial biopsy showed mild myocardial hypertrophy without infiltration.

MANAGEMENT

The patient was brought to the operating room, prepped, and draped in standard fashion. Median sternotomy was performed, and the pericardium exposed, which was thickened and difficult to grasp with instruments (**Figures 2A to 2C**). A combination of electrocautery and blunt dissection was used to create a plane between the fibrous pericardium and the heart. The left ventricle and apex were freed to 1 cm from the left phrenic nerve. Dissection continued inferiorly toward the diaphragm, then the right ventricle to 1 cm above the right phrenic nerve (**Figure 2D**). Excised pericardium measured 8 cm × 2 cm and 11 cm × 4 cm (**Figure 2E**). After excision, the central venous pressure dropped from 26 mm Hg to 15 mm Hg; 2.3 L of bilateral pleural effusion were suctioned. The stripped epicardial surfaces continued bleeding, requiring packing and Arista Absorbable Hemostat (Becton, Dickinson and Company), after which hemostasis was achieved (**Figure 2F**). The patient's sternum, fascia, and skin were closed in standard fashion. The patient was transferred to the cardiovascular intensive care unit where she was extubated on postoperative day (POD) 0. While in the cardiovascular intensive care unit, the patient's central venous pressure further dropped to 10 mm Hg. After transfer to the cardiac surgical ward on POD 1, the patient experienced SOB secondary to fluid overload. This was successfully treated with intravenous furosemide. The patient was discharged on POD 8 without complication and with improving function.

DISCUSSION

ECD is an extremely rare non-Langerhans histiocytosis resulting in systemic infiltration of lipid-laden histiocytes. Only several hundred cases of ECD have been described, often presenting in the fifth to seventh decades.[1-4] Although skeletal infiltration is most common, cardiac manifestations are a common cause of mortality. One such cardiac consequence is constrictive pericarditis, although few case reports have described pericardiectomy for ECD owing to low incidence.[1-3] All previous patients with ECD pericardiectomy were older than 45 owing to later onset of ECD. This case report describes the youngest patient with ECD requiring pericardiectomy to the authors' knowledge.

Signs and symptoms of ECD vary depending on affected systems and include bone pain, diabetes insipidus, dyspnea, cardiac tamponade, congestive heart failure, thromboembolism, peripheral edema, exophthalmos, rash, and fatigue, among others.[1,4-6] This patient presented with a several-month history of dyspnea and SOB secondary to congestive heart failure resulting from constrictive pericarditis compounded by bilateral pleural effusions. This report demonstrates the nonspecific presentation of ECD, highlighting the need for cardiac screening in patients with ECD.

In addition, in patients presenting with unexplained multisystem infiltrative disease with cardiac involvement, a high index of suspicion should be maintained until an alternative diagnosis is made or ECD ruled out, considering cardiac involvement indicates poor prognosis.[7] Because of rarity and systemic involvement, the differential diagnosis of ECD is broad. The differential diagnosis for cardiac involvement includes angiosarcoma, lymphoma, cardiomyopathy, and Takayasu arteritis, among others.[1,4,7]

ECD is often identified in imaging with CT, MRI, PET, and technetium-99m bone scintigraphy. Common findings include femoral diaphyseal and metaphyseal osteosclerosis; dense perinephric fat

