Case Report

Idiopathic Hypereosinophilic syndrome with multiorgan involvement

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Abstract

Idiopathic hypereosinophilic Syndrome (HES) is a rare disorder, and a diagnosis of exclusion of primary and secondary HES. Symptoms develop insidiously and hyper eosinophilia is often detected incidentally. It involves skin, liver, lung, gastro intestinal system, blood, bone marrow and central nervous system.

This case study describes about a patient diagnosed as Idiopathic hypereosinophilic Syndrome with bone marrow, lung and liver involvement, who was treated successfully with steroids.

(Key words: Hypereosinophilia, Idiopathic Hypereosinophilic syndrome, Steroids)

Introduction

Hypereosinophilia (HE) in peripheral blood is defined by absolute eosinophil count >1.5x10^9/L on two occasions at least one month apart and / or pathologic confirmation of tissue HE. (1) Hypereosinophilic syndrome (HES) is characterized by sustained overproduction of eosinophils, in which eosinophilic infiltration and mediator release cause damage to multiple organs. (2) Here we present a case diagnosed as idiopathic HES.

Case report

A 72 years old male presented with low grade intermittent fever and watery diarrhea for 1½ months duration. Diarrhoea frequency was 5-6 times/day; not varied while on fasting or postprandial and during day or night. Stool wasn't mixed with blood or mucus. He had loss of appetite, had lost 8kgs of weight over a period of three months and felt generalised weakness. He was a diagnosed to have Type 11 Diabetes mellitus without complication and hypothyroidism. He was managed with thyroxine and diet control.

On examination he was pale and had 1cm diameter cervical and inguinal lymph nodes. Abdominal examination revealed smooth tender hepatomegaly of 10 cm without splenomegaly, or ascites. There were no signs of cardiomegaly or evidence of cardiac failure and the respiratory system examination was normal.

Full blood count showed a white blood cell count of 36.25 x 10^3/µl (4.0-10.0) with eosinophil of 76.8% (0.5-5%), blood picture revealed severe eosinophilia with marked rouleaux formation. Bone marrow aspirate and Trephine biopsy showed moderately hypercellular marrow with 70% eosinophils of normal morphology, compatible with HES. Investigations revealed hepatic, pulmonary, and bone marrow involvement. No RT-PCR of FILPI-PDGFRA fusion were detected (Table 1).

Diagnosis was made as idiopathic HES and patient was started on prednisolone 40mg/day. He showed dramatic response to prednisolone, that normalize eosinophil count and liver function in three weeks. Prednisolone dose was then tapered gradually every two weeks and continued 10mg as maintenance dose. He has been on regular follow up with full blood count and liver function test every 3 months and pulmonary function test in every 6months.

Discussion

Bone marrow Trephine biopsy finding of "hyperce -llular marrow with 70% eosinophils" confirmed HE, according to the pathologic confirmation criteria specified as "bone marrow section percentage of eosinophils is >20% of all nucleated cells and / or extensive tissue infiltration and / or marked deposition of eosinophil granule proteins in tissues (in the presence or absence of major tissue infiltration by eosinophils). (1)

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HES is a rare, myeloproliferative disorder, usually affects 20-50 years of age. (1, 3 & 4) It may be primary (or neoplastic) or secondary (or reactive) or idiopathic. (1) Onset of the symptoms are often insidious, and hyper eosinophilia is often detected incidentally. In this case symptoms developed over a period of 1½ months and HE was detected on routine investigation.

Idiopathic HES is a diagnosis of exclusion, in which other potential causes for HE and primary and secondary HES should be excluded. (1) This case was investigated comprehensively to exclude all other possible causes for HE prior to be diagnosed as idiopathic HES.

Idiopathic HES involves the skin in 37%, lungs in 25%, Gastro Intestinal Tract (GIT) in 14%, heart in 5% and Central Nervous System (GIT) in 4% of cases. (1) History and examination findings of this case revealed GIT, hepatic and blood involvement. Investigations supported these findings and detected pulmonary and bone marrow involvements.

Hepatic involvement presents commonly as hepatomegaly and mild abnormalities in liver biochemistry; however, presentation with chronic active hepatitis, focal hepatic lesions, eosinophilic cholangitis, or the Budd-Chiari syndrome was also reported. (1,5) Examination detected hepatomegaly and liver profile showed altered with mildly elevated transaminases, very high alkaline phosphate, elevated total and direct bilirubin and low albumin with altered albumin-globulin ratio.

