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Case Reports

Fulminant Eosinophilic Myocarditis Without Peripheral Eosinophilia

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Abstract

Eosinophilic myocarditis is a rare form of myocarditis characterized by eosinophilic infiltration and usually associated with peripheral hypereosinophilia. The clinical spectrum of eosinophilic myocarditis ranges widely, from mildly symptomatic to fulminant disease. When patients have fulminant eosinophilic myocarditis, high-dose corticosteroids can lead to dramatic improvement and peripheral eosinophil counts are used as an indicator of response to treatment. However, in some patients, peripheral eosinophilia is absent at initial presentation; reaching a diagnosis and determining treatment response can be challenging in this situation. This report describes a patient with fulminant eosinophilic myocarditis who initially presented with a normal peripheral eosinophil count, was diagnosed through an early endomyocardial biopsy, and was successfully treated with corticosteroids. Endomyocardial biopsy should be performed to confirm the presence of myocardial eosinophilic infiltration, especially for patients who present with fulminant myocarditis, even when peripheral eosinophilia is absent.

Keywords: Biopsy; eosinophilia; myocarditis

Introduction

Eosinophilic myocarditis (EM) is a relatively uncommon and potentially life-threatening myocardial inflammatory disease characterized by eosinophilic infiltration. It can progress to irreversible myocardial damage, but early corticosteroid therapy can be effective, especially for patients with fulminant disease.[1] Patients with EM usually have peripheral hypereosinophilia at presentation, but some can have normal eosinophil counts; in these patients, endomyocardial biopsy (EMB) is the only way to make the diagnosis. This report describes a patient with fulminant EM without peripheral hypereosinophilia.

Case Report

A 39-year-old woman reported myalgia and generalized weakness for 2 days; she was transferred from an outside hospital to the emergency department of the reporting institution because of hypotension and elevated cardiac enzymes. She had no history of chronic disease or recent medication use. Her blood pressure was 139/108 mm Hg with inotropic support, pulse rate was 104/min, temperature was 36.8 °C, and her respiratory rate was 18/min. Electrocardiography demonstrated sinus tachycardia at 102/min with ST-segment elevations in the anterolateral leads and low QRS voltages in all precordial and limb leads (Fig. 1). Chest radiography revealed pulmonary edema and mild cardiomegaly, with a cardiothoracic ratio of 0.52. Laboratory testing showed leukocytosis ($17.9 \times 10^3/\mu L$; reference range, $4.8\text{-}10.8 \times 10^3/\mu L$) with neutrophilia ($15.3 \times 10^3/\mu L$; reference range, $1.8\text{-}7.8 \times 10^3/mL$) and a normal eosinophil count ($0.44 \times 10^3/\mu L$; reference range, $<0.50 \times 10^3/\mu L$). High-sensitivity cardiac troponin T (1.14 mg/mL; reference range, <0.1 mg/mL), N-terminal pro B-

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type natriuretic peptide (14,676 pg/mL; reference range, <113 pg/mL), and serum lactate (6.0 mmol/L; reference range, 0.7-2.5 mmol/L) levels were also elevated.

Transthoracic echocardiography revealed global hypokinesia and diffusely thickened left ventricular walls, a severely depressed left ventricular ejection fraction of 22%, impaired right ventricular function, and a small pericardial effusion (Fig. 2). Coronary angiography showed normal coronary arteries. Endomyocardial biopsy samples were obtained. Cardiac magnetic resonance imaging demonstrated multifocal myocardial edema on T2-weighted imaging (Fig. 3A) and multifocal increased T1 values (1,100-1,200 ms) on modified Look-Locker inversion recovery T1 mapping (Fig. 3B).

Abbreviations and Acronyms

EM	eosinophilic myocarditis
EMB	endomyocardial biopsy

During the first 2 days of admission to the cardiac intensive care unit, the patient experienced sustained ventricular tachycardia, worsening pulmonary edema, uncontrolled fever (>38.0 °C), and increased vasopressor requirements. Empiric administration of intravenous immunoglobulin was started on the second day for suspected fulminant myocarditis, but there was no noticeable clinical improvement.

