

Hypereosinophilic syndrome with characteristic left ventricular thrombus demonstrated by contrast echocardiography

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Hypereosinophilic syndrome (HES) is a rare condition characterised by idiopathic eosinophilia with organ system involvement. The condition is far more common in males, with a typical onset in the third to sixth decade. Cardiac damage may result in the formation of a characteristic apical thrombus readily visualised on two-dimensional echocardiography. Cardiac involvement portends a less favourable prognosis as it can be complicated by acute embolic events and progressive development of restrictive cardiomyopathy, valvular dysfunction, and heart failure. In this case report, we describe a middle-aged gentleman with HES and characteristic apical thrombus identified on contrast echocardiography. Although the use of contrast agents for assessment of left ventricular thrombus is documented in the literature,¹ this case illustrates the application of contrast echocardiography in the evaluation of eosinophilia. (*Neth Heart J* 2009;17:169-70.)

Keywords: left ventricular thrombus, hypereosinophilic syndrome, contrast echocardiography

A 58-year-old man with a history of coronary artery disease, prostate cancer, and asthma presented with a three-week history of refractory constitutional symptoms that progressed to chest pain. He was hospitalised for further workup and found to have elevated cardiac biomarkers, positive D-dimer, and an eosinophilic leucocytosis. Coronary angiogram showed

moderate left anterior descending artery stenosis proximal to an existing stent. Medical management was pursued due to the patient's systemic illness. The patient proceeded to develop confusion with a non-blanching petechial rash of the face, upper chest, and back prompting magnetic resonance imaging (MRI) of the brain and skin biopsy. MRI revealed numerous lesions suspicious for vasculitis or stroke, and skin biopsy was remarkable for hypereosinophilia. Subsequent extensive infectious disease workup was unremarkable for bacterial, fungal, viral, and parasitic aetiologies. Bone marrow biopsy confirmed hypercellularity and eosinophilia but was otherwise non-diagnostic. A trial of high-dose intravenous corticosteroids resulted in mild clinical improvement, and the patient was transferred to a tertiary care centre for further evaluation.

Transthoracic echocardiography with contrast (LUMINITY (R); Bristol-Myers Squibb, N. Billerica, MA) was performed which showed a layered apical left ventricular thrombus without mobile elements consistent with HES (figure 1A and B) in addition to a restrictive left ventricular diastolic filling pattern (grade 3/4) and moderate mitral regurgitation. The evidence of multiple organ system involvement, characteristic echocardiographic findings, and unrevealing eosinophilia workup was consistent with HES. Treatment with intravenous corticosteroids was continued.

Repeat MRI of the brain showed multiple areas of embolic infarction. Anticoagulation was initiated with intravenous heparin, and antiplatelet therapy with aspirin and clopidogrel was continued due to the findings on recent coronary angiography. Several hours after starting anticoagulation, the patient reported worsening back pain. Clinical assessment revealed sinus tachycardia, fluctuating blood pressure, and significant decrease in haemoglobin. Computed tomography of the abdomen revealed retroperitoneal haemorrhage, which prompted reversal of anticoagulation and empiric embolisation of the suspected culprit arteries. Over the next several days, the patient's mental status continued to decline, and repeat brain imaging identified multiple new infarctions. In view of the patient's deteriorating condition, life-sustaining therapies were withdrawn.

