

CASE REPORTS

A STEMI gone viral

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ABSTRACT

A 65-year-old male with a history of coronary artery disease and ankylosing spondylitis presented with focal ECG changes and elevated cardiac biomarkers suggestive of an acute lateral ST-elevation myocardial infarction. Emergent coronary angiography surprisingly showed non-obstructive coronary artery disease. Further workup including a cardiac MRI, viral serologies, and an endomyocardial biopsy was consistent with focal Coxsackie viral myocarditis. The patient subsequently developed recurrent, pulseless ventricular tachycardia requiring multiple rounds of ACLS, and his left ventricular ejection fraction acutely dropped from 55% to 20%. An emergent intra-aortic balloon pump was placed, and an intravenous lidocaine infusion and high-dose corticosteroids were started for the patient's electrical storm and myocarditis, respectively. The patient was eventually discharged in stable condition with an implantable cardiac defibrillator. No further episodes of ventricular tachycardia were noted at six-month follow-up. In patients with acute ECG changes, elevated cardiac biomarkers, and no evidence of obstructive coronary artery disease, myocarditis should be considered as a leading diagnosis given the potentially life-threatening sequelae as seen in our patient.

Key Words: Myocarditis, Myocardial infarction, Electrical storm

1. INTRODUCTION

Myocarditis is an inflammatory disease of the myocardium with a variety of etiologies including infection, toxins, and immunologic disorders. Diagnosis is often challenging given the diversity of clinical presentations ranging from subclinical disease to chest pain, arrhythmias, heart failure, and cardiogenic shock, all of which can mimic other clinical entities such as acute coronary syndrome.

2. CASE PRESENTATION

A 65-year-old male with a history of coronary artery disease (CAD) with a single right coronary artery stent six years prior and ankylosing spondylitis presented with fever, malaise, decreased exercise tolerance, and palpitations. Ini-

tial vitals and physical exam were grossly unremarkable. An ECG showed 3 mm ST-elevations in leads I and AVL with reciprocal changes in anterior and inferior leads (see Figure 1), and serum troponin-I was elevated > 50 ng/ml. The patient underwent emergent coronary angiography that showed stable, non-obstructive CAD without evidence of in-stent restenosis or acute thrombotic occlusion. Transthoracic echocardiogram showed mild apical hypokinesis stable from prior, left ventricular ejection fraction (LVEF) of 55%, and no pericardial effusion. Further labs showed an elevated erythrocyte sedimentation rate of 39 mm/hr and C-reactive protein of 3.0 mg/dl, thus suggestive of an inflammatory cause of myocardial damage. A cardiac MRI showed severe delayed enhancements with surrounding edema in the left

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ventricle lateral wall suggestive of active, focal myocarditis (see Figure 2). This was confirmed by endomyocardial biopsy that showed an interstitial CD3-positive lymphocytic infiltrate without evidence of giant cells, eosinophils, mast cells, amyloid, granulomas, or significant fibrosis (see Figure 3). An infectious workup showed elevated Coxsackie B virus IgM and IgG titers > 1:320, while echovirus, HIV, and *Trypanosoma cruzi* studies were negative. Anti-nuclear antibody was also negative. The patient's hospital course was also notable for six episodes of sustained, pulseless ventricular tachycardia (VT, see Figure 4) with an acute reduction in

LVEF to 20% for which he required multiple rounds of ACLS and an emergent intra-aortic balloon pump. An intravenous lidocaine infusion and high-dose corticosteroids were started for the patient's VT storm and myocarditis, respectively, and an implantable cardiac defibrillator was placed. The patient was eventually discharged in stable condition with carvedilol, sotalol, lisinopril, and furosemide. At six-month follow-up no additional episodes of VT were noted. Repeat cardiac MRI and endomyocardial biopsy showed residual left ventricular delayed enhancements and no active inflammation or myocarditis, respectively. LVEF remained at 25%.

