Hypereosinophilic Syndrome with Cardiac Involvement in a Pregnant Patient with Multiple Sclerosis

In hypereosinophilic syndrome, the sustained overproduction of eosinophils leads to the dysfunction of one or more organs. Symptoms vary in accordance with which organ is affected. Cardiac involvement leads to substantial morbidity and to most of the deaths that are associated with hypereosinophilic syndrome.

Herein, we present the case of a 31-year-old woman, pregnant for 12 weeks and with a history of multiple sclerosis, who presented with transient vision loss and splinter hemorrhages in her fingernail beds. The diagnosis was hypereosinophilic syndrome with cardiac involvement. Echocardiography revealed 2 echodense structures: one that obliterated the left ventricular apex, and another in the basal lateral wall. The patient underwent therapy with prednisone and heparin but developed heparin-induced thrombocytopenia. This condition resolved when argatroban was substituted for heparin. Two weeks after the patient's release from the hospital, echocardiography revealed improvement in the echodense ventricular structures. The transient vision loss and the splinter hemorrhages were attributed to the hypereosinophilic syndrome.

We believe that this is the first report of a pregnant patient with hypereosinophilic syndrome and cardiac involvement. (Tex Heart Inst J 2011;38(2):163-5)

Hypereosinophilic syndrome (HES) is characterized by the sustained overproduction of eosinophils. Eosinophil infiltration and mediator release cause damage to one or more organs. The symptoms vary, depending upon which organ is involved. The diagnostic criteria for HES include peripheral blood eosinophilia >1,500 × 10^6/L, the absence of a secondary cause of eosinophilia, and evidence of a related organ dysfunction. Hypereosinophilic syndrome frequently affects the skin, central nervous system, gastrointestinal tract, and lungs. Cardiovascular sequelae of HES are commonly seen, and they are a major cause of morbidity and death.

The onset of HES symptoms is frequently insidious, and the eosinophilia is detected incidentally. However, in some patients, the presenting manifestation is severe and life-threatening due to rapidly developing cardiac or neurologic complications.

The treatment of HES largely depends upon the patient's presentation, the laboratory findings, and the results of mutational analysis. First-line therapy in most patients involves glucocorticoids. Herein, we discuss the case of a pregnant patient with HES and cardiac involvement.

Case Report

In December 2009, a 31-year-old woman presented at our neurology clinic, 3 days after suddenly and completely losing the vision in her right eye for a 2-minute period. The patient, who was in week 12 of pregnancy, also reported a 2-week history of bilateral distal fingernail-bed discoloration, consistent with splinter hemorrhages. A review of symptoms revealed palpitations, nausea, and vomiting. Of note, the patient reported having seen floaters and having similar nail-bed discoloration in May 2007, when she was diagnosed with multiple sclerosis at an outside institution.

An urgent ophthalmologic evaluation revealed occlusions of the inferotemporal retinal artery (Fig. 1A). The patient was sent to the emergency department for further evaluation. Notable findings during physical examination included tachycardia (heart rate, 108 beats/min) and splinter hemorrhages in the fingernail beds (Fig. 1B). Her blood pressure (123/79 mmHg) and pulse oximetry results were normal. Auscultation...
tion of the heart and lungs disclosed a normal S1 and S2 with no murmurs, rubs, or gallops. The jugular venous pressure was normal, and vascular examination revealed normal pulses and no bruits. Neurologic examination revealed nothing unusual. There were no skin rashes.

Laboratory findings included leukocytosis (11.5 × 10^9/L) with 19% eosinophils, normocytic anemia (hemoglobin, 11.3 g/dL; and mean corpuscular volume, 91.7 µm³), and an elevated cardiac troponin I level of 0.41 ng/mL (normal range, 0.01–0.1 ng/mL). Results of a complete metabolic profile, platelet count, and urinalysis were normal.

A 2-dimensional transthoracic echocardiogram showed normal left ventricular size and an ejection fraction of 0.60. It also revealed 2 echodense structures in the left ventricle: one that obliterated the apex, and another in the basal lateral wall (Fig. 2). Pulsed-wave and tissue-Doppler echocardiography showed a normal diastolic filling pattern with no mitral regurgitation. Cardiovascular magnetic resonance was contraindicated due to the pregnancy.