ABBREVIATIONS AND ACRONYMS

CT = computed tomography

ECD = Erdheim-Chester disease

FDG = fluorodeoxyglucose

MEK = mitogen-activated protein kinase

MRI = magnetic resonance imaging

PET = positron emission tomography

POD = postoperative day

SOB = shortness of breath

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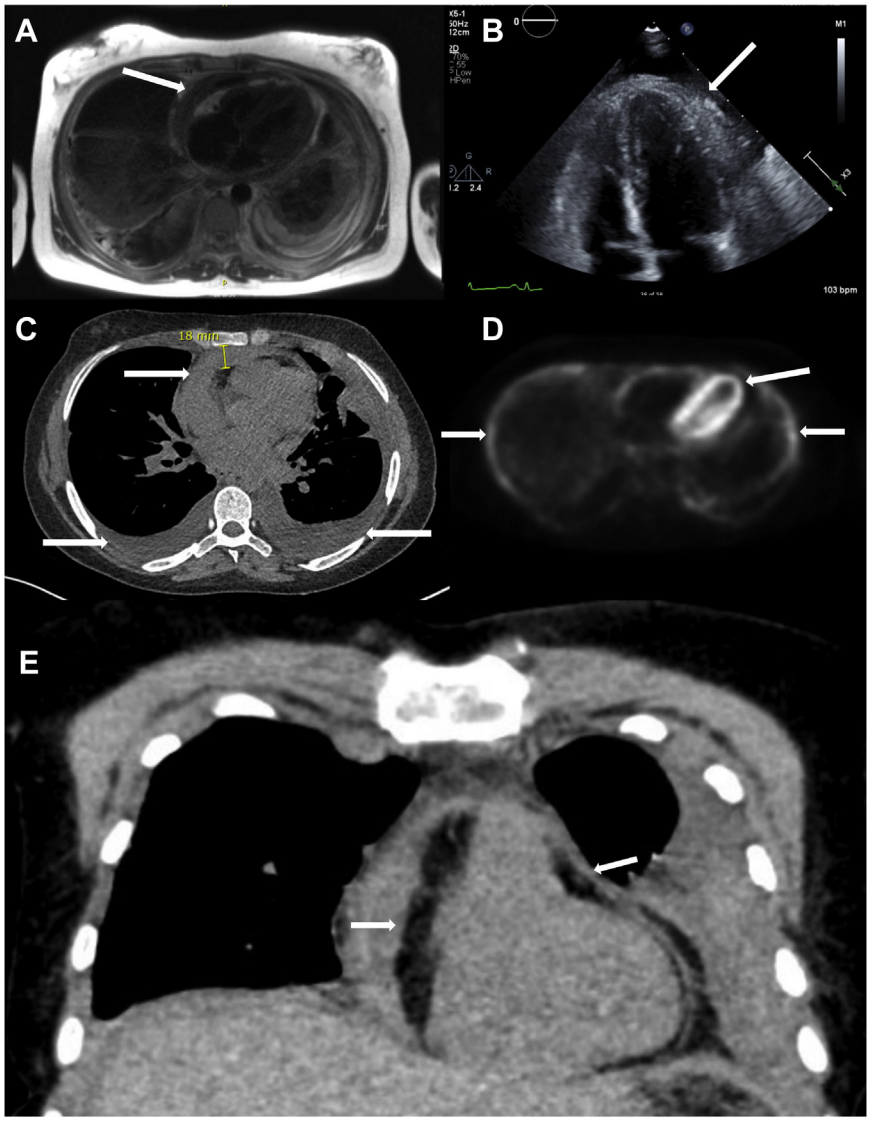
FIGURE 1 Preoperative Imaging