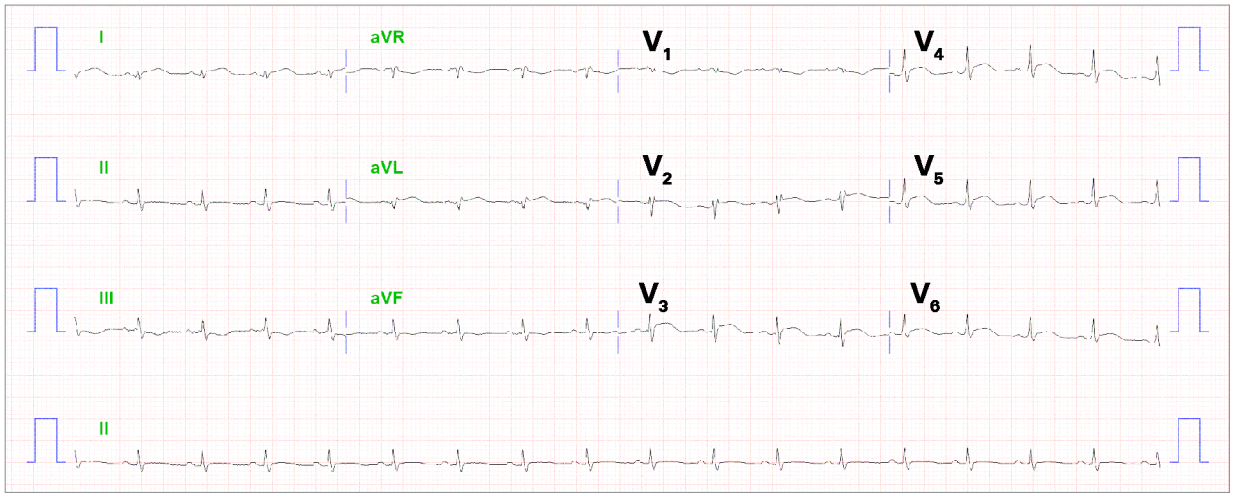

Fig. 1 Electrocardiogram shows sinus tachycardia with a heart rate of 102/min, ST-segment elevations in leads V_2 through V_6 and in leads I and aVL, and low QRS voltages in all precordial and limb leads.

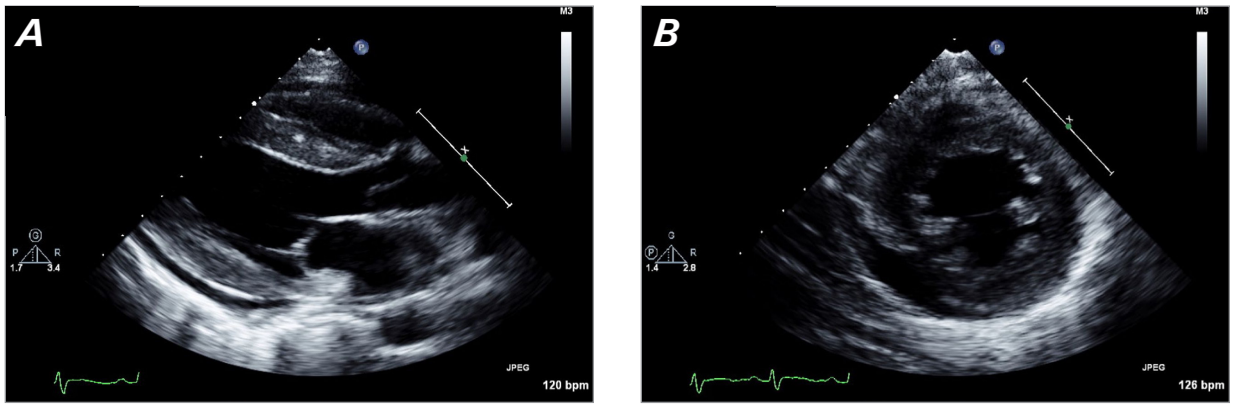

Fig. 2 A) Parasternal long-axis (Video 1) and **B**) short-axis (Video 2) views of a transthoracic echocardiogram on admission shows global hypokinesia, increased left ventricular wall thickness, and a small pericardial effusion.

Supplemental motion images are available for Figure 2A and Figure 2B.

