Cardiac Involvement Mimicking Acute Coronary Syndrome in Idiopathic Hypereosinophilic Syndrome

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ABSTRACT

Hypereosinophilic syndrome (HES) is defined as a persistent eosinophilia lasting longer than 6 months of unknown origin and related to organ involvement. Cardiac involvement, usually leading to morbidity and mortality of HES patients, often mimics other diseases such as acute coronary syndrome. We report a 46-year-old female who came to hospital with atypical chest pains and a known history of eosinophilia. After excluding other possible causes of eosinophilia, we underwent further cardiac investigations. She had normal cardiac size on echocardiography and no thrombus or mass, with only global hypokinesia with systolic and diastolic dysfunction noted. These findings were different from other studies. This patient was then treated as HES with cardiac involvement.

Key words: acute coronary syndrome, cardiac involvement, hypereosinophilic syndrome.
involvement is the most common cause of morbidity and mortality in HES patients.4,5 We reported eosinophilia in 46-year-old female presenting to a tertiary care hospital with atypical chest pains mimicking acute coronary syndrome.

CASE ILLUSTRATION

A 46-year-old woman came to the emergency room with chief complaints of feeling of lethargy and lacking of appetite for a week. She also reported daily epigastric pain radiating to the lower retrosternal area, not worsened by exertion or associated with breathlessness. She had no exertional symptoms, fever, black stools, or travel history. She did not smoke. She had a past medical history of gastritis, asthma, and white coat hypertension hospitalized 3 years ago. At that time hypereosinophilia was observed.

During physical examination, her blood pressure was 112/81 mmHg, pulse was 98 beats per minute, respiratory rate was 16 breaths per minute. Body temperature was 36.6°C. There was slight epigastric tenderness, but with no guarding, rigidity, rebound, or masses. There were no abnormal findings in her heart, lungs, abdomen, and extremities.

ECG showed sinus tachycardia and new ST depression in the inferior and lateral leads. The full blood count on admission showed white blood cell count of 16.58 (normal range [NR] 4.0–10.0 x10⁹/L), eosinophil 50.8% (NR 0-6%), absolute eosinophil 8.42 x10⁹/L (NR 0.04-0.44 x10⁹/L). Other laboratory findings were as follows: Troponin T serum 0.92 ug/L (NR <0.03 ug/L), creatine kinase serum 219 U/L (NR 38-164 U/L), creatine kinase-MB 10.5 ug/L (NR0.5-5.0 ug/L), NT-proBNP serum 11535 pg/mL (NR <150 pg/mL), C-reactive protein 25.9 mg/L (NR 0.2-8.8 mg/L), ESR 56 mm/Hr (NR 3-15 mm/Hr), IgE 264 IU/ml (NR 18-100 IU/ml). Liver and renal functions were normal. No positive results were found for myeloma, lupus anticoagulant, anti-CCP, rheumatoid factor, anti ds-DNA, antinuclear antibody (ANA), or antineutrophil cytoplasmic antibody (ANCA). Stool for parasites was negative.

On the next day, troponin T, creatine kinase, and creatine kinase-MB still remained high at 1.11 ug/L, 128 U/L, 8.1 ug/L respectively. In addition, eosinophil remained high 42.4% and the absolute count was 3.93 x10⁹/L, confirmed with bone marrow biopsy.

Chest x-ray on admission showed a normal heart size. Bibasal atelectasis of the lungs were noted. No masses, consolidation, or pleural effusion were seen. Multislice CT-scan was performed three days after admission. There was bilateral pleural effusion with atelectasis, without any suspicious lesion, masses, or enlargement on heart, liver, kidneys, spleen, and uterus. Transthoracic echocardiography showed normal size of left and right ventricle with moderate to severe global left ventricular hypokinesia, systolic and diastolic dysfunction, moderate left atrium enlargement, and a small circumferential pericardial effusion. There was no intracardiac thrombus, mass, or vegetation. Coronary angiography with a view to percutaneous intervention was performed. However, the angiography showed no significant epicardial coronary stenosis. She was treated for hypereosinophilic syndrome with congestive heart failure. Intravenous methylprednisolone 1 mg/kg per day was given with ACE inhibitor and diuretics. After two weeks of therapy, clinical manifestations rapidly improved and peripheral blood eosinophilia had subsided.

DISCUSSION

The patient came to the hospital with non-specific symptoms. She felt lethargic with lack of appetite for a week. She also had chronic epigastric pain. ECG showed abnormal ST changes and elevated cardiac biomarkers. At first patient was treated for acute coronary syndrome (ACS) and underwent angiography. However, angiography was normal. Blood test showed a highly elevated eosinophil count and persistent elevated cardiac biomarkers. The patient was investigated for myocarditis associated with hypereosinophilic syndrome.

