

# A case report of Löffler endocarditis in idiopathic hypereosinophilic syndrome: recovery is possible

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## Introduction

Hypereosinophilic syndrome (HES) is a myeloproliferative disorder characterized by persistent eosinophilia that is associated with damage to multiple organs.

## Case Presentation

Herein, we describe a case of left ventricular (LV) Löffler endocarditis on top of idiopathic HES leading to inflow and outflow obstruction. The posterior mitral leaflet was involved in the fibrotic process leading to severe mitral valve regurgitation. There was a mural thrombus in the left ventricle, which resulted in thrombo-embolic complications in the form of lower limb ischaemia. The patient was treated with high-dose corticosteroids and anticoagulants with significant improvement of his cardiac condition.

## Discussion

In patients with persistent hypereosinophilia, thorough workup is recommended to identify any possible primary cause and detect associated end-organ damage. Treatment should be started as early as possible after establishing the diagnosis to reduce morbidity and prevent complications. Corticosteroids are the first-line therapy that usually cause a rapid reduction in the level of the eosinophilia and must be started promptly if cardiac involvement is present to attain rapid reduction in the eosinophil level and reverse the cardiac damage.

## Keywords

Hypereosinophilic syndrome • Löffler endocarditis • Endomyocardial fibrosis

## Learning points

- In patients with persistent hypereosinophilia, thorough workup is recommended to identify any possible primary cause and detect associated end-organ damage.
- Treatment should be started as early as possible after establishing the diagnosis to reduce morbidity and prevent complications.
- Corticosteroids are the first-line therapy in hypereosinophilic syndrome and should be started immediately if cardiac complications are present to attain rapid reduction in the eosinophil level and reverse the cardiac damage.

## Introduction

Hypereosinophilic syndrome (HES) is a myeloproliferative disorder (MPD) characterized by persistent eosinophilia that is associated with damage to multiple organs.<sup>1–5</sup>

Hypereosinophilic syndrome is a diagnosis of exclusion when secondary and clonal causes of eosinophilia are excluded. Three features are required for a diagnosis of HES<sup>2</sup>: (i) a sustained absolute eosinophil count >1500/ $\mu$ L, which persists for longer than 6 months, (ii) no identifiable aetiology for eosinophilia, and (iii) signs and symptoms of organ involvement.

The most serious complication of HES is cardiac involvement, which can result in myocardial fibrosis, chronic heart failure, and death.

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## Timeline

Time	Events
Six months before presentation	Start of patient complaint: effort intolerance, loss of weight and intermittent fever
Two months before presentation	Additional symptoms: recurrent transient ischaemic attacks and left lower limb (LL) intermittent claudications Complete blood picture (CBC): mild leucocytosis with persistent hypereosinophilia on repeated measurements
First week of hospital admission	Investigations to diagnose the cause of hypereosinophilia and detect end-organ damage including echocardiography and cardiac magnetic resonance imaging (CMR), which revealed cardiac left ventricular (LV) Löffler endocarditis. Arterial Duplex and multislice computed tomography angiography of LLs showed arterial thrombo-embolism.
One week after admission	Start of corticosteroid therapy + antithrombotic drugs
One month after starting corticosteroids	CBC showed dramatic fall in eosinophils from 42% to 4.5%
Monthly follow-up echocardiography	Showed significant regression of the endomyocardial fibrotic process
Two months after starting corticosteroid therapy	Follow-up CMR revealed resolution of LV subendocardial wall thickening

## Case presentation

A 36-year-old male patient with no previous medical history presented to our hospital complaining of effort intolerance, loss of weight, and intermittent fever for 6 months; he also started to suffer from transient ischaemic attacks and left lower limb (LL) intermittent claudications for 2 months.

Physical examination revealed stable vital signs. Cardiac examination revealed a muffled S1 on apex with a harsh pansystolic murmur and an accentuated P2 over the pulmonary area. Extremities revealed absent pulsations of the dorsalis pedis, posterior tibial, and popliteal arteries on the left LL. However, the limb was warm with no ischaemic skin changes and with normal motor function. Laboratory investigations done over the past few months were all unremarkable, except for his complete blood picture (CBC) that revealed mild leucocytosis with persistent hypereosinophilia on repeated measurements. So, the patient was admitted for further investigations.

His first CBC in the hospital again revealed white blood cell count of  $11.24 \times 10^3$  cells/ $\mu$ L (4.00–11.00) and an absolute eosinophilic count of 4700 cells/ $\mu$ L (up to 0.6), accounting for about 42% of total leucocytic count, but his peripheral blood film revealed no abnormal cell types. Repeated stool and urine analyses were normal. His resting

electrocardiogram showed normal sinus rhythm of 80 b.p.m. with no significant changes. Computed tomography (CT) of the chest revealed few mediastinal lymph nodes, from which needle aspiration was taken and its pathological examination revealed mild inflammatory reaction with no neoplasia or specific granulomatous cells. Computed tomography of the abdomen revealed mild hepatosplenomegaly.