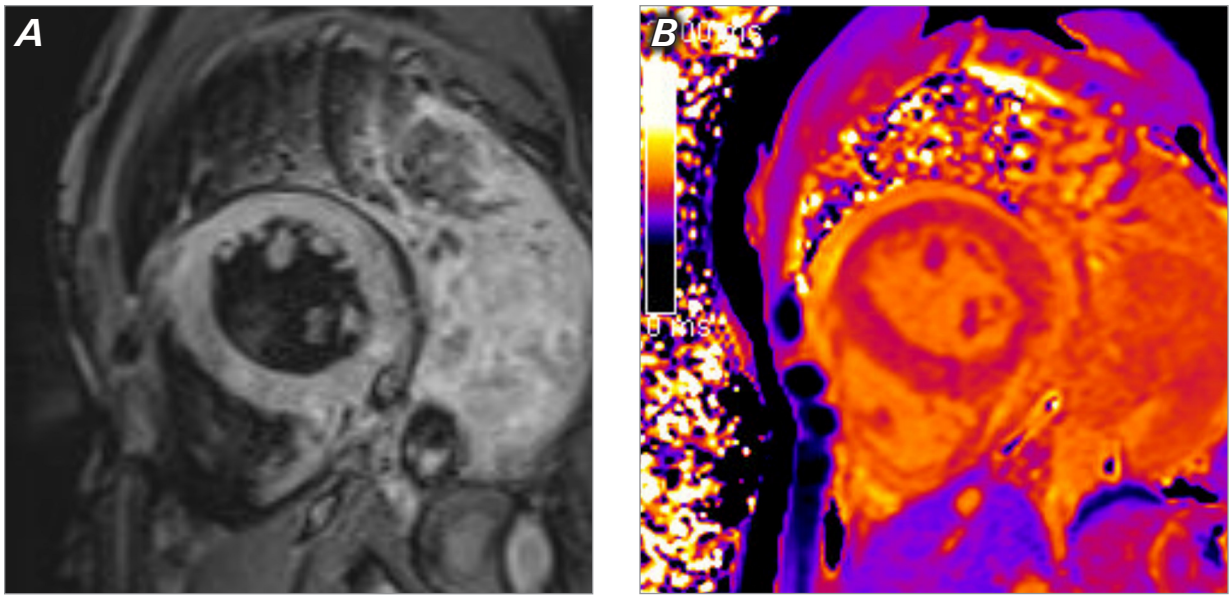

Fig. 3 Cardiac magnetic resonance imaging shows **A**) multifocal high signal intensity in the left ventricular myocardium on T2-weighted images, and **B**) modified Look-Locker inversion recovery T1 mapping shows multifocal increased values (1,100-1,200 ms) in the left ventricular myocardium.

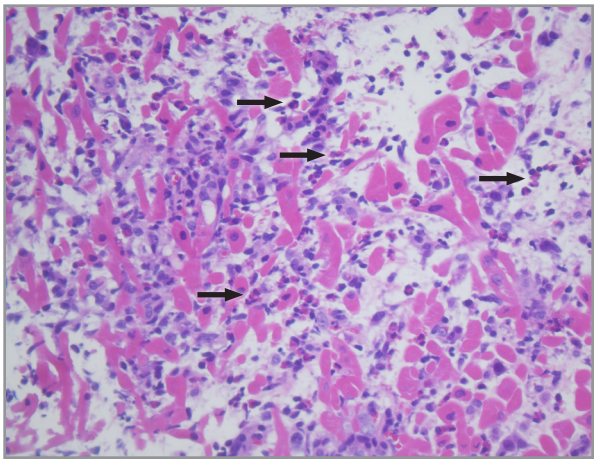

Fig. 4 Histologic examination of the endomyocardial biopsy shows myocardial disarray with mixed inflammatory infiltrates, including numerous eosinophils (arrows); hematoxylin-eosin staining; original magnification, ×400.

The pathologic diagnosis from the endomyocardial biopsies, reported on the fourth hospital day, was diffuse eosinophilic and lymphocytic infiltration, consistent with EM (Fig. 4). Intravenous methylprednisolone was immediately initiated at a daily dose of 1 mg/kg for 3 days, and then changed to daily oral prednisolone at 1 mg/kg. Follow-up transthoracic echocardiography on the third day of steroid therapy showed marked improvement of the left ventricular ejection fraction to 51%, normalized left ventricle wall thickness and right ventricular function, and a minimal pericardial effusion. Over the next few days, her vital signs stabilized and her pulmonary edema gradually improved. Her left ventricular ejection fraction fully recovered to 63% on the seventh day of steroid therapy (Fig. 5). On hospital day 8, her eosinophil count showed an unexpected increase to $1.06 \times 10^3/\mu L$ and peaked at $1.3 \times 10^3/\mu L$ on the next day (Fig. 6). Her care team considered repeating the EMB to rule out exacerbation of EM but did not do so because of the invasive nature of the procedure and the improvement in her clinical status. The team obtained additional elements of her history and supplemental laboratory tests to evaluate the cause of her peripheral eosinophilia. She did not have any pets, but a positive result for immunoglobulin G antibody to *Toxocara canis* was available after discharge. The team assumed that *T canis* infection was the etiology of her EM and started high-dose albendazole (400 mg twice daily for 5 days) upon her first outpatient visit after discharge.