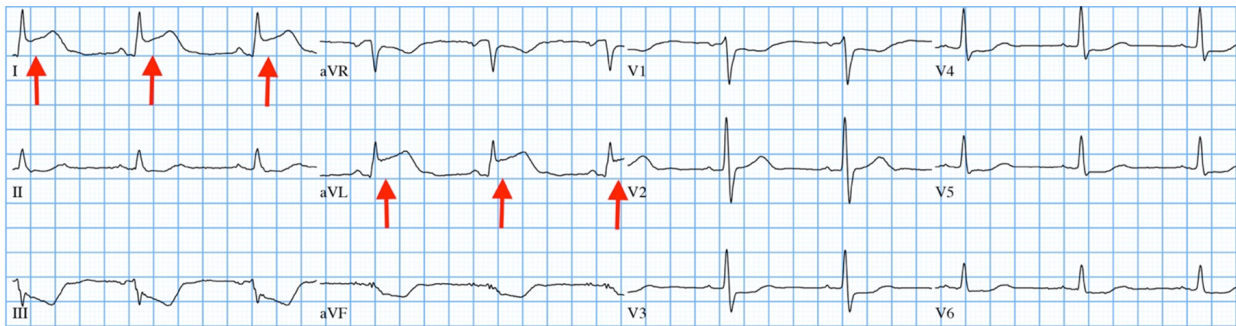


Figure 1. Admission ECG. 3 mm ST elevations in leads I and aVL (red arrows) with reciprocal changes in anterior and inferior leads, suggestive of acute myocardial ischemia and/or necrosis.

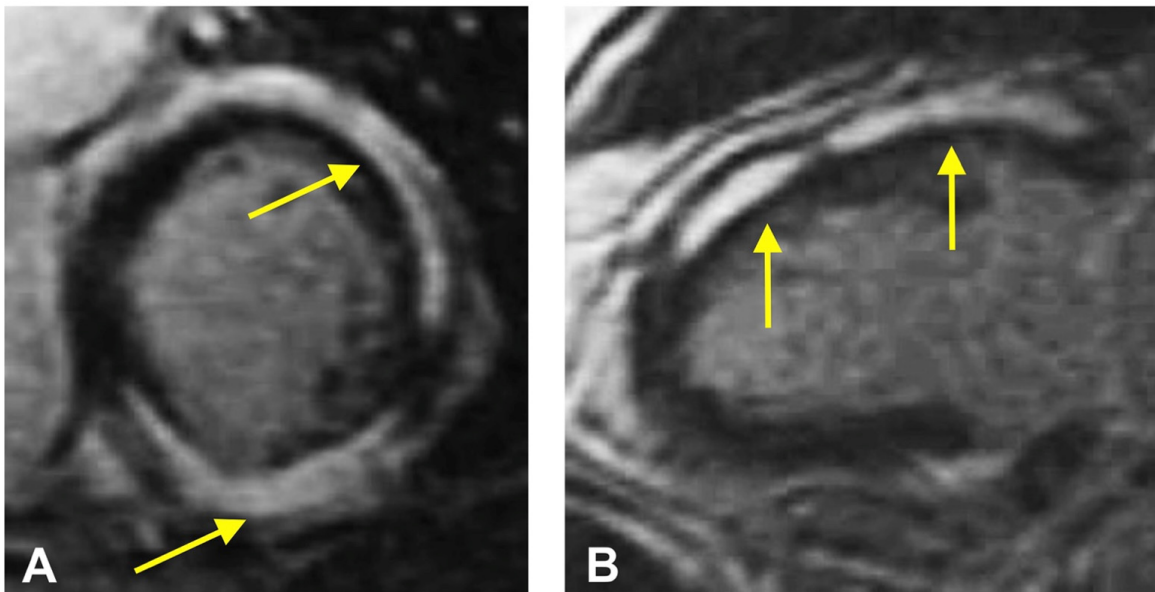


Figure 2. Cardiac MRI. Epi- and mid-myocardial delayed enhancements (yellow arrows) in the lateral left ventricular wall with surrounding edema and relative sparing of the interventricular septum suggestive of focal, active myocarditis as seen on cardiac MRI (A) short axis and (B) 2-chamber views.

3. DISCUSSION

Myocarditis should be considered as a leading diagnosis in patients presenting with focal ECG changes and elevated car-

diac enzymes, but without evidence of obstructive coronary artery disease. A thorough history and physical exam may reveal an important clue such as a viral prodrome and may

help expedite diagnosis given the potentially life-threatening sequelae as seen in our patient. Cardiotoxic enteroviruses (e.g. Coxsackie B) are classically associated with myocarditis. However current literature describes human herpes virus 6, parvovirus B19, human immunodeficiency virus, hepati-

tis C, and Trypanosoma cruzi as other important infectious etiologies.^[1,2] Non-infectious causes of myocarditis include autoimmune disorders, toxins (e.g. anthracyclines, cocaine, etc.), and hypersensitivity reactions from various medications (e.g. sulfonamides, tricyclic antidepressants, etc.).

