Idiopathic Hypereosinophilic Syndrome in a child

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Abstract
The Hypereosinophilic Syndrome, which is characterized by pulmonary infiltrates, cardiomegaly, congestive heart failure and elevated eosinophilic count is a well described but poorly understood entity. We ruled out numerous other causes of eosinophilia. A case of Idiopathic Hypereosinophilic Syndrome is presented here. This patient represents a spectrum of severity and prognosis of some organ dysfunction like damage to the heart and CNS by eosinophilic infiltration. This patient was given chemotherapy without success and died. We detected severe eosinophilic infiltrations in some other organs, as well.

Key words: Idiopathic Hypereosinophilic Syndrome, Chemotherapy, CNS.

Introduction
Idiopathic Hypereosinophilic Syndrome (HES) represents a heterogeneous group of leukoproliferation disorders associated with Eosinophilic count more than 1500 cells/m^3 and persists for at least 6 months unless death intervene. It is a rare disorder in children. The clinical presentation is generally insidious but may be acute with sudden cardiac or neurological complications. We present a child with this uncommon condition.

Report of case:
A 3.5-year old male child presented with complaint of fever, weakness, non-productive, non-spasmodic cough, tachypnea for 3 months, arthralgia and arthritis for 3 days. There were no history of dyspnea or wheezing, jaundice, skin rash, hematuria, weight loss, worm infestation, bronchial asthma, allergic disorder, pica, bleeding tendencies and palpitation or swelling in any part of the body. Growth and development were normal, the child was treated in Yazd and became asymptomatic. The high grade fever, abdominal distension and tachypnea recurred within a week and then child was referred to Tehran.

At admission, the child looked ill, with a pulse rate of 120/min and respiratory rate of 54/min. He looked pale. There was no lymphadenopathy, joint pain, no edema over feet or other skin lesions. Auscultation of chest revealed bilateral crepitations and breathing sound in lower part of right lobe was decreased. Systolic
murmur grade III/VI at tricuspid site was detected. The spleen was palpable 3 cm below the left costal margin and liver 4 cm below the right costal margin in the midclavicular line. The hepatic span was 9 cm, and the systemic examination was normal.

Investigations revealed: Hb 7.7 g/dl, WBC 26,800 cells/mm³ (Polymorph 10%, lymphocytes 12%, eosinophils 71%) and platelet count 265 x 10⁵/mm³. MCV=85 fl and ESR was 12 mm at the end of one hour. Peripheral blood smear examination showed marked eosinophilia with absolute eosinophilic count (AEC) of 1500/mm³.

The bone marrow examination showed myeloid hyperplasia with increased eosinophilia and its precursors. Megakaryocyte and erythroid series are normal. No abnormal cells or parasites were seen. Chest radiography revealed bilateral interstitial infiltrations, there was no biochemical evidence of hepatic or renal dysfunction (ALT 13, AST 12, BUN 23 mg/dl, creatine 0.9 mg/dl). The Mantoux tuberculin skin test result was negative. Ultrasound examination of the abdomen revealed hepatosplenomegaly. Serology for fasciola antibody was 1/20. Hydatid antibody 3.8, toxocara was negative and immunoglobulin levels were normal (IgG=1180, IgM=120, IgA=77, IgE=11).

Antinuclear antibodies and complement levels were negative. Echocardiographic examination showed mild cardiomyopathy and mild MR and TR. EP was 50%.

Karyotyping was normal. Hematological parameters of parents were normal. Repeated stool examination for ova and cyst were negative for common parasitic infection since no cause attributable to hypereosinophilia was found. A diagnosis of Idiopathic HES was made. The child was put on prednisolon (2 mg/kg/day) and followed up with cell blood count including PBS (Peripheral Blood Smear).

There was only a partial improvement blood cell count; hydroxyurea was used for reducing white blood cell count. He suddenly expired because of cardiovascular arrest.

Necropsy study showed severe eosinophilic infiltration of both lungs and the liver.

Discussion

A case of HES was first reported in 1968 by Hard and Anderson but no detail was given. Chusid and Co-workers later used restricted definition and criteria for diagnosis of HES as persistent eosinophilia of more than 1500 cells/mm³ for at least 6 months or death before 6 months with signs or symptoms of HES. Lack of evidence for any recognized cause of eosinophilia and signs and symptoms of multiorgan system involvement. Fewer than 30 cases have been reported in children below 12 years of age. The presentation include: Signs and symptoms of multiorgan involvement like weakness, cough, dyspnea, myalgia, rash, fever, mumps and so on. Any organ may be involved. The characteristic feature of HES in tissue damage is related to the release of basic protein, eosinophil peroxidase, cathepsin protein and eosinophil derived neurotoxin.

In NIH series hematological involvement was seen in all, pulmonary in 40% skin in 59%, Neurological in 64%, Splenomegaly in 45%, Hepatomegaly in 35%, cardiovascular in 54% and ocular involvement in 18%. In our case the BM, liver, spleen and lung were involved. This was compatible with other reports.

Myeloproliferative diseases or acute eosinophilic Leukemias are among the differential diagnoses: characteristics of lymphoproliferative include presence of hypogranular, vacuolated eosinohils, presence of Philadelphia chromosome and decreased alkaline phosphatase. Acute eosinophilic leukemia is unlikely in the absence of immature cells in PBS or BM aspirates and with normal myeloid and erythroid series. Acute eosinophilic leukemia is of special concern as a differential diagnosis. The conversion of idiopathic HES to acute leukemia is rare. The pulmonary infiltration with eosinophilia syndrome (PIE) should also be regarded as a
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differential diagnosis, especially where there is a history of recurrent wheezing or dyspnea.

A patient with HES who has no organ dysfunction or symptoms needs no treatment except for a close follow up, in 3 to 5 monthly intervals. The symptomatic patient should be treated with prednisolone therapy until clinical improvement occurs. And then the dosage should be tapered.

Response to steroid therapy was good in 38% of cases (NIH series) a 31% of patients showed a partial response. Symptomatic patients non-responsive to steroids should be offered chemotherapeutic agents.

Common chemotherapeutic drugs use include Hydroxyurea, Vinoreline (VCR), 6 Mercaptopurine (6 MP), busulfan and chlorambucil. Hydroxyurea because of absence of leukemicogenic effect and oral administration is used frequently. Interferon alpha and cyclosporine have also been found to be useful in HES with a response seen as early as one week after starting treatment though more data are required for its use in children population.

Long term prognosis of patients with idiopathic HES, contribute to be rather poor with a 40% reported mortality at 10 years. Although mortality of HES is high aggressive medical treatment can result in significant clinical improvement. The most common causes of mortality in HES is damage to heart and CNS by eosinophilic infiltration. Thrombectomy in thromboembolism, endocardial resection in endocardial fibrosis and valve replacement in severe regurgitation of mitral and tricuspid valve can be life saving. NIH published a follow up of 60 patients diagnosed and treated over 11 years, with variable survival rates depending on the major organs involvement.

Patients with cardiovascular complications have a lower survival rate. Our case highlights the importance of thorough screening in a symptomatic patient with marked eosinophilia.

References
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