A rare case of eosinophilia-induced endomyocardial fibrosis

Introduction

Eosinophilia-induced cardiomyopathy is rare in the western world. This article describes a case in which this eosinophilia was caused by an equally unusual T-cell lymphoblastic lymphoma.

Discussion

Eosinophilia usually occurs in response to infection (predominantly parasitic or fungal), autoimmune conditions (i.e. Churg–Strauss syndrome) or malignancy. Less frequently (<1% of cases) eosinophilia presents without an obvious trigger (idiopathic eosinophilia); a condition predominantly affecting males (Rothenberg, 1998).

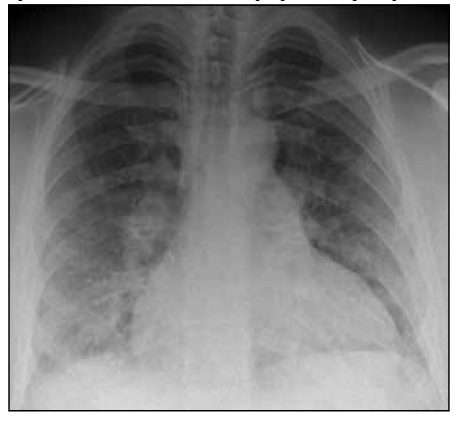
A feature of this case was eosinophilia associated with T-cell lymphoblastic lymphoma – an exceptionally rare condition. The eosinophils infiltrate organs, commonly including the heart (33–75% of cases) and bone marrow (Parillo et al, 1979; Fazel et al, 2009). Cardiac involvement is a major cause of mortality (Parillo et al, 1979).

Loeffler first described eosinophilic endomyocarditis in 1936. Eosinophils infiltrate the myocardium causing inflammation and necrosis (Brito-Babapulle, 2003; Leiferman and Gleich, 2004), which may be demonstrated by late gadolinium enhancement on magnetic resonance imaging. Thrombus frequently forms over fibrosed endocardium, providing a reservoir for embolic phenomena. With time, myocardium is replaced with scar tissue, leading to a restrictive cardiomyopathy. Valvular abnormalities occur as the chordae become less mobile with resultant valve incompetence. The echo, Doppler and magnetic resonance imaging are consistent with a restrictive cardiomyopathy. Despite not performing an endomyocardial biopsy, it is highly probable that the cardiomyopathy is caused by this hypereosinophilic syndrome.

Conclusions

These findings confirmed a diagnosis of myeloid and lymphoid neoplasia with eosinophilia, and abnormalities of PDGFRA, by the World Health Organization classification (Swerdlow et al, 2008). The FIP1L1-PDGFR rearrangement is formed as a result of a cryptic deletion on chromosome 4q12;

Figure 1. Chest radiograph showing an enlarged heart and widespread bilateral interstitial opacities and bilateral hilar lymphadenopathy.



Dr G Rosser *is Specialist Registrar,* **Dr SW Dubrey** *is Consultant Cardiologist and* **Dr MT Dahdal** *is Associate Specialist in the Department of Cardiology, Hillingdon Hospital, Uxbridge, Middlesex UB8 3NN,* **Dr J Wong** *is Consultant Radiologist in the Department of Radiology, Harefield Hospital, Harefield, Middlesex,* **Dr R Grocott-Mason** *is Consultant Cardiologist in the Department of Cardiology and* **Dr K Patel** *is Consultant Haematologist in the Department of Haematology, Hillingdon Hospital, Uxbridge, Middlesex*

Correspondence to: Dr SW Dubrey (simon.dubrey@thh.nhs.uk)

Case Report

A 36-year-old man gave a 3-month history of shortness of breath and ankle swelling. Initial investigations revealed a haemoglobin of 10.1 g/litre, white cell count of 64.1x10^9/litre, eosinophils 16.4x10^9/litre (normal range 0–0.5x10^9/litre) and platelet level of 158x10^9/litre. His serum calcium level was normal at 2.08 mmol/litre as were renal, liver and thyroid function tests.