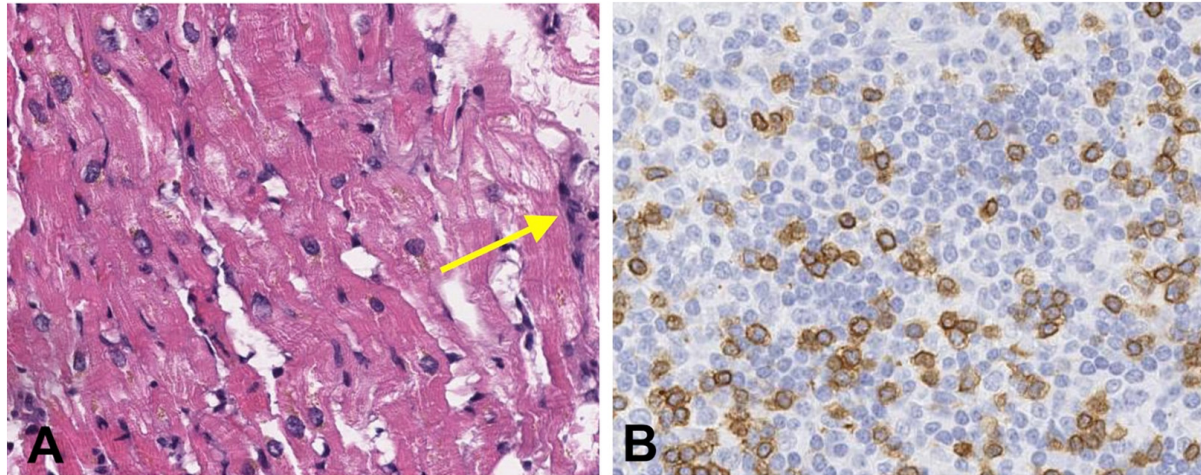


Figure 3. Endomyocardial biopsy. (A) Diffuse lymphocytic infiltrate with focal areas of myocardial necrosis (yellow arrows) seen on endomyocardial biopsy. (B) Dense areas of CD3-positive cells on immunohistochemical stain suggestive of lymphocytic infiltrate.

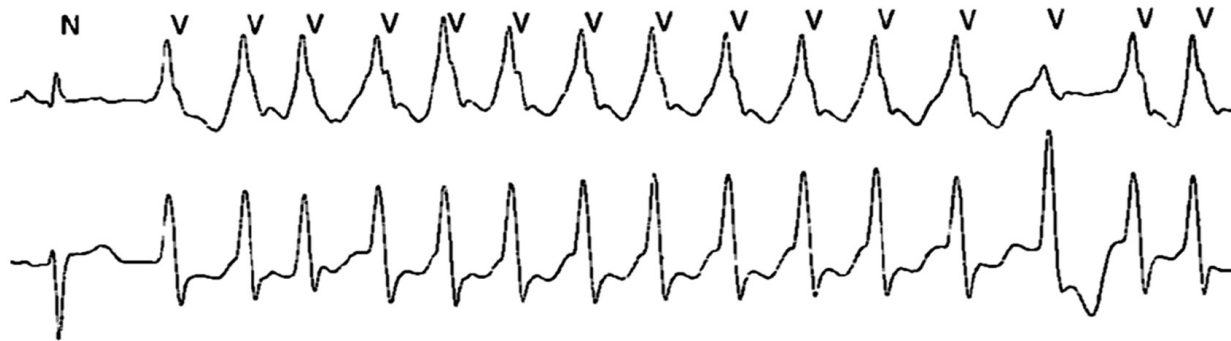


Figure 4. Electrical storm. Sustained ventricular tachycardia noted on telemetry with a sinus beat designated with a “N” and ventricular beats designated with a “V”.

The wide range of etiologies and clinical presentations of myocarditis have made its diagnosis a challenge. Physical exam, routine labs, chest radiography, and ECG findings are often non-specific. Echocardiography can provide useful data towards immediate management and prognosis including ventricular function and geometry, valvular dysfunction, silent intracardiac thrombi, etc. The pattern of late gadolinium enhancement on cardiac magnetic resonance (CMR) can further elucidate between myocarditis and ischemic cardiomyopathy given the former’s preference of epi- and mid-myocardial involvement with relative sparing of the endocardium as

compared to the latter.^[3]

