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CASE REPORT

ADVANCED

CLINICAL CASE

Lymphocytic Perimyocarditis Masquerading as Steroid-Dependent Recurrent Pericarditis

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ABSTRACT

Lymphocytic myocarditis is a pattern of myocardial inflammation typically associated with viral, autoimmune, or idiopathic causes. We present a case of lymphocytic perimyocarditis masquerading as steroid-dependent recurrent pericarditis. This case shows the advantages of using multimodal cardiac imaging and endomyocardial biopsy in clarifying diagnosis in treatment-resistant cases. (**Level of Difficulty: Advanced.**) (J Am Coll Cardiol Case Rep 2023;21:101960)

HISTORY OF PRESENTATION

A 41-year-old male presented for evaluation of multiple recurrences of sharp, mid-sternal chest pain. His chest pain was worse when lying flat and with exertion, improved with leaning forward, and was associated with shortness of breath. Physical examination was pertinent for the absence of jugular venous distention, Kussmaul's sign, murmurs, pericardial friction rub, pericardial knock, abdominal distention, and peripheral edema.

LEARNING OBJECTIVES

- To understand the typical clinical manifestations of perimyocarditis.
- To identify advanced cardiac imaging findings suggestive of perimyocarditis.
- To understand myocarditis management and immunomodulatory therapy's potential role.

PAST MEDICAL HISTORY

At 27 years of age, he had an index episode of symptoms consisting of chest pain worse with lying flat, improved with leaning forward, and associated with dyspnea following an episode of streptococcal pharyngitis treated with antibiotics. He had elevated troponins and diffuse ST-segment elevations in the precordial and limb leads with reciprocal ST-segment depression in lead aVR on electrocardiogram. He underwent cardiac catheterization which showed normal coronary arteries. He required triple-therapy (nonsteroidal anti-inflammatory drugs, colchicine, and corticosteroids), and multiple attempts at tapering his medications resulted in symptom recurrence; therefore, anakinra was added. However, his symptoms remained refractory.

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ABBREVIATIONS AND ACRONYMS

CMR = cardiac magnetic resonance image

EMB = endomyocardial biopsy

FDG = fluorodeoxyglucose

LGE = late gadolinium enhancement

PET = positron emission tomography

DIFFERENTIAL DIAGNOSIS

Differential diagnosis included myocarditis or pericarditis of viral, bacterial, autoimmune, or connective tissue disease etiology, and cardiac sarcoidosis.

INVESTIGATIONS

Laboratory studies revealed elevated troponin T of 0.031 ng/mL (normal: <0.010 ng/mL), high-sensitivity C-reactive protein of 3.1 mg/L (normal: <0.3 mg/L), and N-terminal prohormone brain natriuretic peptide of 254 pg/mL (normal: <125 pg/mL). Erythrocyte sedimentation rate was normal at 5 mm/h. He also had a negative autoimmune workup, including negative antinuclear antibodies.

Electrocardiogram showed sinus bradycardia with nonspecific T-wave abnormalities. Echocardiogram was notable for left ventricular ejection fraction of 62%, no regional wall motion abnormalities, concentric left ventricular (LV) hypertrophy with grade 1 diastolic dysfunction, and no pericardial effusion or constrictive physiology. Cardiac magnetic resonance (CMR) imaging showed near transmural enhancement of the basal-mid inferolateral segments with patchy mid-myocardial late gadolinium enhancement (LGE) in the basal-mid anterolateral segments and increased signaling in the lateral wall on T2 short-tau inversion recovery imaging. There was also mild patchy pericardial LGE (**Figures 1A to 1D**).

