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Case Report

Eosinophilic myocarditis: Case report and brief review of the literature ☆,☆☆

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ABSTRACT

Eosinophilic myocarditis (EM) is a cardiac manifestation of hypereosinophilic syndrome with a high mortality rate. EM shares imaging features similar to other restrictive cardiopathies, and include patchy intramural late gadolinium enhancement on cardiac magnetic resonance with or without presence of biventricular thrombus. Diagnosis is confirmed on histopathology, and is the current gold standard. Here we report clinical presentation and imaging findings of EM in a 70-year-old woman who presented with fever and chills.

Abbreviation: CT, computed tomography; TTE, transthoracic echocardiogram; LV, left ventricle; RV, right ventricle; HES, hypereosinophilic syndrome; CMR, cardiac magnetic resonance; EM, ECG, eosinophilic myocarditis; BNP, B-type natriuretic peptide; IgE, immunoglobulin E; DCM, dilated cardiomyopathy; RCM, restrictive cardiomyopathy; HCM, hypertrophic cardiomyopathy; LGE, late gadolinium enhancement; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; CK, creatine kinase; EF, ejection fraction.

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Background

Eosinophilic myocarditis (EM) is a restrictive cardiomyopathy which can manifest from hypereosinophilic syndrome (HES) due to eosinophilic infiltration causing progressive fibrosis and impaired relaxation [1]. HES is defined as a peripheral eosinophil blood count greater than 1.5 x $mm^3/\mu L$ with end organ damage and secondary causes of eosinophilia excluded [2]. Importantly, this condition is associated with high mortality, with in-hospital death reaching 22%; in the hypersensitivity form, mortality can be increased to 36% [3]. Etiologies of EM include allergic disorders, autoimmune disorders, hypersensitive reactions to certain drugs and vaccines, vasculitis such as Churg-Strauss syndrome, parasitic infections, and neoplasia [4].

Treatment includes high-dose steroids followed by a taper with the possible addition of mepolizumab, an IL-5 monoclonal antibody, or azathioprine [5]. An anticoagulant can also be used due to the hypercoagulable state that develops [5]. While cardiac biopsy remains the gold standard for diagnosis, the sensitivity is only 54%, due to the patchy distribution of disease [6]. Due to the invasiveness of the procedure and lower sensitivity, non-invasive imaging and laboratory tests are used commonly to make the diagnosis.

Here, we present a case of a 70-year-old woman with diagnosis of Eosinophilic myocarditis.

Case report

A 70-year-old woman with a history of hypertension, hyperlipidemia, eczema and obstructive sleep apnea presents with fever and chills for 4 days. She reported a febrile temperature as high as 104 F, though was afebrile on admission. Normal blood pressure, pulse and oxygen saturation. Initial laboratory workup was pertinent for elevated troponin of 14,552 ng/L (normal range: 0-30 ng/L), C-reactive peptide (CRP) of 96.2 mg/L (normal range: $<$ 8.0 mg/L), erythrocyte sedimentation rate (ESR) of 23 mm/h (normal range: 0-20 mm/h), B-type natriuretic peptide (BNP) of 895 pg/mL (normal range: $\leq$ 100 pg/mL), creatine kinase (CK) of 2,584 U/L (normal range: 25-190 U/L) and normal total leukocyte count of 8.7 x $mm^3/\mu L$ (normal range: 3.7-11.0 $mm^3/\mu L$).

Patient was subsequently admitted for further workup. CT Chest, abdomen and pelvis was performed which showed no pertinent findings to clinical presentation. Blood culture were negative. Differential counts was pertinent for a peak absolute eosinophil count of 0.67 x $mm^3/\mu L$ (normal range: $\leq$ 0.50 x $mm^3/\mu L$).

A transthoracic echocardiogram (TTE) was performed during the admission which was pertinent for concentric myometrial hypertrophy. Cardiology recommended further evaluation with Cardiac magnetic resonance (CMR).

CMR shows diffuse mid-wall to near transmural left ventricular (LV) patchy enhancement throughout the myocardium suggesting an infiltrative pattern (Fig. 1). No subendocardial enhancement in vascular territory distribution to suggest infarct. Constellation of these findings were compatible with non-ischemic myocarditis, and in the setting of elevated eosinophil counts highly suggestive of eosinophilic cardiomyopathy.

A 3-day course of steroids was started for management of myocarditis. Right heart catheterization was performed for endomyocardial biopsy which showed acute myocarditis with an eosinophil rich infiltrate (Fig. 2), confirming the diagnosis.

The patient was started on a 2-month high-dose steroid taper beginning with 50 mg of prednisone daily, and she continues to follow cardiology in the clinic.