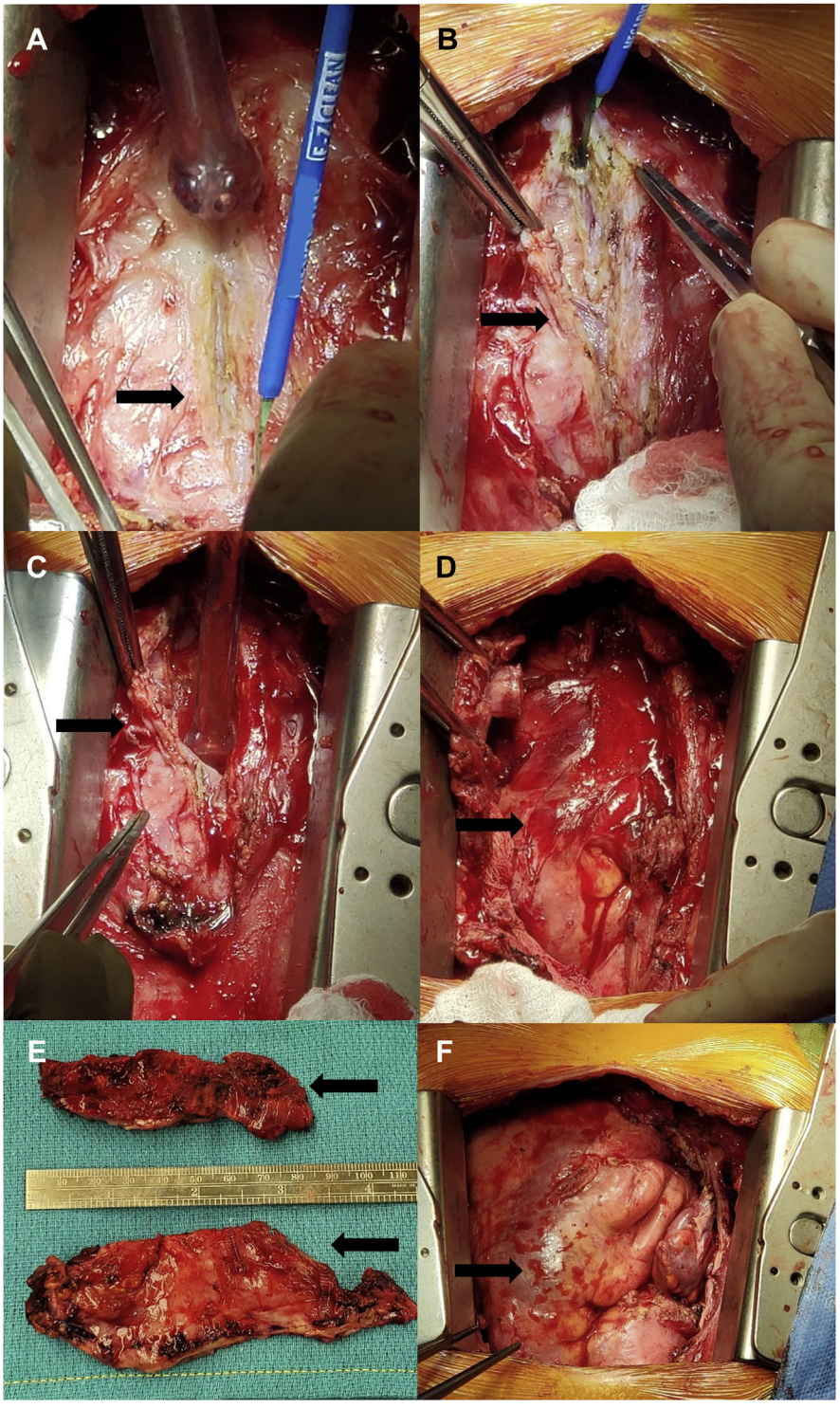


(A) MRI demonstrating thickened pericardium, pericardial effusion, and prominent pericardial uptake of gadolinium. **(B)** Echocardiogram showing hyperechoic pericardium. **(C)** CT demonstrating thickened pericardium up to 18 mm, moderate pericardial effusion, bilateral moderate pleural effusions, and pleural thickening. **(D)** FDG PET showing increased diffuse intense hypermetabolism throughout pericardial sac overlying the right ventricle and atrium, in left ventricular myocardium and pleura. **(E)** Moderate pericardial effusion.

infiltration (hairy kidneys); orbital mass lesions; and pericardial, pleural, and aortic infiltration.[1,5-7] Definitive diagnosis is established through clinical-pathological correlation with pathological tissues exhibiting foamy histiocytes, Touton Giant cells, and surrounding fibrosis. Histiocytes are $CD68^{+}$, $CD1a^{-}$, and $S100^{-}$. Analysis of mutations of BRAF V600E or mitogen-activated protein kinase (MEK) pathway genes are often used to guide management.[1,4,5]

Current first-line therapy for ECD is interferon-α, which is the most widely studied and efficacious treatment. Second-line therapies vary based on identified mutations, but may include cladribine (purine analog), anakinra (interleukin-1 receptor antagonist), vemurafenib (BRAF enzyme inhibitor), MEK inhibitors, corticosteroids, methotrexate, and chemotherapy, along with radiation therapy and surgical intervention for localized lesions with

FIGURE 2 **Intraoperative Images**



(A) Initial incision into thickened pericardium. **(B and C)** Dissection of fibrous pericardium. **(D)** Remaining visceral pericardium after fibrous pericardium excision. **(E)** Sections of the excised pericardium measuring 8 × 2 cm and 11 × 4 cm. **(F)** Heart post excision of the visceral pericardium and after hemostasis showing normal cardiac structures.