Fluorodeoxyglucose (FDG) positron emission tomography (PET) obtained to evaluate for active cardiac and extracardiac inflammation showed FDG uptake in the basal anterolateral, basal inferolateral, and basal inferior segments suggesting active cardiac inflammation but no extracardiac inflammation (**Figures 1E and 1F**). Because of lack of a definitive diagnosis of the cause of his inflammation and poor response to prior therapy, he underwent endomyocardial biopsy. Pathology showed multiple foci of mononuclear infiltrates in the interstitium associated with myocyte encroachment and foci of replacement fibrosis (**Figure 2**). Pathology was negative for eosinophils, granulomas, giant cells, sarcoplasmic inclusions or vacuolations, abnormal glycogen accumulation, iron, and amyloid. He was diagnosed with recurrent myocarditis due to lymphocytic myocarditis of likely viral or idiopathic etiology.

MANAGEMENT

Given the diagnosis of lymphocytic myocarditis, the patient was started on mycophenolate mofetil 500 mg twice daily in lieu of anakinra, which was tapered off. His prednisone was increased to 20 mg daily, and he continued colchicine 0.6 mg twice daily.

DISCUSSION

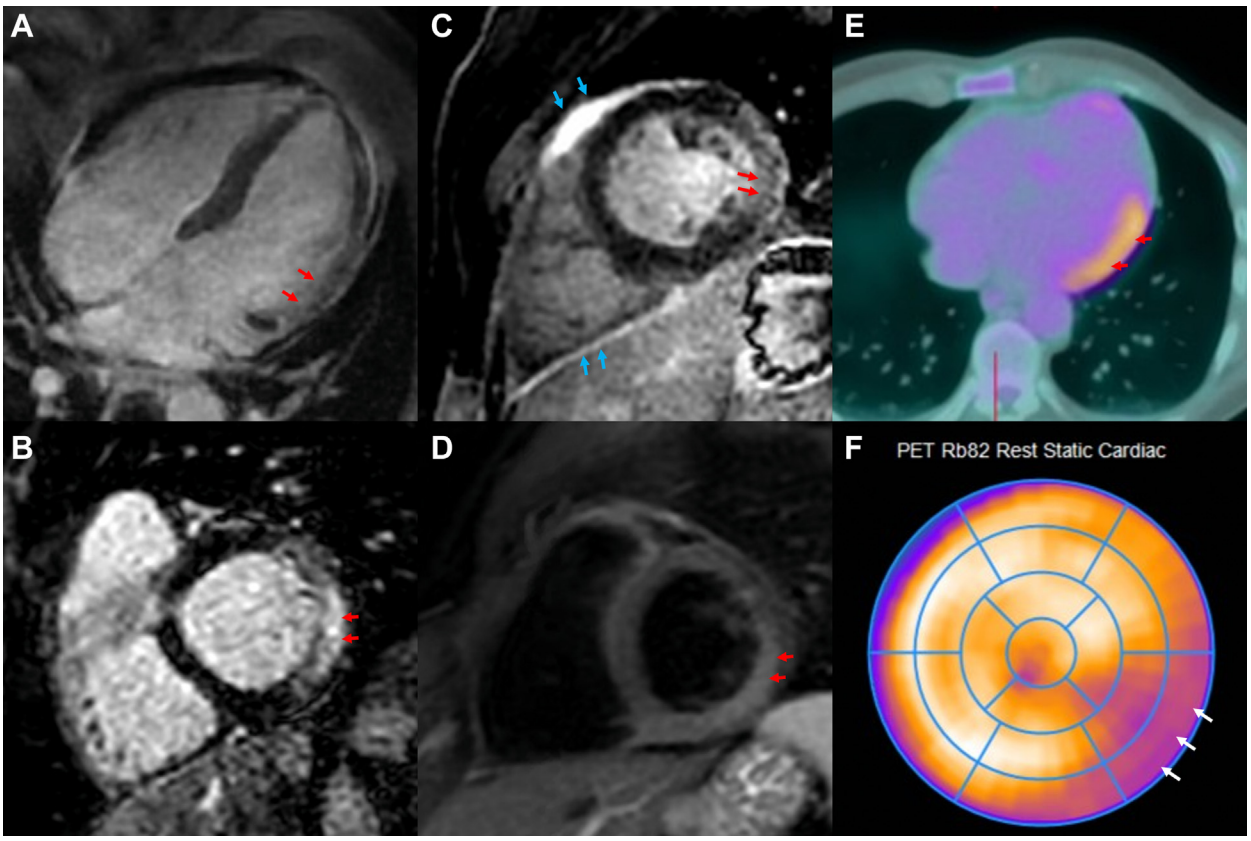
Myocarditis is defined as inflammation of the myocardium. Perimyocarditis occurs when there is concomitant pericardial inflammation due to primary myocardial pathology. In many cases of myocarditis, the etiology is unknown and are diagnosed as idiopathic. In cases with a diagnosed etiology, viral infection is the most common.[1] Patients with myocarditis can present with chest pain, heart failure, and arrhythmia. Chest pain can be pericarditis-like, especially if there is concomitant pericardial inflammation such as in this case.[2] Lymphocytic myocarditis presenting as recurrent episodes of chest pain mimicking medication resistant pericarditis without associated heart failure or LV dysfunction has not been previously documented.

