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Letter to the Editor



# Eosinophilic Myocarditis Progresses to Giant Cell Myocarditis Requiring Heart Transplantation: A Case Report

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To the Editor,

Cardiac involvement in drug-induced hypersensitivity syndrome (DiHS) can be diagnosed as eosinophilic (or hypersensitivity) or acute necrotizing eosinophilic myocarditis (ANEM) according to histologic findings.[1] Meanwhile, there have been several cases of giant cell myocarditis (GCM) due to drug hypersensitivity with a notably devastating clinical course.[2] Herein, we report a case showing progression from eosinophilic myocarditis to giant cell myocarditis in a patient with DiHS who underwent heart transplantation.

A 32-year-old previously healthy female visited our hospital in July 2019. Three months prior, she initiated a dietary supplement that included *Carnicia cambogia* extract for weight reduction. Approximately 8 weeks later, she developed fever, skin rash, palpable lymph nodes around her neck as well as motor weakness in the lower extremities. Upon arrival, her temperature was 39.0°C. Initial laboratory tests showed a white blood cell count of 12,700/mm$^3$ with neutrophil dominance (83.9%) and 635/μL eosinophils. Other laboratory data revealed the following: aspartate transaminase, 133 IU/L; alanine aminotransferase, 297 IU/L; creatine kinase, 1,598 IU/L; myoglobulin, 4,883 ng/mL (reference < 110 ng/mL); creatine kinase-MB, 52.1.5 ng/mL (reference < 5 ng/mL); troponin I, 11.153 ng/mL (reference < 1.5 ng/mL); and C-reactive protein, 2.85 mg/dL. Her electrocardiogram (ECG) showed sinus tachycardia with ST elevation in the inferior and V2 to V6 leads. Meanwhile, transthoracic echocardiogram (TTE) and computerized tomography coronary angiogram reported normal findings. Other autoimmune, infectious, or malignant causes for her symptoms, and abnormal tests were evaluated and ruled out. The endomyocardial biopsy showed marked lymphocytic and eosinophilic infiltration with myocyte damage, consistent with eosinophilic myocarditis (**Figure A**). Consequently, her Registry of Severe Cutaneous Adverse Reaction (RegiSCAR) score was 6 and *Carnicia cambogia* extract was considered the culprit.[3]

Treatment was initiated with 1 mg/kg of methylprednisolone (approximately 70 mg). However, weakened strength of legs, eosinophilia, and elevated cardiac enzyme were relatively refractory to corticosteroids. After increasing methylprednisolone up to 2 mg/kg, the patient seemed to recover. We added 100 mg of cyclosporine while attempting to reduce methylprednisolone. However, on the 20th day of hospitalization, the patient complained of newly developed chest pain. ECG showed a more prominent elevation of the ST segment at leads II, III, and V2 to V6. On TTE, the ejection fraction of the left

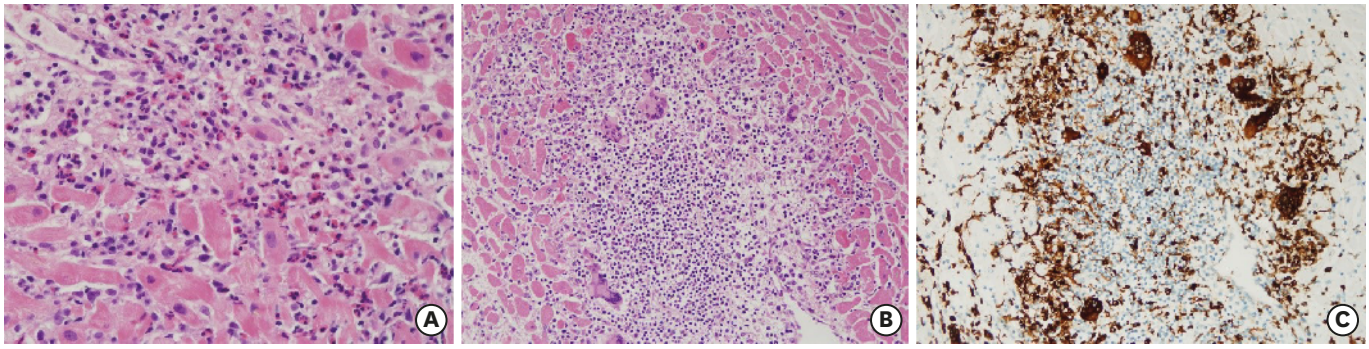


**Figure.** Histologic findings of the cardiac muscle during initial evaluation (A) and from the explanted heart (B and C). Endomyocardial biopsy (A) reported marked lymphocytes with eosinophilic infiltration at the beginning (×400). After 4 weeks, an abundance of lymphocytes and scattered giant cells with more prominent myocyte damage were noted (B) (×200). The presence of giant cells was confirmed by CD68 immunostaining (C).

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ventricle decreased to 49% along with right ventricular dysfunction. Due to concerns about progression to fulminant heart failure, the patient received an additional 1 mg/kg of methylprednisolone. On the next morning, 500 mg of methylprednisolone and 750 mg of cyclophosphamide were administered. To target eosinophils, reslizumab (200 mg) was infused. Nevertheless, her blood pressure gradually decreased. This led to cardiac arrest and veno-arterial extracorporeal membrane oxygenation (VA-ECMO) was applied. After 10 days of ECMO, she underwent heart transplantation. Histology of the explanted heart revealed diffuse infiltration of lymphocytes and scattered giant cells with myocyte damage, consistent with GCM (**Figure B and C**). Intriguingly, there were no eosinophils. She recovered without complications and remains clinically stable 8 months after the transplant.

GCM is a rare type of myocarditis, usually affecting young to middle-aged previously healthy adults.[4] Regarding GCM as a result of drug hypersensitivity, post-mortem autopsy cases have mostly been reported due to its rapid progression.[2,5] To our knowledge, this is the first survival case of GCM induced by drug hypersensitivity.[6] *Carnicia cambogia* extract is also first reported as a causative agent, which was once reported to provoke ANEM.[7] Another importance of this case is that histological findings of both eosinophilic myocarditis and GCM were observed in one patient at different time points. It provides direct evidence that these conditions are present in the same spectrum of disease with different severity, a possibility suggested only by indirect evidence.[5,6] However, what drives this progression remains inconclusive. As of yet, there is no marker for predicting GCM or management guidelines for patients with eosinophilic myocarditis, especially when corticosteroids are insufficient. Future studies on underlying pathophysiology are warranted.

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