NON-ST ELEVATION MYOCARIDAL INFARCTION AS THE INITIAL PRESENTATION OF CHRONIC EOSINPHILIC LEUKEMIA: A CASE REPORT

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Abstract

Cardiac dysfunction occurs in hypereosinophilic syndromes is a major cause of morbidity and mortality. In patients with high clinical suspicion for acute myocarditis and confirmed peripheral eosinophilia, timely diagnosis and treatment is imperative to avoid the catastrophic consequence of irreversible fibrotic changes to the cardiac tissue.

INTRODUCTION

The HES are rare and have an unknown prevalence. It is more common in men compared to women and rates increase with age to peak in the range of 65-74 years[2]. Only some patients with persistent eosinophilia develop organ dysfunction that characterizes HES. Essentially, all organs may be susceptible to the effects of sustained eosinophilia and the heart is no exception. Cardiac involvement can cause significant morbidity and mortality[3]. Eosinophilic myocarditis is a rare presentation of HES but poses a diagnostic challenge since initial investigations are non-specific and definitive diagnosis requires either endomyocardial biopsy or cardiac magnetic imaging which may not be readily available. The diagnosis may be further delayed where other sinister etiologies of chest pain need to be ruled out such as Acute Coronary Syndrome requiring cardiac catheterization. However, in patients with high clinical suspicion for acute myocarditis and confirmed peripheral eosinophilia, timely diagnosis and treatment is imperative to avoid the catastrophic consequence of irreversible fibrotic changes to the cardiac tissue. We present a case of eosinophilic myocarditis as the initial presentation of HES and discuss the pathophysiology, diagnosis and management of such cases.

CASE PRESENTATION

A 65 year old man had been having fever, chills and a productive cough with yellow sputum for four days prior to his presentation. He developed right sided parasternal chest pain twenty-four hours before presenting to the emergency department. The pain was worse on inspiration and he was able to localize it with one finger. The past medical history was significant for hyperlipidemia and coronary artery disease with ST elevation myocardial infarction (STEMI) requiring stent placement in the left anterior descending artery (LAD) 10 years prior to his admission.

On presentation, his blood pressure was 143/54, pulse rate 107, respiratory rate was 18 and oxygen saturation was 98%. His temperature was 102.7 F. He showed no signs of cardiopulmonary distress and clinical examination of his cardiac, respiratory and abdominal systems showed no abnormalities.

His initial investigations were significant for leukocytosis of 18.5k/uL (neutrophil 57%, lymphocyte 6%, eosinophil 35%, monocyte 2%). His cardiac troponin was elevated (5.77ng/ml). Electrocardiogram (EKG)

showed normal sinus rhythm and left bundle branch block which was unchanged from prior EKGs. Chest X-ray reported right upper lobe infiltrate concerning for pneumonia.

He was admitted for management of Non-ST Elevation Myocardial Infarction (NSTEMI) in the setting of Pneumonia with high suspicion for myopericarditis given his symptomatology. He was treated with aspirin, clopidogrel, pravastatin, ceftriaxone and doxycycline and admitted to cardiac telemetry unit.

His Echocardiogram (ECHO) showed left ventricular ejection fraction of 36-40% with moderate diastolic dysfunction which was not significantly changed from a prior study one year ago. Left cardiac catheterization showed non-obstructive coronary artery disease with patent LAD stent. Over the ensuing days, he developed worsening peripheral eosinophilia of 72%. Peripheral smear showed normocytic normochromic anemia, leukocytosis with eosinophils (no blasts) and normal platelets. Serum Vitamin B12 was elevated (>1500pg/mL) and serum tryptase was within normal limits (9ng/dl). He showed clinical improvement after initiation of high dose steroids for the management of eosinophilic myopericarditis. Bone marrow biopsy showed chronic myeloproliferative neoplasm with eosinophilia with fusion of FIP1L1 and PDGRA genes. He was eventually discharged with outpatient hematology/oncology follow-up and commenced treatment with Imatinib.

DISCUSSION

The hypereosinophilic syndrome (HES) constitutes a rare hematological group of disorders defined by the association of hypereosinophilia (absolute eosinophil count >1.5 x 10^9/L) with eosinophil mediated organ damage and/or dysfunction in the absence of other etiologies of eosinophilia including parasitic infection and allergies[4].

The incidence and prevalence of HES are not well characterized. The Surveillance, Epidemiology and End Result (SEER) database recorded a crude incidence of ˜0.035 per 100 000 over a five year period (2001-2005). The syndrome is more common in men than women (male: female ratio 1.47) and rates increased with age to a peak in the range of 65 to 74 years. As seen in this case, the HES may result from the novel fusion of tyrosine kinase FIP1L1-PDGRA genes as a result of chromosomal deletion on 4q12 which has more frequently been detected in males[2].