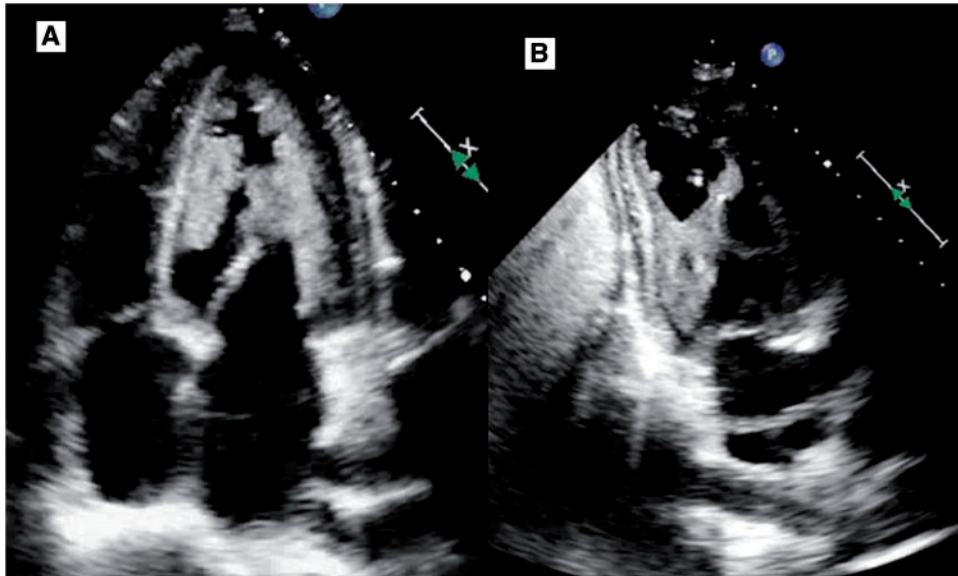
Arterial Duplex of the left LL revealed a thrombus in the left common femoral artery with distal monophasic flow. Multislice CT angiography of both LLs revealed partial thrombosis of the right common femoral artery with normal distal flow, while the left common femoral artery was seen totally occluded by a thrombus just proximal to its bifurcation with extension of thrombosis to superficial femoral artery that was attenuated distal to the occluded segment.

Transthoracic echocardiography (TTE) revealed marked thickening and fibrosis of left ventricular (LV) endocardium with heavy involvement of mitral subvalvular apparatus (*Figure 1A and B*), resulting in inflow and outflow obstruction with Doppler maximal LV outflow tract velocity of 3.8 m/s and peak systolic gradient of 58 mmHg (*Figure 2A*). The posterior mitral leaflet was completely embedded in the fibrotic tissue with poor coaptation of mitral valve leaflets causing severe mitral regurgitation (*Figure 2B*). The left atrium was dilated, but both right and left ventricles had normal size and systolic function. There was also mild-to-moderate tricuspid valve regurgitation with peak systolic gradient of 65 mmHg signifying a resting pulmonary artery systolic pressure (PASP) of 70 mmHg. Cardiac magnetic resonance (CMR) imaging revealed the same echocardiographic findings in addition to subendocardial oedema and late gadolinium enhancement (LGE) at the basal and mid-ventricular lateral walls as well as the thickened subvalvular apparatus of the mitral valve (*Figure 3A and B*). It also revealed an LV mural thrombus that was not visualized on previous TTE.

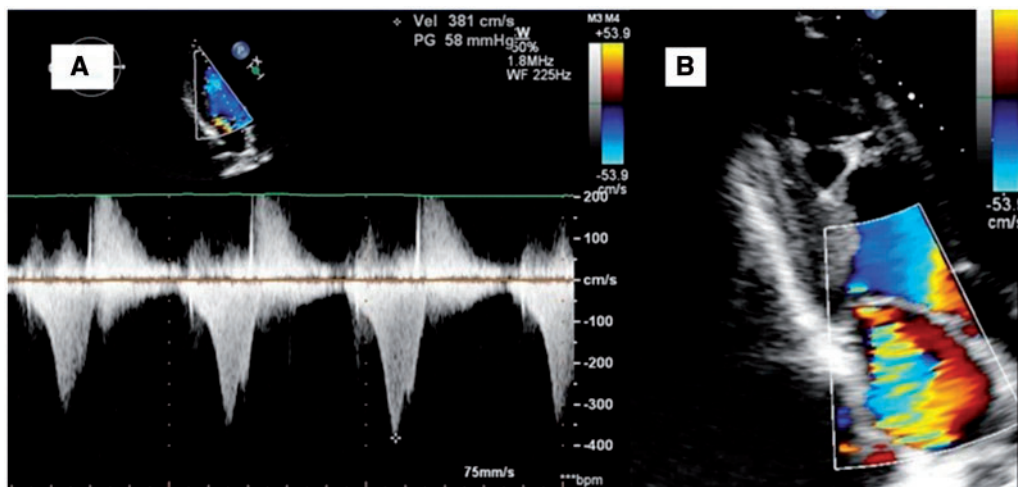
Bone marrow aspiration, cytogenetics, and molecular genetic studies detected no primary cause for hypereosinophilia. So, the patient was diagnosed to have idiopathic HES complicated by LV Löffler endocarditis and peripheral arterial thrombo-embolism.