Lymphocytic myocarditis is the most common histopathological pattern of inflammation and is most often seen in viral, autoimmune, or idiopathic myocarditis.[2] The proposed mechanism includes immune system activation after infection and molecular mimicry between viral and cardiac antigens resulting in lymphocyte infiltration of the myocardium.[3]

The gold standard for diagnosing myocarditis is EMB which can identify the pattern of inflammation on histology.[4] However, EMB is an invasive procedure with a low yield of successful diagnostic samples in patchy diseases due to sampling error. Advanced multimodality cardiac imaging is a complementary and noninvasive method to evaluate for myocarditis. It can assess cardiac function and patterns of inflammation to aid in diagnosis.

Echocardiography may have low sensitivity for myocarditis in cases with mild disease.[5] Findings can include reduced cardiac function, diastolic dysfunction, and dilated ventricles, depending on chronicity.[6] CMR provides a more comprehensive assessment for myocarditis. CMR diagnosis is based on the revised Lake Louise criteria, requiring features including: 1) myocardial edema; 2) myocardial hyperemia or global relative enhancement; or 3) myocardial fibrosis or LGE.[7] LGE patterns for

FIGURE 1 Advanced Cardiac Imaging With CMR and FDG-PET



(A) Cardiac magnetic resonance (CMR) 4-chamber view shows late gadolinium enhancement (LGE) in the mid-lateral wall in an epicardial distribution **(red arrows). (B)** CMR short-axis view shows LGE in the basal-lateral wall in an epicardial distribution **(red arrows). (C)** LGE in the mid-lateral walls **(red arrows)**. LGE is seen in the pericardium **(blue arrows)**. **(D)** CMR short-axis view shows edema in the lateral wall **(red arrows)** on T2 sequence. **(E)** Fluorodeoxyglucose (FDG) positron emission tomography (PET) imaging reveals a large amount of focal FDG uptake in the anterolateral basal-mid segments. **(F)** Rb82 PET image reveals resting perfusion defect in basal-mid inferolateral segments corresponding to regions of FDG uptake.