He had no past medical or family history of significance, took no medication or illicit substances and exercised regularly at a gym. He smoked occasionally and drank 14 units of alcohol/week.

On examination he was dyspnoeic at rest, pulse 92 beats/minute and blood pressure 115/58 mmHg. The heart sounds were normal. The jugular venous pressure was not elevated but peripheral oedema was significant to the knees. The spleen was palpable at 4 cm below the costal margin and lymph nodes were palpable in both groins, left axilla and submandibular region.

A chest radiograph showed bilateral interstitial shadowing and hilar lymphadenopathy (*Figure 1*). A computed tomographic scan of the chest, abdomen and pelvis revealed widespread lymphadenopathy, pulmonary infiltrates and splenomegaly. Blood tests were negative for HIV, cytomegalovirus and hepatitis. Echocardiography revealed a dilated left ventricle of globular appearance (*Figure 2*), with mildly impaired systolic function and reduced long axis function. There was apical hypertrophy and an impression of thrombus at the apex. Significant diastolic dysfunction was supported by a dilated left atrium (51 mm) and restrictive features on Doppler mitral inflow pattern (*Figure 2*). Moderate mitral incompetence was also present. A cardiac magnetic resonance image scan showed dilated ventricles and a globally hypokinetic left ventricle. There was delayed enhancement with gadolinium at the left ventricular apex, consistent with endomyocardial fibrosis (*Figure 3*).

Losartan and anticoagulation with warfarin were commenced, with low molecular weight heparin overlap therapy.

A bone marrow biopsy was performed which was consistent with a myeloproliferative disorder. Fluorescent in-situ hybridization analysis revealed the FIP1L1-PDGFR (Fip1-like1 - platelet-derived growth factor receptor alpha) fusion gene rearrangement. An axillary lymph node biopsy revealed a diagnosis of T-cell lymphoblastic lymphoma. Treatment was commenced with imatinib mesilate at 400 mg orally daily.

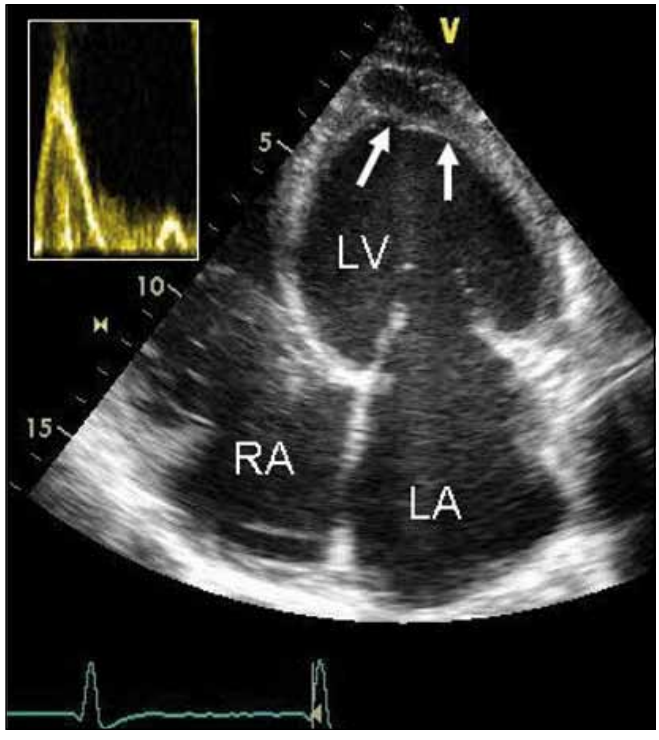


Figure 2. Transthoracic echocardiogram. Four chamber view showing a globular looking left ventricle (LV) with the suggestion of a rim of apical thrombus (white arrows). Doppler image shows a restrictive ventricular inflow pattern with an E:A ratio of 3.5. LA = left atrium; RA = right atrium.

