Hypereosinophilic syndrome with isolated Loeffler’s endocarditis: Complete resolution with corticosteroids

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ABSTRACT

Hypereosinophilic syndrome (HES) is classically defined as prolonged, unexplained peripheral eosinophilia in a patient presenting with evidence of end-organ damage. The heart is involved in two forms; endomyocardial fibrosis (Davies disease) and eosinophilic endocarditis (Loffler’s endocarditis). It was first reported in 1968 by Hard and Anderson. Chusid and co-workers formulated a definition with strict criteria for the diagnosis of HES as 1) peripheral blood eosinophilia more than 1500 cells/cu mm for at least six months duration 2) signs, symptoms of end-organ (heart, lungs, gastrointestinal tract, skin, bone-marrow, brain) involvement with eosinophil tissue infiltration/injury 3) exclusion of known secondary causes of eosinophilia. We report a case of hypereosinophilic syndrome with Loffler’s endocarditis, in the absence of endomyocardial fibrosis. The patient presented with a eosinophilic vegetation over the posterior leaflet of the mitral valve. There was complete resolution of the vegetation after two months of corticosteroid therapy.

KEY WORDS: Hypereosinophilic syndrome, Loeffler’s endocarditis, response to steroids

Hypereosinophilic syndrome (HES) is characterized by eosinophilic tissue damage related to the release of basic proteins, neurotoxin, eosinophil cationic protein. Our patient had hematological, cardiac, pleural and bone-marrow involvement. The unique feature was the isolated involvement of the endocardium, without endomyocardial fibrosis (EMF) and the complete resolution of the endocardial eosinophilic infiltration with steroids alone.

Management options include steroids and chemotherapeutic drugs like hydroxyurea, vincristine, 6-mercaptopurine, busulphan and chlorambucil.

Interferon alpha and cyclosporine have also been found to be useful in HES. [1,5]

Case History

A 41-year-old male presented in 2000 with high-grade continuous fever, dry cough, breathlessness for a duration of 10 months. Blood investigations revealed a persistent increase in the eosinophil count in the peripheral blood in the last 10 months with the absolute eosinophil count ranging from 3000-6000 cells/cu mm. His chest X-ray revealed a left-sided pleural effusion. Pleural fluid analysis showed 38% eosinophils. His chest computerized tomography (CT) scan revealed features of pericardial effusion, constrictive pericarditis with thickening of the pericardium > 5 mm, calcification of the pericardium, biaatrial dilatation.

2D-Echo revealed thickened pericardium. He underwent pericardiectomy. The histopathology was reported as non-specific pericarditis, no granulomas. Bone-marrow biopsy revealed hypercellular marrow with predominant eosinophil precursors.

The patient was treated with steroids for one month but was lost to follow-up.

After five years, in 2005, he re-presented with fever, breathlessness. He had a striking peripheral eosinophilia with an absolute eosinophil count of 4800 [30% of 16,000]. 2D-Echo revealed a 2.5 cm × 1.5 cm pedunculated mass attached to the atrial aspect of the posterior mitral valve leaflet (PML) [Figure 1]. This showed heterogeneous echogenicity and a mobility independent of the leaflet. These features were highly suggestive of vegetation. Four consecutive blood cultures were negative, ruling out infective endocarditis. The patient was started on oral steroids (prednisolone 40 mg daily) and oral anticoagulation with warfarin 5 mg daily to prevent any embolic episodes. He was also started on amoxicillin and clavulanic acid for seven days. Since all his four blood cultures were negative, antibiotics were stopped. After two months of treatment, on follow-up, the absolute eosinophil count was down to 500 cells/cu mm and the 2D-Echo showed complete resolution of the vegetation over the mitral valve [Figure 2]. The steroid dose was tapered gradually and warfarin was stopped.
At follow-up, one year later, he has a normal eosinophil count on a maintenance dose of 2.5 mg daily of prednisolone. The mitral valve remains normal and free of any vegetation.