Discussion

Cardiomyopathies have been commonly divided into dilated, hypertrophic, arrhythmogenic right ventricular, and restrictive cardiomyopathies [7].

Dilated cardiomyopathy (DCM) is defined by the presence of dilated left ventricles and systolic dysfunction in the absence of abnormal loading conditions or ischemic heart disease that is extensive enough to cause global systolic impairment [8]. Though in clinical practice DCM has been divided into ischemic and nonischemic despite the formal definition to account for the similar morphologic changes seen after ischemia [9]. Nonischemic DCM can be caused by an extensive list of conditions including alcohol, peripartum cardiomyopathy, infection, hypersensitivity myocarditis, infiltrative diseases, and Churg-Straus vasculitis [8,10]. Importantly, myocarditis represents the etiology in 12% of dilated cardiomyopathy patients [11]. Nonischemic and ischemic dilated cardiomyopathy have been found to have differentiating imaging findings, though both have a dilated and thin walled LV [12]. In ischemic DCM there will be subendocardial or transmural late gadolinium enhancement (LGE) on CMR in the distribution of a coronary artery [13]. In contrast, Nonischemic DCM can show a LGE in a mid-myocardial distribution not associated with a coronary artery [13,14], though most will not show LGE. Midwall fibrosis identified by late gadolinium enhancement on CMR has been identified in 35% of DCM patients and is a predictor of mortality in dilated cardiomyopathy, likely due to increased LV wall stiffness [15].

Hypertrophic cardiomyopathy (HCM) is classified as a hypertrophied, nondilated LV in the absence of another disease that can produce a similar wall thickening [16] and has a phenotypic prevalence of 1:500 in the general population. For the initial assessment, significant findings on echocardiography include LV wall thickness of $\geq$ 15 mm, a pressure gradient over the LV outflow tract obstruction of $\geq$ 50 mmHg, restricted LV diastolic function and an enlarged left atrium (LA) [17]. Though CMR is vital in differentiating the phenotypes of HCM, accurate maximal wall thickness measurements, risk stratification, identifying asymptomatic HCM mutant carriers and evaluating aspects of the heart echocardiography is suboptimal for, such as the apical variant of HCM [18].

Arrhythmogenic right ventricular cardiomyopathy is heritable condition defined by fibro-fatty replacement of the myocardium, primarily in the right ventricle, that underlies ventricular dysfunction and predisposes to ventricular arrhythmias [19]. The recently produced “Padua criteria” for diagnosis have been shown to be more accurate than the previous criteria and include: morpho-functional ventricular ab-

