CASE REPORTS

A case of eosinophilic myocarditis

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ABSTRACT

A 83-year-old female presented with shortness of breath and was found to be in acute decompensated heart failure with a reduced ejection fraction. Bloodwork revealed significant eosinophilia and endomyocardial biopsy confirmed eosinophilic myocarditis (EM). One month prior, she had been hospitalized for a new diagnosis of heart failure while on vacation in Colorado. During that hospitalization, work-up included a heart catheterization showing non-obstructive coronary disease leading to a new diagnosis of non-ischemic cardiomyopathy. Bloodwork at that time showed a normal eosinophil count. She had been given prednisone for a suspected asthma exacerbation a few days prior to presentation likely normalizing the eosinophil count. We report a case of EM and the difficult diagnostic dilemma it presents due to low incidence, broad clinical symptoms, and past medical history that can confound the diagnosis. A thorough work-up was completed, and in this patient's case, the etiology was likely drug-induced from the home medication hydrochlorothiazide.

Key Words: Eosinophilia, Systolic heart failure, Eosinophilic myocarditis, Non-ischemic cardiomyopathy

1. INTRODUCTION

Eosinophilic myocarditis (EM) is a difficult diagnosis due to its broad clinical presentation and low incidence rate. If left untreated, EM can be fatal.[1] When cardiac symptomology occurs in conjunction with peripheral eosinophilia, clinicians must maintain a high index of suspicion for EM as it requires cardiac biopsy for formal diagnosis.[2] Even after the diagnosis of EM is confirmed, a physician's work is just beginning as one must also determine the underlying etiology of the hypereosinophilia. Peripheral eosinophilia has a wide range of differential diagnoses including infectious, allergic, and hematologic causes which will often guide treatment of the underlying disease. Treatment for the majority of patients with EM is steroids.[3] We report a case of EM presenting with new heart failure with reduced ejection fraction with the diagnosis confounded by prior steroid use.

Due to the low incidence of the disease, no large randomized control trials exist to establish treatment guidelines, instead management is often based upon expert opinion. Successful treatment has been documented with corticosteroids in combination with immunosuppressive agents such as azathioprine.[4] Other case reports have documented high dose corticosteroids followed by a taper which have resulted in complete resolution of the disease.[5] Doses of steroids utilized in clinical care can be varied, but often courses of treatment are initiated with methylprednisolone regimen of 1 mg/kg/day, followed by a taper with varying durations.[4–6] Depending on the severity of the disease, high dose pulse therapy for up to three days is often included in the treatment regimen for those presenting in cardiogenic shock, later

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followed by starting 1 mg/kg/day regimen.[6] It is unclear what the optimal dose, duration, or taper administration of corticosteroids is needed to optimize cure rates, and prevent disease remission. Corticosteroids in isolation, have also reported cases of failed treatment.[6] In addition, it is uncertain if adding an immunosuppressive agent has utility in improving cure rates or preventing relapses of EM, although it may be appropriate in certain clinical scenarios. To guide therapy of EM, clinicians should consider the severity of the presenting disease to determine the dosing, duration, taper regimen of corticosteroids, as well as the suspected underlying etiology to elect if there is any theoretical benefit to adding an immunosuppressive agent.

2. Case presentation

A 83-year-old female with a past medical history of hypertension, asthma, and a recent diagnosis of non-ischemic cardiomyopathy of unclear etiology presented to an outside hospital with shortness of breath and right-sided chest pressure. At that time, her troponin was 12 (< 0.04 normal, > 0.5 consistent with cardiac damage) and electrocardiogram demonstrated sinus tachycardia with t-wave depressions in V4-V6. Chest pain improved with nitroglycerin and she was transferred to a tertiary care center for further work-up.