WHO defines idiopathic HES in those fulfilling Chusid’s criteria with no cause found for the eosinophilia. HES is a very rare syndrome, more frequently found in males than females, and most common in patients 20-50 years age group.1,3

Our patient was a 46-year-old female, who
fulfilled the diagnostic criteria of HES. She had eosinophilia three years ago. Previous studies suggested that any patients with documented absolute eosinophilic count greater than 1500 x10^9/µL on at least 2 occasions should be evaluated for HES, regardless of the presence of symptoms. Hypereosinophilia in our patient was confirmed by bone marrow biopsy.

As the first step of establishing the diagnosis of HES, we excluded other possible causes for the eosinophilia. The differential diagnosis of HES including both familial and acquired causes were excluded. There was no history of familial eosinophilia, which is an autosomal dominant disorder. Our patient was also negative for allergic and autoimmune diseases, malignancies, connective tissue disorder, skin diseases, leukemia, and parasitic infections. She came with sign and symptoms of cardiac origin indicating cardiac involvement.

The heart is the most common organ system affected in HES besides the nervous system, skin, lungs, and gastrointestinal tract. Cardiac complications are a leading cause of morbidity and mortality. Cardiac involvement was reported in 40-64% patients with other symptoms such as fatigue, cough, breathlessness, muscle pains, angioedema, rash, and fever.

Also known as eosinophilic myocarditis, cardiac involvement can occur in three stages. The first stage is eosinophil infiltration of the myocardium causing early acute necrosis. This may be asymptomatic and last from days to months. The second stage is a thrombotic stage characterized by mural thrombi and thrombus formation along the damaged endocardium. The predisposed location is the left ventricle and its apices where stasis mostly occurs. This process can take up to ten months. How the eosinophil infiltration lead to thrombotic diathesis in HES is not fully understood. However, four main granular proteins released by eosinophil-major basic protein (MBP) may cause hypercoagulability. They are eosinophil-derived neurotoxin (EDN), eosinophil cationic protein (ECP), and eosinophil peroxidase (EPO).

The last stage is the fibrotic stage. The thrombus is organized into a thick layer of granulation tissue replacing normal endocardium and is further characterized by hyaline fibrosis. In this stage there are no more deposits of eosinophil granule proteins.

As fibrosis progresses in the left ventricle, its compliance will decrease and resulting in a restrictive cardiomyopathy. Papillary muscle dysfunction and mitral regurgitation occur when the fibrosis affects the papillary muscle and chordae tendineae. At this stage, murmurs may be heard and the patient may show clinical manifestation of heart failure. In the acute stage, embolic events from the thrombus can be found in 25% of cases. The thrombotic and structural changes of the myocardium can also provoke arrhythmias. Patients may feel chest discomfort, with elevated cardiac biomarkers and ST changes in ECG. On the other hand, patients may appear asymptomatic or have normal results of echocardiography and other tests.

Our patient showed relatively normal cardiac size in echocardiography and no thrombus, but global hypokinesia with systolic and diastolic dysfunction was noted. It is quite different with previous reports that showed thrombus in left ventricle. Our patient also had high cardiac biomarkers mimicking acute coronary syndromes (ACS). Similar cases have been reported in 2012 by Amini et al and Wociechowska et al. Amini reported an old woman came with typical chest pain. ACS was suspected but angiogram showed no obstructive coronary artery disease. Cardiac magnetic resonance imaging showed neither infiltrative myocardial disease nor any evidence of infarction. Hematologic work-up for her eosinophilia was consistent with HES. She then underwent endomyocardial biopsy to confirmed HES. Therefore, cardiac involvement secondary to HES should be considered as a differential diagnosis to ACS even in patients with no clinical symptoms of eosinophilia.

It is suggested that if HES is clinically suspected, cardiac biopsy should be done. Our patient did not have biopsy performed. However, studies show that biopsy is not very sensitive (50%) as the infiltrate is often focal. Treatment is much more important than waiting for laboratory results. The management of HES includes treatment with steroids and standard of care treatment for heart failure. In
a case report by Aggarwal et al., a combination of azathioprine and steroids has been used to prevent the recurrence of HES. In other cases, endocardectomy and cardiac transplantation have been performed. Our patient received high dose corticosteroid (methylprednisolone 1 mg/kg per day) and standard treatment for heart failure and showed improvement in 2 weeks.

CONCLUSION

Hypereosinophilic syndrome is a rare condition. The heart is one of the most common organ system affected in HES. The symptoms are not typical and often found mimicking acute coronary syndrome or other heart diseases.

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REFERENCES