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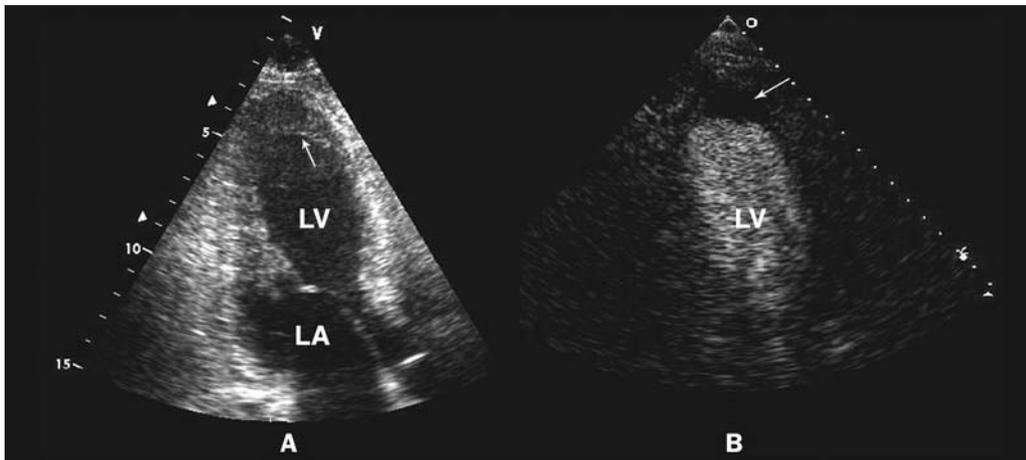


Figure 1. A) Non-contrast two-dimensional transthoracic echocardiogram revealing apical left ventricular thrombus (arrow). B) The addition of LUMINITY (R) contrast clearly defines the borders of the layered left ventricular thrombus (arrow) and confirms absence of mobile elements. LV=left ventricle, LA=left atrium.

Discussion

HES is defined by three criteria: 1) sustained eosinophilia ($>1500/\mu\text{l}$) for six months, 2) absence of other aetiology (e.g. parasitic infection, allergy, eosinophilic pneumonia), and 3) evidence of organ system involvement.² The syndrome is more common in men compared with women (9:1), and the typical age at presentation is 20 to 50 years of age.³ Initial presentation can be quite variable ranging from flu-like symptoms to sudden cardiac or neurological complications. Cardiac complications may evolve through three stages: necrosis, thrombosis, and fibrosis. The initial necrotic stage consists of eosinophilic infiltration of the endocardium and myocardium with subsequent eosinophil degranulation.⁴ Cardiac findings may be minimal at this stage, and imaging with echocardiography and angiography are often unrevealing. After several weeks, the thrombotic stage arises as thrombi form along the damaged ventricular endocardium with the potential to embolise systemically. Finally, the damaged endomyocardium undergoes fibrosis often resulting in valvular regurgitation and restrictive cardiomyopathy.³ Depending on the stage of the disease, two-dimensional echocardiography may visualise a layered intracardiac thrombus with varying degrees of increased endomyocardial echogenicity representing fibrosis. Prognosis of HES is variable depending on timing of diagnosis and extent of disease. Cardiac involvement is recognised as a major cause of morbidity and mortality in HES.³

Recently, a deletion at chromosome 4q12, resulting in the fusion of the FIP1L1 and PDGFRA genes (FIP1L1-PDGFR α), has been shown to be associated with clinical HES.⁵ The protein product of the altered gene is an activated tyrosine kinase that transforms haematopoietic cells and can be inhibited by imatinib. Of note, a study of clinicopathological correlation of 89 consecutive patients with eosinophilia demonstrated that essentially all FIP1L1-PDGFR α cases were histologically classified as systemic mastocytosis⁶ and the condition may be more appropriately labelled systemic mastocytosis-chronic eosinophilic leukaemia.⁷ Our

patient was tested for the gene abnormality; however, results were within normal limits. Imatinib is the preferred therapy in FIP1L1-PDGFR α patients even in the absence of symptoms for prevention of cardiovascular complications. Prednisone (1 mg/kg per day) is recommended as at least part of the initial treatment regimen for HES patients with cardiac involvement. Combination therapy with hydroxyurea (500 mg twice daily) may be considered as well.⁷

Conclusion

This case report demonstrates the characteristic apical thrombus of hypereosinophilia using contrast echocardiography. Due to potential systemic thromboembolisation as well as development of restrictive cardiomyopathy and valvular regurgitation, cardiac involvement is recognised as a major cause of morbidity and mortality in HES. In certain cases of HES, a genetic abnormality has been identified that results in production of an activated tyrosine kinase that can be inhibited by imatinib. Prednisone is recommended for treatment of HES patients with cardiac involvement. ■

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