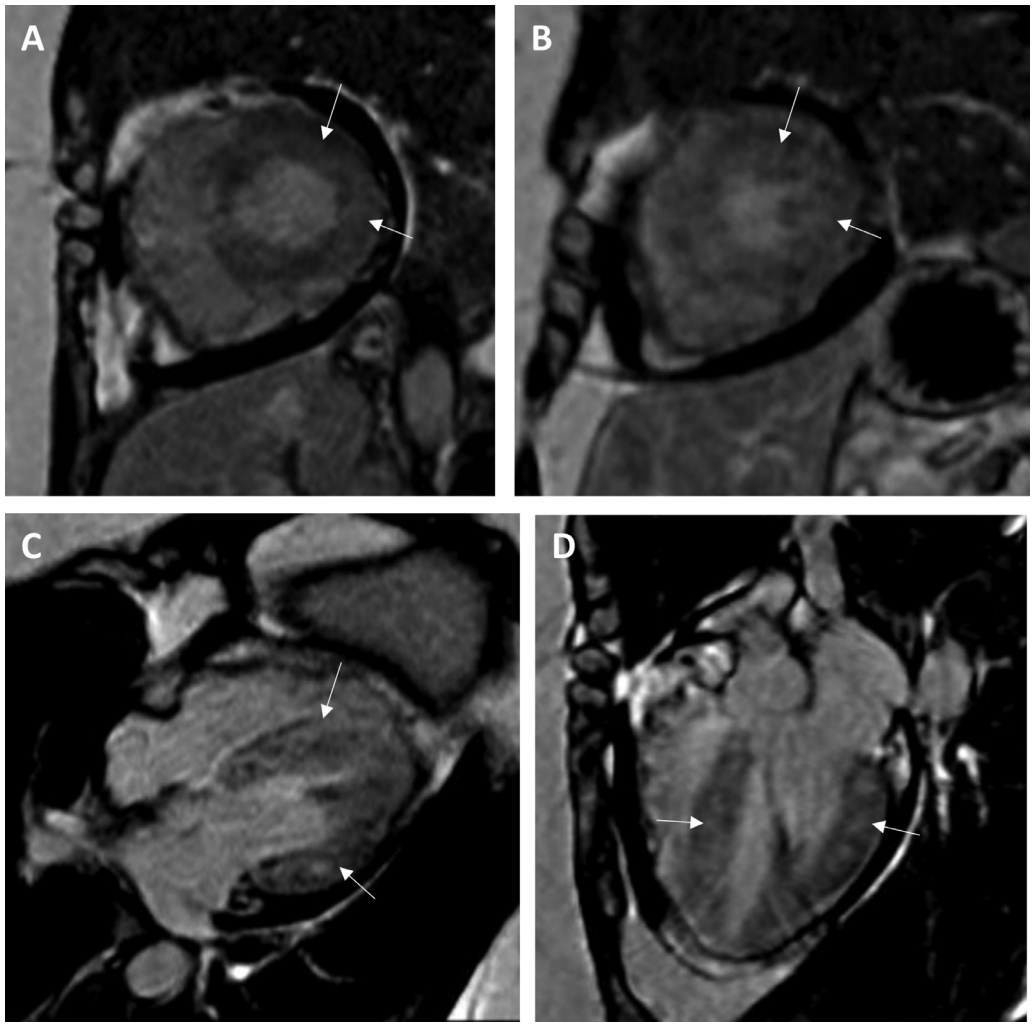

Fig. 1 – Cardiac MRI (CMR) late gadolinium images, short axis view (A, B), 4-chamber view (C) and 3-chamber view (D). Patchy mid-wall to near transmural LV myocardial late gadolinium enhancement (LGE) is present throughout the myocardium suggesting infiltrative pattern (arrow).

normalities, structural myocardial abnormalities, repolarization abnormalities, depolarization abnormalities, ventricular arrhythmias, and family history [20]. In terms of imaging the major findings include regional right ventricular (RV) akinesia, dyskinesia, or bulging and either global RV dilation or global RV systolic dysfunction [20,21].

Restrictive cardiomyopathy (RCM) is defined as diastolic dysfunction of a non-dilated left ventricle, caused by a variety of etiologies broadly grouped as infiltrative, storage diseases, non-infiltrative, and endomyocardial diseases [22,23]. Typically, restrictive cardiomyopathy is characterized by near-normal systolic function and suspicion of a restrictive filling pattern on echocardiography, though echocardiography is unable to differentiate between subtypes for RCM [8]. The diastolic dysfunction observed in restrictive cardiomyopathy is similar to constrictive pericarditis, so either echocardiography with Doppler or cardiac magnetic resonance (CMR) imaging is required to differentiate the 2 [22,24]. Late gadolinium enhancement found on CMR is a way to differentiate between the subtypes of RCM [25]. Cardiac amyloidosis, for example, has a circumferential LGE pattern affecting the subendocardium or less commonly transmurally, along with concentric hypertrophy seen on CMR [25,26]. In contrast cardiac sarcoidosis can present with a LGE pattern at the midmyocardial wall or epicardium in a patchy distribution [27], though the pattern is variable and myocardial thickness can fluctuate based on disease activity so sarcoidosis is more difficult to distinguish based on LGE [28].

Eosinophilic myocarditis is a RCM classified with the endomyocardial diseases with a progression that has historically been separated into 3 stages [29]. (1) The acute stage is characterized by infiltration and deposition of eosinophils leading to cytokine mediated damage to the endocardium. This causes progression to (2) the thrombotic stage, where a layered thrombus forms due to activation of tissue factor by the eosinophils. Finally, the damage progresses to (3) the last stage, myocardial fibrosis causing wall stiffness [30]. Echocardiography is useful in monitoring changes in cardiac function, wall thickness and cardiac chamber size as well as the development of mitral regurgitation and apical thrombus formation as the disease progresses [31]. The inflammation with EM seen on CMR is consistent with the Lake Louise crite-