The varied clinical presentations of HES reflect the heterogeneous nature of the disease. Essentially, all organs may be susceptible to the effects of sustained eosinophilia and the heart is no exception. Cardiac disease (unrelated to hypertension, Rheumatic heart disease and atherosclerosis) was identified in 20% of patients (37/188) of patients in a clinical analysis of data taken from 2001-2006[1].

Essentially, the cardiac pathology of HES has been divided into three stages: acute necrosis, thrombosis, and fibrosis. The acute necrotic stage is characterized by eosinophilic infiltration into the myocardium and degradation with release of toxic cationic proteins leading to myocardial necrosis[5]. The stimulus for thrombosis in the second stage is ventricular wall vascular damage leading to exposure of von Willebrand factor, collagen, and tissue factor (TF) that ultimately lead to generation of a fibrin thrombus[6]. The majority of patients who have HES may not be diagnosed with cardiac involvement until the final pathological stage where they present with scarring of the chordae tendinae and endocardium leading to a restrictive or dilated cardiomyopathy and progressive valvular incompetence most commonly from regurgitant atrioventricular valves[7].

Eosinophilic myocarditis may present in many different ways, ranging from asymptomatic cases to life-threatening conditions such as cardiogenic shock or sudden cardiac death due to malignant ventricular arrhythmias. In this case, our patient presented with eosinophilic myocarditis which an uncommon initial presentation. However, there was high clinical suspicion in the setting of his febrile illness, pleuritic chest pain and elevated cardiac biomarkers. Elevations in serum troponin levels can be sensitive indicators of early and ongoing eosinophil-associated myocardial damage in forms of HES[8]. Additionally, peripheral hypereosinophilia remained the only initial clinical clue to suggest eosinophilic myocarditis in this patient. However, there are cases reported where peripheral hypereosinophilia is not present initially and found solely

on endomyocardial biopsy[9]. It is also recommended to assess serum tryptase and Vitamin B12 levels since increased concentrations support a diagnosis of myeloproliferative disorder. Although EKG and ECHO are both non-specific for the diagnosis of eosinophilic myocarditis, it was done to rule out other sinister causes of chest pain.

In the acutely ill patient, endomyocardial biopsy is the gold standard but can lead to significant complications such as ventricular perforation, arrhythmia or conduction abnormalities[10]. Additionally, patchy or focal myocarditis can lead to significant sampling error which limits its effectiveness. As such, there is now an emerging role for cardiac magnetic imaging for diagnosing eosinophilic myocarditis[11]. However, its use is constrained by high expense and limited availability. In this case, given that our patient had a positive tissue biopsy showing showed chronic myeloproliferative neoplasm with hypereosinophilia, we opted to initiate treatment based on the clinical diagnosis.

Corticosteroids have long been the standard treatment for HES and EM. The goal of corticosteroid therapy is to prevent or reduce eosinophil-mediated organ damage[12]. Additionally, the early initiation of steroid therapy can achieve substantial improvements in clinical outcomes, prognosis and long-term survival. However, as seen in this case, it may not always be clinically feasible to do so when there is need to rule out other credible etiologies of chest pain such as acute coronary syndrome. Our patient had significant improvement of symptoms with prednisone dosed at 1mg/kg/day. Additionally, there was a substantial decrease in peripheral eosinophilia with initiation of Imatinib in the outpatient setting.

In conclusion, eosinophilic myocarditis is a rare initial presentation of hypereosinophilic syndrome. Peripheral eosinophilia is a valuable clue to point clinicians in the direction of eosinophilic myocarditis as a possible diagnosis. In patients with high clinical suspicion for acute myocarditis and confirmed peripheral eosinophilia, timely diagnosis and treatment is imperative to avoid the catastrophic consequence of irreversible fibrotic changes to the cardiac tissue.

CONCLUSION

The HES are a heterogeneous group of rare disorder characterized by the sustained overproduction of eosinophils, in which eosinophilic infiltration and mediator release result in multiple organs damage. Cardiac involvement can cause significant morbidity and mortality. Eosinophilic myocarditis is a rare initial presentation of HES. It poses a diagnostic challenge since initial investigations are often non-specific and other common causes of chest pain need to be ruled out. However, in the setting of high clinical suspicion for eosinophilic myocarditis and persistent peripheral eosinophilia, timely diagnosis and treatment with steroids is imperative to avoid the catastrophic consequence of irreversible fibrotic changes to the cardiac tissue.

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