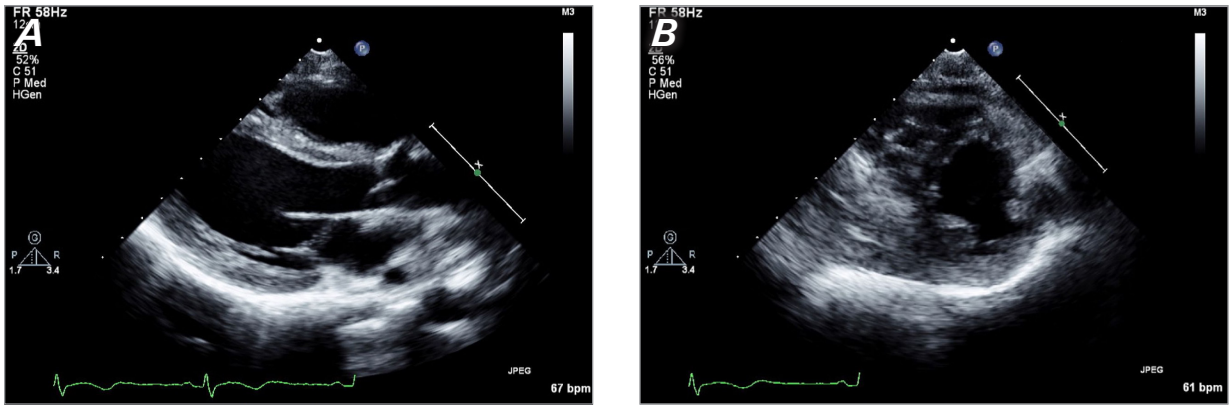

Fig. 5 A) Parasternal long-axis (Video 3) and **B**) short-axis (Video 4) views of transthoracic echocardiogram performed on the 10th day of hospitalization show normal left ventricular wall thickness and no pericardial effusion.

Supplemental motion images are available for Figure 5A and Figure 5B.

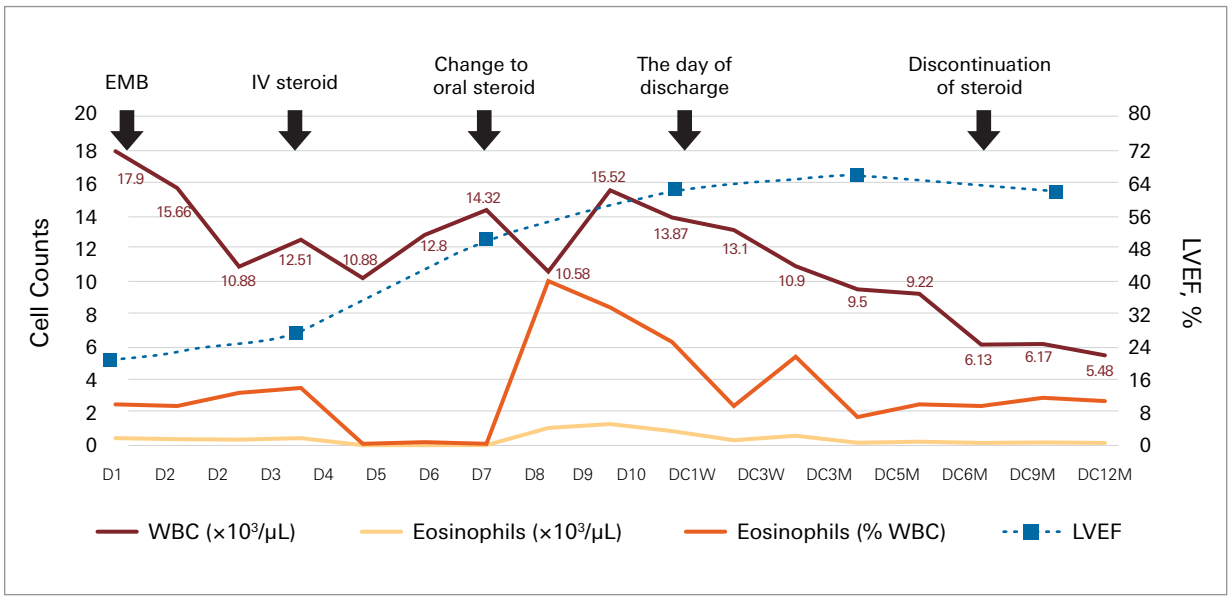

Fig. 6 Diagram illustrating the absolute WBC eosinophil counts, percentage of eosinophils on the WBC differential, and the LVEF during hospitalization and after discharge. The eosinophil count was normal at presentation and increased during steroid therapy; it then gradually decreased and stayed within the normal range.