**Discussion**

Hypereosinophilic syndrome is a group of leukoproliferative disorders with overproduction of eosinophils resulting in end-organ damage.\(^2\)

The recognized causes of eosinophilia are allergy and asthma, infections like parasitic, fungal, interstitial lung disease like histiocytosis X, sarcoidosis, collagen vascular diseases, malignancy, including non-Hodgkin’s lymphoma, myeloblastic leukemia, non-small cell carcinoma of the lung, pulmonary eosinophilic syndromes like tropical pulmonary eosinophilia, Churg Strauss syndrome, and chronic eosinophilic pneumonia.

Hypereosinophilic syndrome occurs at any age, though most cases occur between 20-50 years of age.\(^3\)

Cardiac involvement occurs in more than 60% of patients with HES; the commonest finding is EMF. Vegetations may involve atrio-ventricular valve leaflets. Progressive scarring, especially on the posterior mitral valve leaflet restricts valve movement.\(^4,5\)

In our case the patient was diagnosed with HES, according to Chusid’s criteria. Bone marrow analysis confirmed the diagnosis. The patient had a eosinophilic pleural effusion, presumable eosinophilic pericardial effusion, bone-marrow involvement and a eosinophilic vegetation on the mitral valve [Loeffler’s endocarditis]. Initial presentation with constrictive pericarditis in HES has never been reported and is not clear. Histopathology revealed nonspecific pericarditis, without eosinophil.

There was, however, no echocardiographic evidence of associated EMF. The Echo findings were more suggestive of vegetation than a thrombus because a thrombus has low echogenicity, with a central lucency. Thrombus does not have independent mobility (except a ball valve thrombus in mitral stenosis). The commonest location of thrombus is left ventricular apex in patients with apical infarction, left atrial appendage in mitral stenosis with atrial fibrillation. Valve leaflets are mobile structures, and do not ever attract thrombus. The echocardiographic difference between vegetation and thrombus being uncertain, the mass is probably a pile of thrombus and eosinophils as described in the papers of Hendren.\(^6\)

He responded dramatically to steroids with complete resolution of the vegetation.

Symptomatic patient with EMF should be treated with steroid therapy, prednisolone in a dose of 1 mg/kg/day until clinical improvement occurs, after which the dose should be tapered gradually.\(^5\) Symptomatic patients non-responsive to steroids, should be offered chemotherapeutic agents. The common chemotherapeutic drugs used include hydroxyurea, vincristine, 6-mercaptopurine, busulphan and chlorambucil. Haematological remission can be achieved and maintained with vincristine alone or in combination with 6-mercaptopurine and 6-thioguanine. Interferon alpha and cyclosporine have also been found to be useful in HES.\(^1,7\)

Although mortality is high, aggressive medical and surgical treatment can result in significant clinical improvement. The commonest cause of mortality in HES is damage to the heart and central nervous system, by eosinophilic infiltration. Endocardial resection in endocardial fibrosis and valve replacement in severe regurgitation of the mitral and tricuspid valve can be lifesaving.\(^9\)

Chusid et al.,\(^2\) reported an average survival of nine months, a three-year survival of 12%. Spry et al.,\(^8\) suggested that patients with HES should be divided into three subgroups: predominant pulmonary involvement, which is steroid-responsive, with the best prognosis; predominant cardiac or central nervous system involvement with a bad prognosis; and eosinophilic leukemia with cytogenic abnormalities of the eosinophils. This third group is rare and carries the worst prognosis. There have been recent case reports\(^9-11\) on HES and Loffler’s endomyocarditis.
Our case was a confirmed case of HES [by Chusid’s criteria and bone marrow analysis]. There were two features of distinction that make this case worthy of reporting. Isolated eosinophilic vegetations in the absence of EMF are extremely rare in HES. Within two months of steroid therapy there was echocardiographic evidence of complete resolution of the previously seen vegetation without any residual valve scarring or regurgitation.

Conclusions
This patient had hematological, cardiac, pleural, bone-marrow involvement. The unique feature was the isolated involvement of the endocardium, without EMF and the complete resolution of the endocardial eosinophilic infiltration with steroids alone.

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