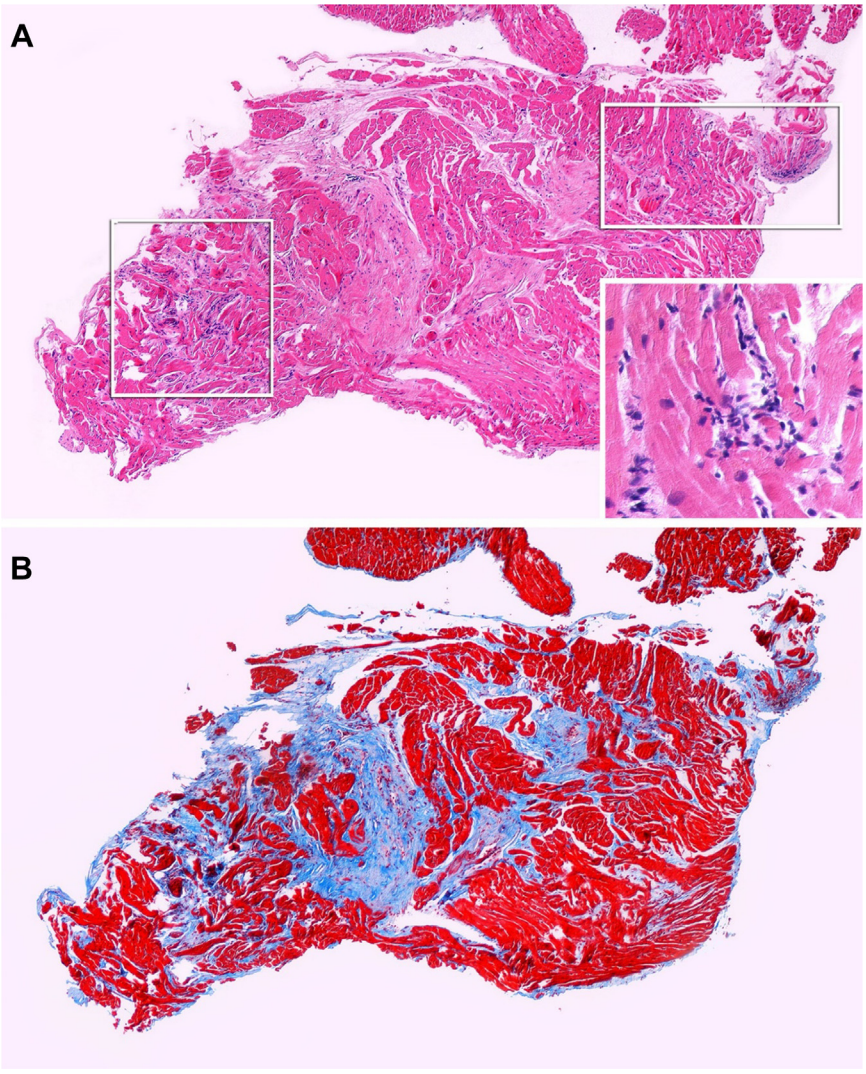
myocarditis can be epicardial but can vary.[4] In particular, coronary disease should be excluded as a potential cause of transmural LGE. FDG-PET is another imaging modality that can identify myocardial inflammation by detecting increased glucose use by the myocardium.[4]

Management of lymphocytic myocarditis focuses on managing heart failure symptoms and potential arrhythmias.[8] The role of immunosuppressive therapy has shown mixed results. Some studies showed that they increase left ventricular ejection fraction and functional capacity, whereas others have not shown similar benefits.[9] Our patient was not responsive to anakinra, which suggested a pathway of immune system activation that was not predominantly mediated by interleukin-1. The use of immunosuppression to treat myocarditis is an area of ongoing study.

FOLLOW-UP

On follow-up after 2 months, the patient's symptoms had improved. He had one recurrence of chest pain and palpitations associated with an upper respiratory infection which improved by temporarily increasing his steroid dose. He had no additional emergency department visits or hospitalizations. Event monitoring was negative for arrhythmias. The patient had successfully tapered off anakinra and weaning off steroids while he remained on mycophenolate mofetil.

FIGURE 2 Endomyocardial Biopsy Pathology



(A) Biopsy specimen shows 2 foci of mononuclear infiltrates **(boxed areas)** on the hematoxylin and eosin stain. **(B)** Trichrome stain highlights the extent of replacement fibrosis seen as **blue areas**.

CONCLUSIONS

We present an atypical case of lymphocytic perimyocarditis presenting with chest pain without heart failure symptoms or LV dysfunction that masqueraded as steroid-dependent, recurrent pericarditis. This case shows the importance of distinguishing pericarditis from myocarditis or, as in our case, perimyocarditis. Further, idiopathic pericarditis that does not respond to standard therapy should prompt further investigations to elucidate the cause of recurrent inflammation, such as myocarditis. CMR and FDG-PET can noninvasively assess for myocardial inflammation, but EMB can aid in definitive diagnosis. Treatment of myocarditis is an ongoing area of study and includes the management of heart failure, arrhythmias, and potentially immunomodulatory therapies.

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