D, day of hospitalization; DC, time after discharge; EMB, endomyocardial biopsy; IV, intravenous; LVEF, left ventricular ejection fraction; M, month; W, week; WBC, white blood cell count.

She was discharged on hospital day 11, and her prednisolone dose was reduced as scheduled. Her eosinophil counts gradually decreased and remained within the normal range until the seventh month after discharge, when steroid therapy was discontinued. The patient has been asymptomatic, with normal cardiac function and without peripheral hypereosinophilia, for 1 year.

Discussion

Eosinophilic myocarditis is a rare type of heart muscle inflammation that features eosinophilic infiltration, usually accompanied by varied degrees of peripheral hypereosinophilia. Its prevalence was reported as 0.1% in a cohort that underwent biopsy for suspected

myocarditis[2] and 2.8% in patients undergoing heart transplantation.[3] The clinical spectrum is very wide, ranging from mildly symptomatic to life-threatening conditions.[4] Eosinophilic myocarditis can be associated with clinical conditions that cause eosinophilia, such as hypersensitivity reactions, hypereosinophilic syndrome, parasitic infections, and malignancy. However, the etiology is not always apparent and, in a report involving 179 patients, was undefined in 35.7% of those with histologically proven EM.[1] *T canis* infection accounted for 3.4% of that cohort,[1] but toxocariasis as a cause of EM can be overlooked and misdiagnosed in a substantial portion of patients. It is often asymptomatic, and humans can become infected by ingesting contaminated foods even if they do not own pets.[5]

Because of its rarity, evidence-based treatment guidelines for EM are not available. If the cause of eosinophilia is identified, specific treatment should be implemented: for example, albendazole for *T canis* infection was used for the patient in this report. Early high-dose corticosteroid therapy effectively reverses cardiac injury and improves the prognosis; therefore, timely diagnosis is crucial for appropriate management of EM.[6,7] When peripheral hypereosinophilia is present in patients with a clinical scenario of myocarditis, EM is suspected; the diagnosis is confirmed by EMB.[8] However, the degree of peripheral eosinophilia may be variable over the course of the disease. Peripheral eosinophil counts can be within the normal range during the entire disease course or in the early stage of the disease. The patient in this report only developed peripheral eosinophilia after 8 days of hospitalization. Brambatti et al[1] report that peripheral hypereosinophilia was absent at presentation in 25% of 179 patients with biopsy-proven EM and developed during hospitalization in 5 patients. Morimoto et al[9] suggest that, in the acute phase of EM, peripheral blood eosinophils migrate to tissues and the bone marrow fails to immediately increase production in response.

The absence of peripheral eosinophilia can interfere with the diagnosis of EM, and EMB is the only alternative for these patients. In addition, as resolution of eosinophilia following steroid therapy can be considered an indicator of response to therapy in patients with initial peripheral eosinophilia, determining treatment response can be challenging in patients with normal eosinophil counts.[10] When deciding whether to taper or discontinue steroids, biomarkers and imaging studies—along with the clinical response—should be considered comprehensively. If these are insufficient, repeat EMB should be considered.[11]

The patient in this report presented with cardiogenic shock suggestive of fulminant myocarditis, but she had a normal eosinophil count. Early EMB allowed for a timely diagnosis of EM and prompt administration of corticosteroids. Although hypereosinophilia developed during steroid therapy, the dose of steroids was successfully reduced and discontinued based on her clinical recovery. *T canis* infection was considered to be the cause of EM and treated with albendazole.

In conclusion, EM is a rare but potentially fatal form of myocarditis and can occur in the absence of peripheral hypereosinophilia. Early diagnosis through EMB and immediate steroid therapy can improve the prognosis. Comprehensive clinical judgment—including the patient's clinical status and results of laboratory testing—is needed to determine the response to treatment in patients with EM who do not have peripheral eosinophilia.

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