However, an endomyocardial biopsy (EMB) can provide a definitive, histological diagnosis via the Dallas criteria, which defines active myocarditis as “an inflammatory infiltrate of the myocardium with necrosis”.^[4] EMB sensitivity and specificity ranges from 35 to 60 percent and 80 percent respectively.^[5,6] This variability is likely due to the transient, focal nature of myocarditis with the epicardial left ventricular wall as the most common site of involvement instead of the right ventricular endocardium where most EMBs are performed.^[5] Different gold standards (e.g. autopsy versus

clinical/functional diagnosis) may also be contributory. Current guidelines recommend EMB in cases of new onset heart failure of unclear etiology (*e.g.* non-ischemic, non-valvular, *etc.*) of less than two weeks duration with hemodynamic compromise, or of two weeks to three months duration with a dilated left ventricle, ventricular arrhythmias, second or third degree heart block, or failure to respond to usual care within one to two weeks.^[5,6]

EMB should also be considered in cases of myocarditis where tissue diagnosis may affect management and prognosis. This is especially important given the homogeneity of clinical presentations and non-invasive diagnostic testing among different causes myocarditis, each of which with different therapeutic strategies. For example, a viral prodrome may suggest viral myocarditis. Viral serologies and/or PCR may be non-diagnostic given the multitude of potential viral etiologies; however a lymphocytic infiltrate on EMB can provide definitive diagnosis. Corticosteroids appear to improve LVEF at one- and three months in patients with viral myocarditis compared to placebo, yet no difference in mortality was noted.^[7] Peripheral eosinophilia, helminthic or new medication(s) exposure may suggest eosinophilic myocarditis, and can be definitely diagnosed by an eosinophilic infiltrate on EMB. Treatment involves identification and withdrawal of the potentially offending agent(s), and high-dose IV and/or oral steroids with a gradual taper.^[8,9] Giant-cell myocarditis, a rare but often fatal cause of myocardial disease, has no associated prodrome and/or exposure history. Diagnosis typically requires targeted, often repeat EMB. Treatment involves combined immunosuppressive therapy (*e.g.* high-dose steroids and cyclosporine) which has been shown to improve transplant-free survival.^[10] It should be noted that these and other potential causes of myocarditis occur at the cellular level, which in turn can only be detected by EMB.

The role of intravenous immune globulin (IVIG) in myocarditis remains controversial. Several case reports and case series describe short-term improvement in LVEF and NYHA functional class after early administration of high-dose IVIG (2 mg/kg) in both children and adults with acute myocarditis and/or idiopathic dilated cardiomyopathy.^[11–13] Similar benefits to LVEF were also noted in a randomized control trial of 83 pediatric patients diagnosed with acute viral encephalitis with myocarditis who were treated with IVIG compared to

placebo.^[14] These studies have led to routine use of IVIG for acute myocarditis at several institutions. Common side effects include headache, fever, and chills. Serious side effects include anaphylaxis/hypersensitivity reactions, aseptic meningitis, renal impairment, and thromboembolic events. However, another randomized control trial in 62 adult patients with recent-onset dilated cardiomyopathy and/or myocarditis showed no significant difference in LVEF or functional capacity at 6 and 12-months with IVIG compared to placebo. Further, no difference in transplant-free survival was noted at 1 and 2-years. It should be noted that only 10 patients in this latter trial demonstrated cellular inflammation on EMB, which in turn suggests that at least some participants may not have had viral myocarditis.^[15,16] Further RCTs may elucidate further insight into the role of IVIG towards treatment of adults with biopsy-proven viral myocarditis.

In the case of our patient, his viral prodrome, ECG changes, elevated cardiac biomarkers, coronary angiogram without obstructive CAD, and cardiac MRI demonstrating late gadolinium enhancement were suggestive of focal viral myocarditis. He did not have peripheral eosinophilia, nor any drug, helminthic, or protozoal exposures suggestive of eosinophilic myocarditis. Of note, he was never on immunomodulators for his ankylosing spondylitis, and as such we were less suspicious for atypical infections like mycobacteria. We proceeded with an EMB given the patient's hemodynamic compromise and acute decompensation. We decided to treat with empiric corticosteroids given that the etiology of the patient's myocarditis was uncertain at the time (*e.g.* pending EMB pathology and viral serologies) and concern for giant cell myocarditis given similarities with our patient's clinical presentation. We also considered IVIG, however deferred treatment given the lack of definitive evidence showing benefit in adult populations with acute myocarditis.

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CONFLICTS OF INTEREST DISCLOSURE

The authors have declared no conflicts of interest.

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