The eosinophilia, emboli, and cardiac findings led us to suspect HES. The patient was started on a heparin drip, and a hematologist was consulted. A bone marrow examination with genetic analysis was recommended to confirm and characterize the syndrome. The patient was started on 40 mg/d of prednisone, and the eosinophilia resolved. On hospital day 3, she developed worsening thrombocytopenia. Heparin-induced platelet aggregation and serotonin release assays were positive, and the diagnosis was heparin-induced thrombocytopenia. The therapy was switched to argatroban, and the thrombocytopenia resolved.

Investigation into the HES revealed no secondary causes, including medications, allergies, asthma, parasitic infections, malignancy, or collagen vascular diseases. The bone marrow examination disclosed increased eosinophils (32%). There was no increase in blast cells on flow cytometry or clonal abnormalities on cytogenetic analysis to suggest acute leukemia. Genetic studies, including that for FIP1L1-PDGFRα or rearrangement, were negative. These findings confirmed the diagnosis of HES. Prednisone was slowly tapered and anticoagulant therapy was continued. The patient was discharged from the hospital after 15 days with instructions to take
fondaparinux (7.5 mg/d) and prednisone (20 mg/d) and to follow up with our cardiology, hematology, and high-risk obstetrics departments. Upon examination 2 weeks later, she was doing well. An echocardiogram showed near-resolution of the echodense structures (Fig. 3), and the pregnancy was viable.

Our neurology service retrospectively concluded that the transient vision loss and splinter hemorrhages in 2007 were probably sequelae of HES and not of multiple sclerosis. In June 2010, the patient delivered a healthy baby girl. The patient’s ongoing daily medical regimen included warfarin and 10 mg of prednisone.

Discussion

Cardiac manifestations contribute to most of the deaths that are associated with HES. The pathogenesis of cardiac involvement is characterized by an acute necrotic stage, an intermediate thrombotic stage, and a final fibrotic stage. The acute necrotic stage involves eosinophilic infiltration of the endocardium and the myocardium, followed by endocardial and myocardial necrosis caused by eosinophilic degranulation and the release of toxic proteins. Granulomas and microabscesses can also form. Typically, this stage is clinically silent, although some investigators have reported finding conjunctival and subungual splinter hemorrhages.

In the intermediate stage, thrombi form along the injured endocardium. Thrombi can involve both of the ventricles, subvalvular regions, and ventricular outflow tracts. Echocardiography and cardiovascular magnetic resonance are ideal methods by which to identify thrombi. Major sequelae of intracardiac thrombi include pulmonary emboli, limb or cutaneous thromboemboli, intra-abdominal emboli, and embolic strokes or transient ischemic events.

The final stage involves scarring of the heart due to fibrous replacement of the endocardial and myocardial tissue. The fibrosis can lead to impaired diastolic function and result in severe restrictive cardiomyopathy. Some patients also present with progressive valvular incompetence from thickening and fibrosis of the chordae tendineae or valve leaflets.

Our pregnant patient presented with HES complicated by embolization and cardiac involvement. Although the combination of HES and cardiac disease is well described in the medical literature, very few case reports discuss HES in pregnant patients. To the best of our knowledge, ours is the 1st report of pregnancy complicated by HES with cardiac involvement.

The pharmacologic treatment of HES includes either glucocorticoids or imatinib mesylate (a tyrosine kinase inhibitor). The choice of initial agent depends on the presence or absence of the FIP1L1-PDGFRα fusion gene. Patients with FIP1L1-PDGFRα-positive disease have had effective remission with imatinib mesylate. The goals of treatment are to reduce the signs and symptoms of eosinophilic disease and to maintain the eosinophil count within normal range.

This case highlights unresolved questions about HES, including the possible need for lifetime anticoagulation, the risk of repeat thrombus development, the duration of tapered steroidal therapy, and the potential risks to a fetus.

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References