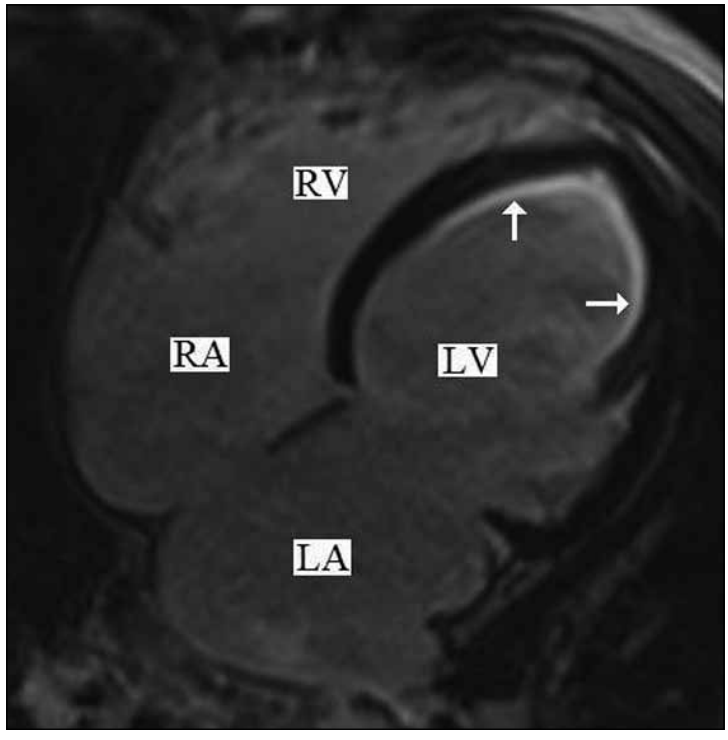


Figure 3. Cardiac magnetic resonance imaging scan showing delayed gadolinium enhancement in an apical endomyocardial distribution (white arrows). Bi-atrial dilatation was marked. LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle.

this results in the formation of a fusion gene encoding a constitutively active tyrosine kinase. Treatment with imatinib mesylate, an orally active tyrosine kinase inhibitor, developed as a treatment for chronic myeloid leukaemia, has shown extremely encouraging results in the treatment of this rare disorder (Gleich et al, 2002). BJHM

Brito-Babapulle F (2003) The eosinophilias, including the idiopathic hypereosinophilic syndrome. *Br J Haematol* **121:** 203–23

Fazel R, Dhaliwal G, Saint S et al (2009) A Red Flag. *N Engl J Med* **360:** 2005–10

Gleich GJ, Leiferman KM, Pardanani A et al (2002) Treatment of hypereosinophilic syndrome with imatinib mesilate. *Lancet* **359:** 1577–8

Leiferman KM, Gleich GJ (2004) Hypereosinophilic syndrome: case presentation and update. *J Allergy Clin Immunol* **113:** 50–8

Parrillo JE, Borer JS, Henry WL et al (1979) The cardiovascular manifestations of the hypereosinophilic syndrome: prospective study of 26 patients, with review of the literature. *Am J Med* **67:** 572–82

Rothenberg ME (1998) Eosinophilia. *N Engl J Med* **338:** 1592–600

Swerdlow SH, Campo E, Harris NL et al (2008) *WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues* 4th edn. IARC Press, Lyon, France

LEARNING POINTS

- Eosinophilia may occasionally be associated with a T-cell lymphoblastic leukaemia.
- Genetic analysis confirmed a FIP1Li-PDGFR (fip1-Like 1-platelet-derived growth factor receptor alpha) fusion gene rearrangement, thus confirming a myelodysplastic syndrome.
- Confirmation of a haematological aetiology in this case was useful in excluding a reactive autoimmune condition such as Churg–Strauss syndrome.
- Anticoagulation is important because of the propensity for thrombus to form over an immobile and fibrosed endocardium.