Further history-taking revealed recent travel to Colorado one month prior where she had developed productive cough, dyspnea, and wheezing. She presented to an urgent care clinic and was treated with doxycycline and prednisone for a presumed asthma exacerbation. Symptoms did not improve with steroids, so she was admitted to the hospital. While hospitalized, troponin was 4 and ejection fraction (EF) on transthoracic echocardiogram (TTE) was reduced to 20% (EF on TTE twelve days prior was 45%). A left heart catheterization was performed that demonstrated non-obstructive coronary disease. Eosinophils at that time were normal, but of note, she had been on prednisone. She was started on appropriate heart failure medications given the new diagnosis of non-ischemic cardiomyopathy and returned home from her vacation. She had been on losartan/hydrochlorothiazide previously for hypertension, but this medication was stopped while in the hospital.

Table 1. Patient labs and imaging data on admission to the tertiary hospital

Lab/Imaging	Admission values	Units	Normal values
White blood cell count	15.5	10^9/L	4.4-10.3
Neutrophil count	8.21	10^9/L	1.60-5.50
Eosinophil count	**4.12**	**10^9/L**	**0-0.4**
Cardiac ejection fraction	20%	N/A	50%-55%
Troponin	12	ng/ml	0-0.03

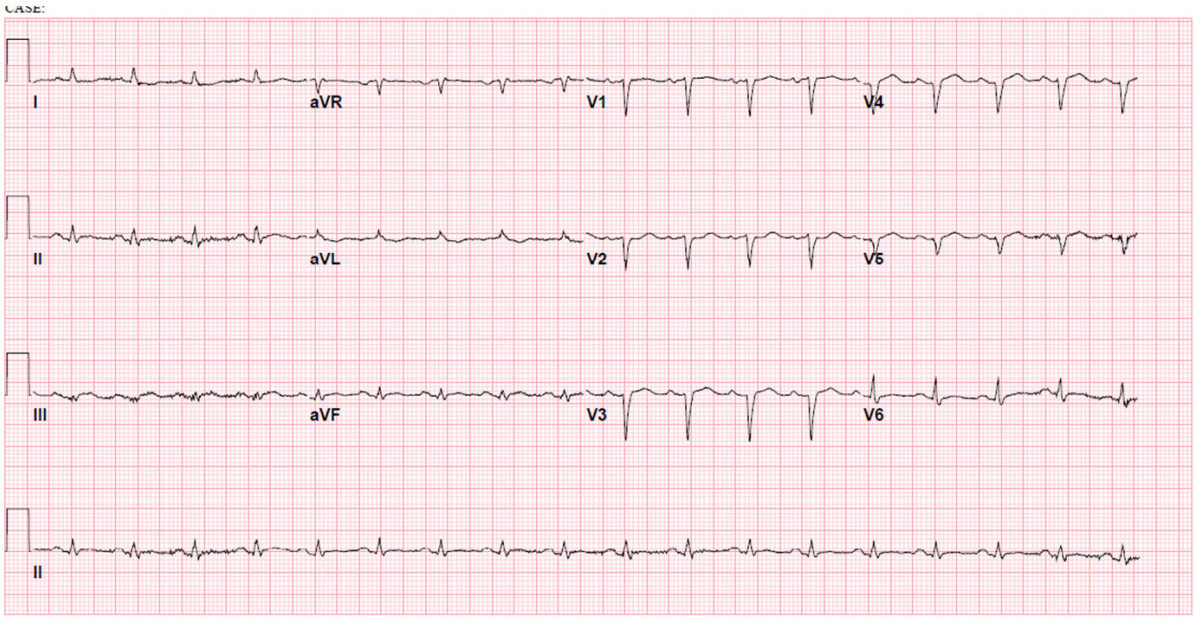
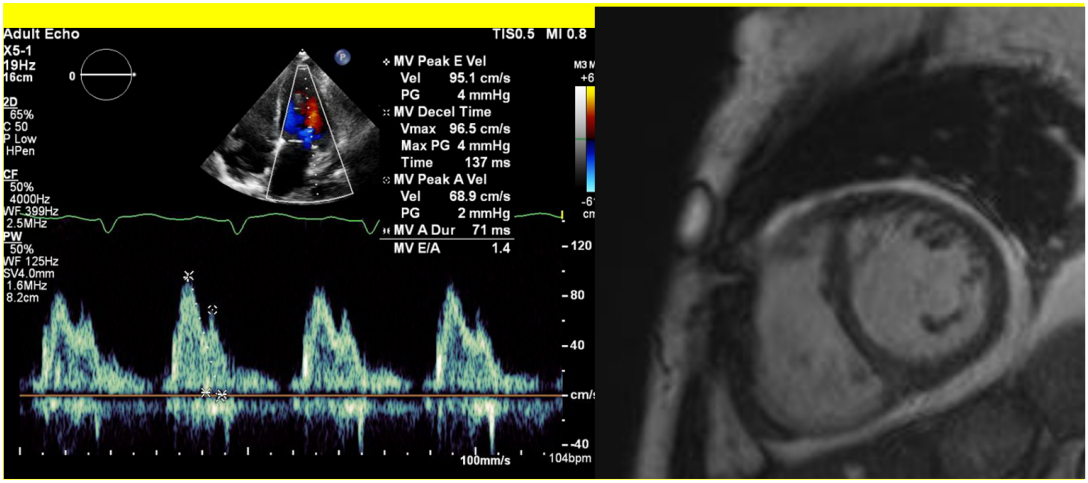