The patient was treated with high-dose corticosteroid therapy in the form of pulse parenteral steroids, dexamethasone (16 mg) for 3 days, then 8 mg for 5 days, followed by oral prednisone (60 mg/day); patient was also prescribed aspirin (75 mg/day, which was stopped after 3 months), an oral vitamin K antagonist to reach a target international normalized ratio between 2 and 3, and statins.

Regular follow-up of the patient was scheduled to assess response to therapy, his CBC revealed dramatic fall in eosinophils from 42% to 4.5% (normal range 1–6) over 1 month. The patient also reported improvement in his exercise tolerance with no evidence of any new embolic events. Monthly follow-up TTE showed significant regression of the fibrotic process with almost complete relief of the LV mid-cavity obstruction (*Figure 4A and B*). Despite persistence of severe mitral valve regurgitation, LV dimensions remained normal with preserved systolic function. Tricuspid regurgitation regressed and resting PASP decreased from 70 mmHg to 40 mmHg. Follow-up CMR 2 months after the start of therapy revealed resolution of LV subendocardial wall thickening. It also showed regression of oedema and LGE which was limited to a thinner subendocardial layer of LV lateral wall and posteromedial papillary muscle with resolution of the LV thrombus. We started gradual tapering of corticosteroid therapy after 2 months of its



**Figure 1** (A and B) Echocardiographic apical four- and two-chamber views showing marked left ventricular endomyocardial fibrosis causing mid-cavity obstruction.



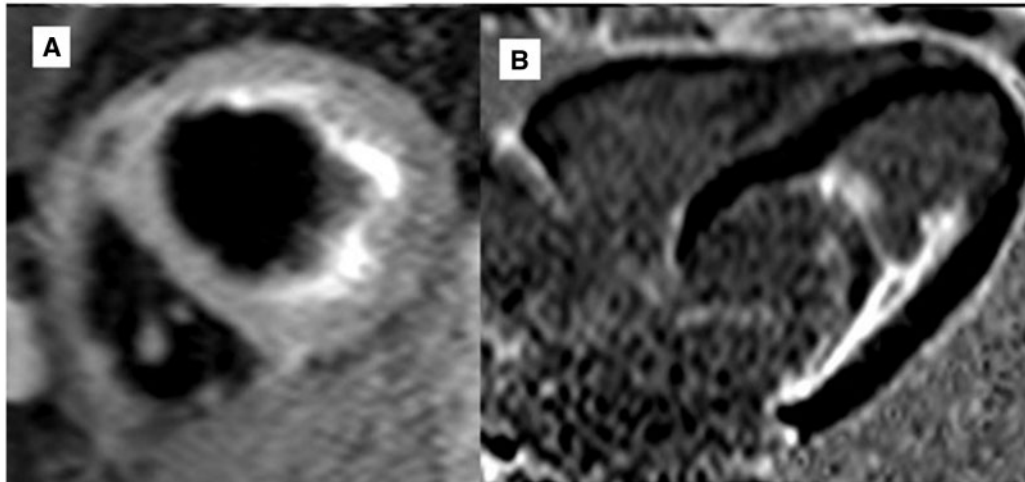
**Figure 2** (A) Continuous-wave Doppler showing dynamic left ventricular outflow tract obstruction. (B) Colour flow Doppler in apical long-axis view showing jet of severe mitral regurgitation.

initiation aiming at reaching the lowest possible maintenance dose and guided by his follow-up echocardiography and laboratory findings. Very gradual tapering was attempted by decreasing the prednisone dose by 10 mg every one and half month initially till reaching 30 mg/day then by 5 mg every one and half month thereafter. The last follow-up of this patient was 10 months after the start of corticosteroid therapy, and we reached a dose of 20 mg/day of prednisone. Further tapering will be intended on subsequent visits.

