Case Reports

Idiopathic Hypereosinophilic Syndrome - Unusal presentation

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A case of idiopathic hypereosinophilic syndrome who had an unusual presentation in the form of pericardial effusion is being presented here. The child initially responded to corticosteroids but could not maintain normal eosinophil counts on tapering of steroids. Therefore he was put on hydroxyurea and low dose of steroids with regular monitoring of absolute eosinophil counts.

Key words: *Hypereosinophilic syndrome, Hydroxyurea*

Idiopathic Hypereosinophilic Syndrome (HES) is a rare condition with organ damage secondary to high eosinophilic counts and marked eosinophilic tissue infiltration. The presentation is generally in the adult age group. We report a child with this syndrome who along with the usual features of the syndrome also had the unusual presentation of pericardial effusion, which resolved after treatment.

Case Report

An 11-year-old boy was admitted with complaints of low-grade continuous fever, along with non productive, non spasmodic cough, bilateral diffuse chest pain increasing on coughing, generalized weakness and dyspnea for a period of 2 months. There was no history of any rash, ear discharge, burning micturition, orthopnea, paroxysmal nocturnal dyspnea, wheezing, hematuria, anuria or dysuria. There was no history of palpitation or swelling in any part of the body, jaundice or any bleeding tendencies, joint pains, limitation of movements or any history of worm infestation or allergic disorders. There was no history of contact with a tuberculous patient. The child was not consuming any medications and was on a vegetarian diet. There was no history of a similar illness in the family.

At admission, the child was sick with a pulse rate of 116/min, respiratory rate of 44/min with subcostal and intercostal retractions and a blood pressure of 104/80 mmHg. He had raised jugular venous pressure. There was no pallor, icterus, cyanosis, clubbing, edema or significant lymphadenopathy. The anthropometry was normal. Examination of the chest revealed diminished chest excursions with a dull percussion note at the lung bases, auscultation revealed bilateral decreased air entery in the lower zones. Cardiac apex was at the left 5th intercostal space just outside the mid clavicular line with distant heart sounds, though both heart sounds were normal and no murmurs could be heard. Liver was palpable 2 cm below the costal margin in the mid clavicular line. It was non tender, soft in consistency with a smooth surface. Spleen was palpable 2 cm below the costal margin in the mid clavicular line, it was non tender, firm in consistency. Fundus examination was

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Manuscript received: January 24, 2003;
Initial review completed: March 26, 2003;
Revision accepted: May 1, 2003.

normal. Rest of the systemic examination was within normal limits.

Investigations revealed: Hb: 12gm%, TLC: 39,600/mm^3, DLC: Polymorphs 14%, Lymphocytes 8%, Eosinophils 78%, Absolute eosinophilic count (AEC) of 30,800/mm^3 and a platelet count of 2.0 lac/mm^3. ESR was 90 mm/1st hour. Peripheral blood smear examination showed marked eosinophilia with normal morphology of other cells. *X*-ray chest revealed bilateral pleural effusion and bilateral perihilar opacities with pericardial effusion; confirmed by echocardiography. Pleural tap showed 9,600 eosinophils/mm^3, Gram stain, cultures and staining for Acid Fast Bacilli was negative. Pericardial tap also revealed mainly eosinophils. Bacteriological and fungal cultures of the pericardial fluid were negative. PCR for tuberculosis of the pericardial fluid was also negative. Liver biopsy revealed a normal architecture but marked eosinophic infilteration. SGOT, SGPT, Alkaline Phosphatase, Blood Urea, Serum Creatinine were within normal limits. Mantoux test (administered as 5 Tuberculin Units) was non-reactive. Stool examination was normal. Peripheral smear for malarial parasite was negative. Filarial serology as well as smears were negative. ELISA for Human Immunodeficiency Virus (HIV) was non reactive. Rheumatoid factor and anti-nuclear antibodies were negative. Ultrasound abdomen was within normal limits. Bone marrow examination did not reveal any abnormal cells or parasites however there was preponderance of eosinophils and eosinophilic precursors. Hematological parameters of the parents were normal.

Child was started on albendazole and was given ceftriaxone and ampicillin for a period of 2 weeks but there was no change in the clinical, radiological or pleural tap findings. In view of the persisting eosinophilia he was given a 21 day course of diethylcarbazine (at 6 mg/Kg/day) but still there was no change in clinical, radiological or hematological findings. Repeated stool examinations for ova and cysts were negative for common parasitic infections. Since there was no other cause to attribute to the above findings and with persistence of hypereosinophilia, a diagnosis of Idiopathic Hypereosinophilic Syndrome was made.