Figure 1. Low voltage ECG on admission to tertiary medical center

After returning home to Ohio, the patient again noted shortness of breath with chest pain and presented to an outside facility where bloodwork showed significant eosinophilia. She was transferred to a tertiary care center for endomyocardial biopsy. Upon arrival to the tertiary care center, vital signs were significant for tachycardia with a heart rate of 118, BP 100/59, and oxygen saturation 95% on 2 liters NC. Bloodwork revealed leukocytosis to 15.5, with the differential demonstrating an elevated absolute neutrophil count of 8.21 and elevated eosinophil count of 4.13 (normal up to 0.4×10^9/L). Table 1 demonstrates pertinent admission lab values and imaging. ECG on admission as seen in Figure 1, was notable for a low voltage ECG.

As shown in Figure 2A, a repeat echocardiogram demonstrated an EF of 35%-40% with restrictive pattern of diastolic filling. In addition, as seen in Figure 2B, a cardiac MRI was performed that demonstrated diffuse elevation in T2 values consistent with myocardial edema, focal inferior subepicardial scarring consistent with inflammation scar, and mild pericardial effusion; these findings were consistent with acute myopericarditis.



A B

Figure 2. (A) Cardiac Echocardiogram mitral inflow and (B) Cardiac MRI

She was given a trial of IV diuresis, but when her oxygenation did not improve, a CT chest was performed demonstrating extensive pulmonary edema, peripheral ground class opacities, moderate size pleural effusions, small pericardial effusion, and mediastinal lymphadenopathy. There was concern for pulmonary involvement of her hypereosinophilia causing hypoxia which did not resolve with diuresis. Pulmonary was consulted, but ultimately was unable to perform a BAL/EBUS with biopsy given significant oxygen requirements. Right heart catheterization and endomyocardial biopsy were performed confirming the histological diagnosis of EM.

As shown in Figure 3, pathology from the endomyocardial biopsy was suggestive of eosinophilic inflammation of the myocardium, perivascular, interstitial eosinophilic infiltrates, and rare myocyte necrosis. Neither necrotizing vasculitis, nor granulomatous inflammation was seen.