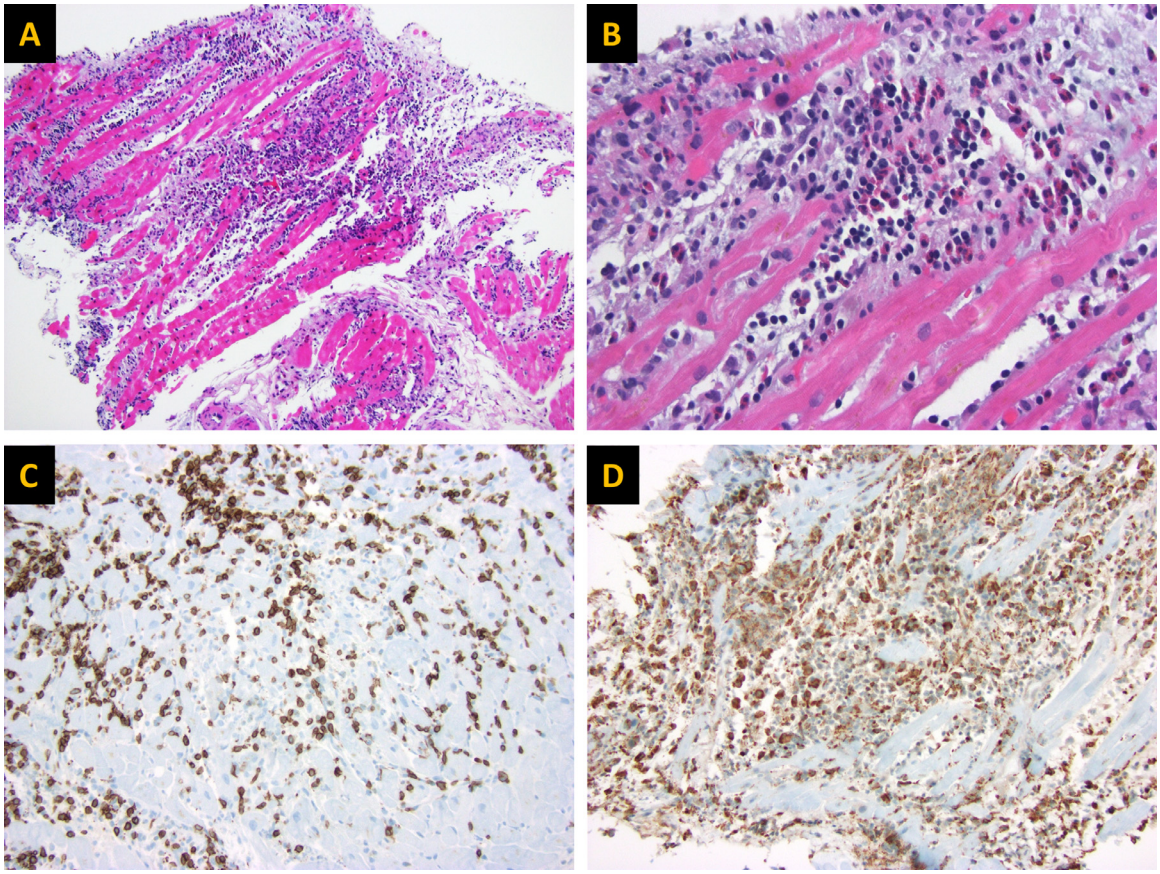

Fig. 2. (– A) Low magnification image of the biopsy shows a diffuse inflammatory infiltrate throughout the myocardium. Scale bar = 150 micrometer. (B) Higher magnification image shows the infiltrate is eosinophil rich and also contains lymphocytes, plasma cells and histiocytes. Foci of myocyte injury and dropout are easily appreciated. Scale bar = 50 micrometer. (C) CD3 immunostain highlights the infiltrating T-cells. Scale bar = 100 micrometer. (D) No giant cells per se are seen in the infiltrate. But CD68 immunostain highlights the numerous histiocytes. Scale bar = 100 micrometer.

ria for myocarditis which require at least 2 of: (1) regional or global increase myocardial signal in T2-weighted images, (2) increased global myocardial early gadolinium enhancement ratio between myocardium and skeletal muscle in gadolinium enhanced T1-weighted images or (3) at least one focal lesion with non-ischemic regional distribution in gadolinium-enhanced T1-weighted images [32]. The EM pattern of LGE is subendocardial with patchy or diffuse distribution without association to a coronary artery distribution [33]. Due to the cardiomyocyte damage, myocarditis can present with elevated troponin, erythrocyte sedimentation rate, reactive C protein and creatine kinase, non-specific ECG changes and/or an elevated BNP due to resulting heart dysfunction [3,34]. Endomyocardial biopsy is still the definitive test though it has a low sensitivity and the invasiveness of the test may limit its use [5,35].

The endomyocardial biopsy was a core component in reaching the correct diagnosis in this case, as the absolute eosinophilic count never reached the 1.5 x $mm^3/\mu L$ threshold. The CMR findings of patchy late gadolinium enhancement in the mid inferior and apical walls, indicating regional injury, small pericardial effusion, and global hypokinesis, are all highly suggestive of myocarditis according to the Lake Louise Consensus Criteria [32]. The patient, however, never developed the layered thrombus which would be more specific for eosinophilic myocarditis. With these findings the differential was able to be narrowed to myocarditis, though the etiology was still broad, allowing for an invasive endomyocardial biopsy to be justified. This case shows the utility of non-invasive imaging in narrowing a differential to support the use of an invasive endomyocardial biopsy in diagnosis of eosinophilic myocarditis.

Patient consent

Consent was obtained for the publication of current case. No patient identifiers disclosed.

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