The child was subsequently put on prednisolone at 1mg/kg/day and followed up. After 1 week of this therapy, there was clinical improvement with lowering of the absolute eosinophilic count to 1,100/mm^3 and improvement in chest *X*-ray with resolution of pericardial effusion. The child over the next two weeks developed features of severe gastritis (documented on endoscopy) and therefore steroids were tapered. Over the next week the child again had increased eosinophilic counts (AEC 3000/mm^3) and also developed erythematous papulo-nodular swellings allover the body with predominance on the trunk. Skin biopsy revealed marked infiltration of eosinophils. Steroids were reintroduced and within 2 weeks ABC had fallen to 1,000/mm^3. Child remained stable for a period of 6 weeks. There was reduction in hepatosplenomegaly (liver and spleen regressed to 1 cm each below the costal margin). Subsequently, he developed pneumonitis, which was confirmed by a chest *X*-ray and due to which the steroids were tapered. His pneumonitis improved after 2 weeks of IV Ceftazidine, Amikacin and Ampicillin. His AEC again rose, this time to 6,250/mm^3. Steroids were again added but this time eosinophils showed only a marginal reduction in numbers. At this point, hydroxyurea was added and there was reduction in the eosinophilic counts over the next 15 days. Presently, the child is being maintained on low dose steroids (0.5 mg/Kg)

and hydroxyurea (at 20mg/Kg/day). After 2 months of starting hydroxyurea, his AEC is 450/mm^3. He is remaining asymptomatic on this regime and is on regular follow up for the past 6 months.

Discussion

The defining characteristics of this rare entity were first described by Chusid, *et al.*(1) as peripheral blood eosinophilia >1500/μL persisting for more than 6 months; absence of parasitic, allergic, or other causes of eosinophilia; and manifestations of organ involvement or dysfunction. The syndrome is generally seen after the second decade of life with very few reports in the pediatric population. Acute eosinophilic leukemia should be kept in the differential diagnosis. Some of the common causes of hyper-eosinophilia should be ruled out before a diagnosis of Idiopathic Hypereosinophilic Syndrome is made(2).

The clinical presentations include weakness, fatigue, cough, dyspnea, myalgia, angioedema, rashes, fever, rhinitis. The symptomatology of Idiopathic HES is due to the eosinophilic tissue damage related to the release of major basic proteins, eosinophil peroxidase, eosinophil cationic proteins and eosinophil-derived neurotoxins(2-4). Although almost any organ may be involved, the heart, skin, nervous system, lungs, spleen, liver, eyes and the GI tract are typically affected. Cardiac involvement is the most prominent cause of morbidity and mortality(5,6). The course of events of cardiac involvement can be staged as the Acute necrotic stage (5.5 weeks): Presenting as a clinically silent stage with damage to the endocardium and infiltration of the myocardium with eosinophils and histopathologic evidence of myocardial necrosis, eosinophilic degranulation and micro abscesses. This is followed by the thrombotic Stage (10 months) with evidence of thrombosis along the endocardium and valve leaflets. The last stage is the fibrotic stage where there is progressive scarring that may lead to entrapment of the chordae tendinae, causing Mitral or Tricuspid regurgitation, endocardial fibrosis and features of restrictive cardiomyopathy. Mural thrombi provide a source for systemic or pulmonary emboli. At this stage patients often present with dyspnea, chest pain, signs of heart failure or new onset murmurs. Our case also had the unusual presentation of pericardial effusion. Cutaneous manifestations include urticarial lesions, angioedema, purpuric papules and nodules, cutaneous micro thrombi. Neurological manifestations are generally impaired cognition, altered behavior, spasticity and occasionally ataxia, focal deficits from cardiac emboli and peripheral neuropathy. Pulmonary manifestations include a chronic persistent, generally nonproductive cough. Symptoms secondary to emboli, thrombosis and cardiac failure are the other pulmonary presentations. Hepatosplenomegaly, blurring vision and diarrhea are some of the less common presentations. Our patient had hepatosplenomegaly and pulmonary manifestations.

The primary aim of the management is to keep the eosinophilic counts low. Some of the treatment options as summarized by Weller and Bubley(5) are as follows. Patients with no organ dysfunction or symptoms despite high AEC, without defining features of HES need a close 3 to 6 monthly follow up(2,5,7,8). Steroids started at lmg/Kg/day are indicated in the symptomatic patient with subsequent tapering and maintenance as per clinical and laboratory parameters. Those unresponsive to steroids can be given hydroxyurea. Acute reductions in eosinophilic counts can be

brought about by vincristine. The onset of a decrease in blood eosinophilia is within 1 to 3 days. Vincristine treatment may become limited by its neurologic complications. Imatinib mesylate is a promising drug in the treatment of Idiopathic Hypereosinophilic Syndrome with response seen as early as one week after starting treatment, though more data are awaited for its use in the pediatric population(9).

Long term prognosis of patients with Idiopathic HES continues to be rather poor with a 40% reported mortality at 10 years(5). With maintainence of low eosinophilic counts and aggressive medical and surgical treatment (managing thrombo-embolism, mitral or tricuspid valve replacements in severe regurgitation, endocardial resection in marked cardiac fibrosis) significant reduction in morbidity and mortality have been noted.

Contributors: AJ did the literature search and prepared the manuscript. APD conceived the idea, revised the manuscript and will act as the guarantor for the paper. AJ, APD and SS all were involved in the treatment of the patient.

Funding: None.

Competing interests: None stated.

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