After 3 days, eosinophil counts returned to normal without any intervention. To determine the etiology of the eosinophilia, an infectious work up was sent including blood cultures, urine cultures, stool studies, fungal cultures, and strongyloides antibody. Infectious workup was negative. Hematology was consulted for a bone marrow biopsy that demonstrated slightly hypercellular bone marrow (20%-30%) with trilineage hematopoiesis and marked eosinophilia. There was no evidence for a myeloid neoplasm and genetic/molecular testing was sent off which is normal to date. Due to concern for pulmonary involvement, ANA, ANCA, rheumatoid factor, tryptase, SPEP/UPEP, flow cell cytometry, immunoglobulins IgA, G, and M were sent and all within normal limits with an elevation of IgE suggesting that the patient's presentation may be more consistent with an allergic disease. Review of old medication lists prior to her hospitalization in Colorado included losartan/hydrochlorothiazide for hypertension. Hydrochlorothiazide is a well-documented cause of hypersensitivity myocarditis and is likely the culprit of her eosinophilia.[8] She was treated with IV solumedrol 1,000 mg daily for 3 days and then discharged on 40 mg oral prednisone. Eosinophilia resolved prior to initiation of steroid treatment, and clinically the patient improved with an ejection fraction about 40% prior to discharge. She was discharged home without oxygen to complete a prolonged steroid course and is currently doing well.

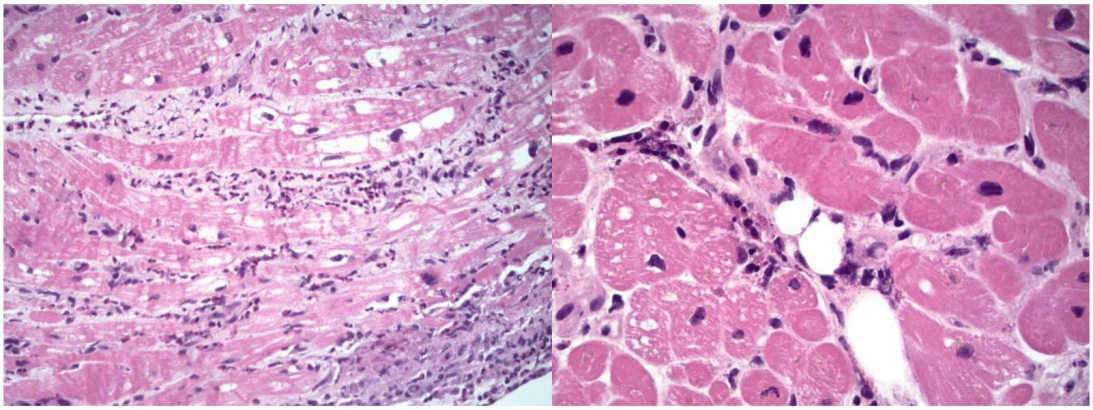


Figure 3. Histopathology from cardiac biopsy

3. Discussion

EM is a difficult diagnosis as it encompasses a wide spectrum of clinical presentations. In this case, our patient presented with acute decompensated heart failure with reduced ejection fraction. At the time of original presentation in Colorado, the diagnosis of EM was likely confounded due to normal eosinophil levels. Other case reports for EM confirmed via endomyocardial biopsy have found varying levels in peripheral eosinophil accounts including normal counts.[7] This further demonstrates the difficulty of this diagnosis and supports the utility of a cardiac biopsy in non-ischemic cases of cardiomyopathy that do not have a clear underlying etiology.

There are many medications that can cause eosinophilia. Acuity of the hypersensitivity reaction can occur after initiating a medication or over a prolonged period of time on the medication. In this case, the patient was previously on losartan/hydrochlorothiazide prior to her presentation to Colorado hospital. Hydrochlorothiazide is a well-documented cause of eosinophilic myocarditis.[8–10] It is important to take a thorough drug history as a part of the workup for EM.

Treatment of this patient was initiated with a burst of solumedrol for 3 days, due to the severity of her disease requiring an ICU admission, which was later de-escalated to 1 mg/kg/day, and discharged on a prednisone taper regimen over a period of weeks, this appears in line, with other expert opinion in treatment regimens for EM.[4–6] The decision was made to not add an immunosuppressive agent to their treatment regimen, as the offending drug agent had been removed, and it was theorized that it would likely not add any benefit. Patient improved clinically on corticosteroids and with removal of the offending drug agent. She has been doing well, with no known EM disease relapse to date.

Conflicts of Interest Disclosure

The authors have declared no conflicts of interest.

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