Pulmonary involvement results in nocturnal cough, productive sputum, wheezing and dyspnea which may be misdiagnosed as bronchial asthma. It may be secondary to congestive heart failure or emboli originating from right ventricular thrombi or primary eosinophilic infiltration of lung parenchyma. (1) Though history and examination of our patient didn't suggest any pulmonary involvement, Chest X-ray had consolidation in right middle lobe and High-resolution computed tomography (HRCT) detected right middle lobe patchy peripheral consolidation with background of ground glass changes suggestive of simple pulmonary eosinophilia. Further lung function test showed moderate restriction, which improved with bronchodilator therapy, and peripheral airflow limitation.

Necessity and options for the treatment of HES depends on clinical presentation, laboratory findings, and mutational analysis. Asymptomatic patients don't need treatment and should be on regular monitoring to detect organ involvement; in contrast patients presented with myeloproliferation and FIP1L1-PDGFRA should be treated vigorously.[4] Steroids are first line of choice and second line drugs such as interferon alpha, or hydroxyurea should be considered for cases refractory to steroids.[3] Our patient, who had myeloproliferation without FILPI-PDGFA gene mutation showed marked response to prednisolone.

Conclusion:

Idiopathic HES with multiorgan involvement can be treated with steroids.

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Table 1: Investigations and results

Investigation	Results (Normal range)
Full blood count	36.25 x 10^3/µl (4.0-10.0), Neutrophil - 8.6% (50-70%), Lymphocyte 11.0% (20-40%), Monocyte 3.2% (3.0-12%), Eosinophil **76.8%** (0.5-5%), Basophil 0.4% (0-1%), Hb 9.5g/dl Platelet 279 x 10^3/µl.
Blood picture	Severe eosinophilia with marked rouleaux formation.
ESR	150mm/1st hour
CRP	80.2mg/l
Bone marrow aspirate and Trephine biopsy	Moderately hypercellular marrow shows 70% eosinophils with normal morphology compatible with Hypereosinophilic syndrome and no evidence of eosinophilic leukaemia
Serum protein electrophoresis	Increased polyclonal response and no monoclonal bands
AST	58U/l (10-35)
ALT	60U/l (10-40)
ALP	291U/l (30-120)
Total bilirubin	57.2µmol/l (5-21)
Direct bilirubin	47.8 (<3.4)
Total protein	93g/l (61-77)
Albumin	20.3g/l (36-48)
Globulin	72.7g/dl (22-40)
INR	1.4
Stool full report	Negative for pus cell, amoeba, ova and cyst and stool for occult blood was negative
Ultrasound abdomen	Mild to moderate hepatomegaly with altered liver architecture (possible liver parenchymal disease), mild free fluid, mild prostatomegaly without splenomegaly
LDH	845U/l (230-460)
Hepatitis BsAg, Hepatitis C Ab & Retroviral Ab	Negative
GI endoscopy	Severe portal hypertensive gastropathy
Colonoscopy & biopsy	Colonoscopy – Normal; Biopsy - Sigmoid colonic polyp and histology showed Tubular adenoma with low-grade dysplasia

Contrast enhanced CT abdomen and pelvis	Mild to moderate hepatomegaly with ascites, no focal liver lesion and mild thickening of small bowel wall with subcutaneous tissue oedema
Liver biopsy	Marked portal expansion with eosinophils with mild chronic active hepatitis
Ultrasound neck	Atrophic thyroid gland and left side level 11 cervical lymph node enlargement
Lymph node biopsy	Reactive lymph node and no evidence of granuloma, atypical cells, inflammation or malignancy
TSH	8.94mIU/L (0.55-4.78)
Free T4	0.88ng/dl (0.89-1.76)
Chest X-ray	Consolidation in right middle lobe
Sputum AFB and sputum culture	Negative and no growth
HRCT chest	Right middle lobe patchy peripheral consolidation with background of ground glass changes could be due to simple pulmonary eosinophilia
Lung function test	Moderate restriction and peripheral airflow limitation
IgE	141 IU/ml (20.4-87)
RT-PCR of FILPI-PDGFRA gene mutation	Not detected
Toxoplasma antibodies (IgM and IgG) and Toxacara antibodies	Negative
ANA	Negative
Serum creatinine	107µmol/l
Na^+	131mmol/l
K^+	4.2mmol/l