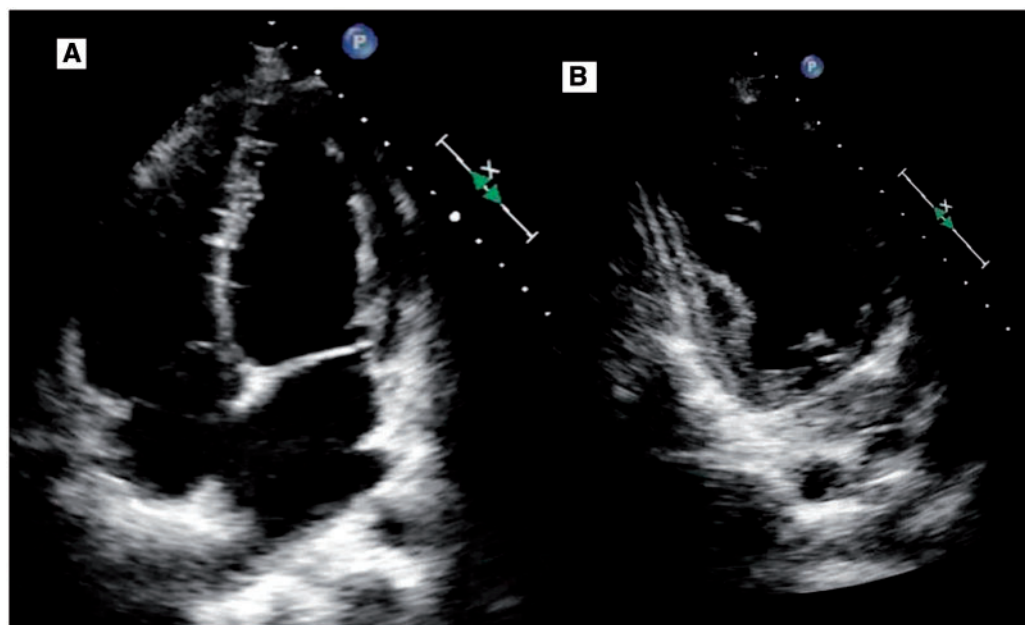
## Discussion

Acquired eosinophilia can be classified into secondary, clonal, and idiopathic categories.<sup>6</sup> Hypereosinophilic syndrome is a diagnosis of exclusion when secondary and clonal causes of eosinophilia are excluded.

Hypereosinophilic syndrome affects mostly men with a peak incidence in the 4th decade of life.<sup>7</sup> Clinical manifestations of HES are heterogeneous, and the presentation can be sudden and dramatic, but



**Figure 3** (A) Cardiac magnetic resonance imaging black blood T2-weighted image short-axis view showing left ventricular subendocardial oedema. (B) Cardiac magnetic resonance delayed enhancement image of four-chamber view showing left ventricular subendocardial late gadolinium enhancement.



**Figure 4** (A and B) Follow-up echocardiographic (2 months after the start of corticosteroid treatment) apical four- and two-chamber view showing significant regression of left ventricular endomyocardial fibrosis.

more frequently, the onset is insidious.<sup>8,9</sup> Virtually any organ system may be involved in HES. The cardiac system is one of the most frequently involved systems, and cardiac complications are a leading cause of mortality. Damage typically occurs in three stages: (i) initial acute necrosis, (ii) thrombotic phase, and (iii) endomyocardial fibrosis.<sup>7</sup>

There are three primary goals for the management of HES: (i) reduction of peripheral and tissue levels of eosinophils, (ii) prevention

of end-organ damage, and (iii) prevention of thrombo-embolic events in patients at risk.<sup>10</sup> Patients without progressive organ system dysfunction typically do not require specific treatment; however, these patients should be monitored closely.<sup>11</sup> Corticosteroids were initially the mainstay of HES treatment and are currently recommended as the first-line therapy.<sup>3</sup> Corticosteroids usually cause a rapid reduction in the level of eosinophilia and must be started promptly if cardiac

involvement is present. About one-third of these cases do not respond to steroids. In such patients, interferon alpha and hydroxyurea are the second-line drugs of choice.<sup>12</sup> For those individuals whose conditions do not respond to first- and second-line therapies, high-dose imatinib is the treatment of choice.<sup>12</sup> Allogenic stem cell transplantation has also been reported to be a potentially curative therapy. It is the ultimate therapeutic measure in case of therapeutic refractoriness or intolerance to available therapies.<sup>13</sup> Our patient showed favourable response to corticosteroid therapy with improvement of his symptoms and reversal of the endomyocardial damage.

## Conclusion

In patients with persistent hypereosinophilia, thorough workup is recommended to identify any possible primary cause and detect associated end-organ damage. Treatment should be started as early as possible after establishing the diagnosis to reduce morbidity and prevent complications. Corticosteroids are the first-line therapy that usually cause a rapid reduction in level of the eosinophilia and must be started promptly if cardiac involvement is present to attain rapid reduction in the eosinophil level and reverse the cardiac damage.

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**Consent:** The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

**Conflict of interest:** none declared.

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