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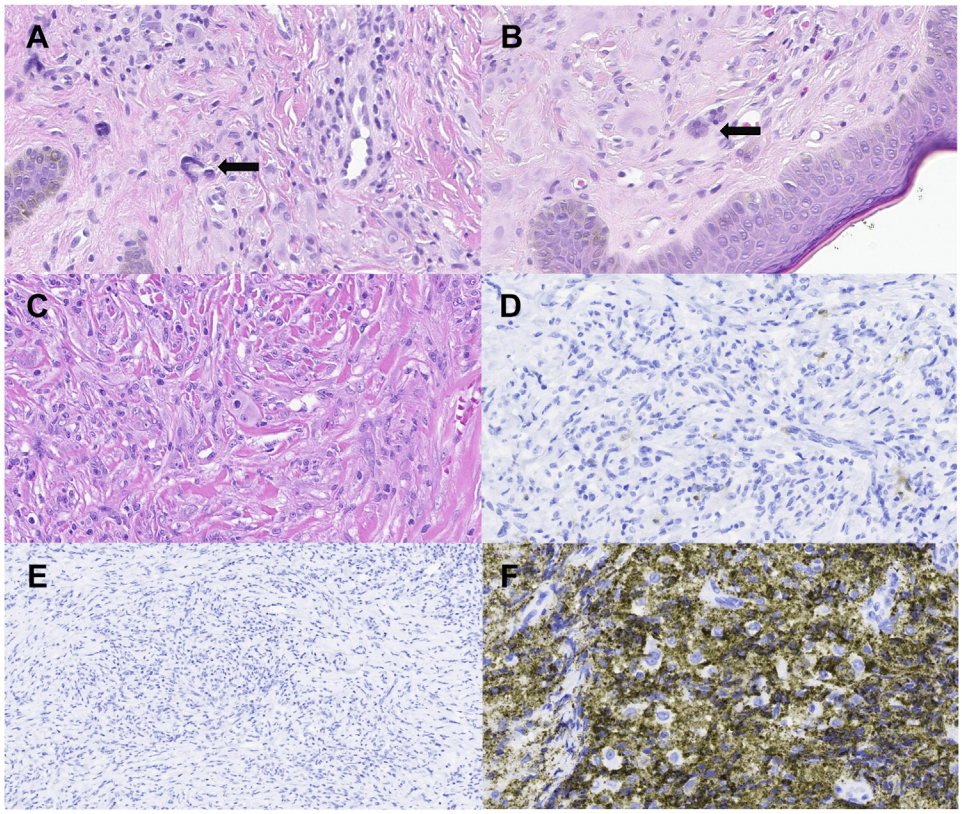
FIGURE 3 Staining of Samples



(A and B) Hematoxylin and eosin (H&E) stain of skin samples (×400 magnification) showing Touton Giant cells. **(C)** H&E stain of pericardial sample (×400 magnification) showing fibrosis, chronic inflammation, small lymphocytes, significant population of histiocytic cells demonstrating spindly and epithelioid morphology with abundant foamy cytoplasm and slightly atypical nuclear features. **(D)** Negative uptake of S100 stain in pericardial sample (×400 magnification). **(E)** Negative uptake of CD1a stain in pericardial sample (×200 magnification). **(F)** CD68 stain of pericardial sample (×400 magnification) showing diffuse, strong cytoplasmic staining.

mechanical complications.[1,5,7] In this case, pericardiectomy with diuresis was successful in relieving the patient's symptoms related to constrictive pericarditis and fluid overload.

FOLLOW-UP

Ten weeks postoperatively, the patient reports no SOB, improved peripheral edema, 50 lb weight loss, and good wound healing. Excised pericardium was sent for pathology. Hematoxylin and eosin stain of skin samples found Touton Giant cells (Figures 3A and 3B), hematoxylin and eosin stain of pericardium identified fibrosis, chronic inflammation, small lymphocytes, and significant population of histiocytic cells demonstrating spindly and epithelioid morphology with abundant foamy cytoplasm and slightly atypical nuclear features (Figure 3C). Immunohistochemical staining was $S100^{-}$, $CD1a^{-}$, and $CD68P^{+}$ (Figures 3D and 3F). Molecular genetic sequencing demonstrated MAP2K1 drive mutation without BRAF K-ras and NRAS mutations. Cobimetinib, a MEK inhibitor, has been initiated with cycled dosing regimens alternating between 60-mg dose taken once daily for 21 days followed by a 7-day period without treatment, then restarting the dosing regimen.

CONCLUSIONS

ECD is a rare condition, although should be considered in the differential diagnosis for young patients presenting with infiltrative disease and constrictive pericarditis. Surgical pericardiectomy is an effective and safe treatment for constrictive pericarditis secondary to ECD and should be considered where potential benefit exists.

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KEY WORDS constrictive pericarditis, Erdheim-Chester disease, pericardiectomy

APPENDIX For a supplemental video, please see the online version of this paper.