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CASE REPORT

Chromosomal mosaicism for inversion of chromosome 3(p25, p26) in a case of idiopathic hypereosinophilic syndrome (IHES)

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Abstract Cytogenetic analysis and molecular genetic studies help for diagnosis of IHES and differentiation between IHES and other hematologic disorders with eosinophilia. We want to present a case of IHES with chromosomal mosaicism for inversion of chromosome 3(p25, p26), who achieved complete remission after treatment with Imatinib and short course of prednisolone.

Keywords Idiopathic hypereosinophilic syndrome · Cytogenetic analysis · Inversion

Introduction

Hypereosinophilia is described by eosinophil counts more than 1,500/μl. The most frequent causes are: autoimmune diseases, allergies, infectious diseases and malignancies. IHES is defined by triad of hypereosinophilia (eosinophil counts exceeding 1,500/μl) more than 6 months, no other apparent etiologies for eosinophilia and organ damage due to tissue infiltration by eosinophils and mediator release [1–4].

IHES has two variants: myeloid and lymphoid.

The most chromosomal abnormality is a deletion in Chromosome 4q12 that leads to fusion of two genes: FIP1-Like1 (FIP1L1) and PDGFR Alpha [5].

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Case Report

A 53-year-old male was admitted with fever, night sweating, dyspnea and wheezing since 7 months ago. He had no history of parasitic, allergic and inflammatory disorders. Drug history was unremarkable except for inhaler of seretide. Family history was unremarkable. Physical examination revealed: Temperature = 37°C, Pulse rate = 110/min, Respiratory rate = 30/min, blood pressure = 110/80 mmHg, pallor, right eye blindness, a posterior cervical lymphadenopathy (1.5 × 1.5 cm, firm, mobile and non tender), bilateral inguinal lymphadenopathies (1 × 1 cm, firm, non tender and mobile), bilateral wheezing in both lung fields and hepatosplenomegaly. Abdominal sonography showed hepatomegaly (liver span = 165 mm) and splenomegaly (span of spleen = 190 mm).

Laboratory findings are included in Table 1.

HIV Ab, HCV Ab, HBS Ag, ANA, Anti-Ds DNA, C-ANCA and P-ANCA all were negative. Stool examination and urine analysis were unremarkable.

Echocardiography showed normal ejection fraction with mild to moderate right ventricular enlargement.

Pulmonary function test showed obstructive pattern with FEV1/FVC = 57%.

Chest HRCT scan was reported normally. Cervical lymph node was excised and reported suspicious for T-cell type non-Hodgkin lymphoma, but this diagnosis was not confirmed despite microscopic review by an expert pathologist.

EMG and NCV revealed evidences of right median nerve and left peroneal nerve mononeuritis multiplex. Sural nerve biopsy was reported unremarkable.

Study of peripheral blood smear showed WBC = 35 × 10^3/μl (45% neutrophil, 45% eosinophils,

Table 1 Lab data on admission in hematologic ward

WBC	35 × 10^3/μl
Hb	9.5 g/dl
Plat	84 × 10^3/μl
MCV	100 fl
ESR	60 mm/h
FBS	153 Nl: 70–115 mg/dl
Uric acid	4.5 Nl: 2.3–6.1 mg/dl
Direct Bilirubin	0.2 Nl: <0.2 mg/dl
Total Bilirubin	0.75 Nl: 0.75 mg/dl
AST	11 Nl: <50 U/l
ALT	8 Nl: <50 U/l
Alk ph	154 Nl: 80–306 U/l
LDH	556 Nl: up to 480 U/l
IgE	355 Nl: <100 IU/ml

5% monocytes, 5% lymphocytes). Bone marrow aspiration and biopsy showed hypercellular bone marrow with increase in numbers of eosinophils.

Since in our center the karyotype analysis is not available, thus we referred him to another research center for cytogenetic analysis.

Conventional G-banded karyotype analysis was done. Three bone marrow cultures including 24 h high resolution culture, over night culture and direct culture were established for this sample. Then the cells were harvested i.e. hypotonic solution treatment followed by chilled fixative treatment to fix the cells. Fixed cells were dropped on slides and stained for Giemsa banding karyotypes then analyzed and defined according to recommendations of the International System for Human Cytogenetic Nomenclature. At least 20 metaphase plates were analyzed from each sample and 3–4 well spread plates were photographed and karyotyped with using Cytovision Software. In only two cells an abnormal chromosome 3 with inversion between bands p25 and p26 was detected.

Result of karyotype analysis was: 46, XY, inv(3)(p25 p26)[2]/46, XY[18].[Figure 1].

Because of unexplained hypereosinophilia and evidences of organ involvement (dyspnea, wheezing and mononeuritis multiplex) and hepatosplenomegaly the diagnosis of idiopathic hyper eosinophilic syndrome was made and treatment with prednisolone 50 mg (1 mg/kg) and Imatinib 100 mg daily and inhaler of bronchodilator was started.

1 week after administration of Imatinib, WBC count was diminished to 2,300/μl but, hemoglobin level and platelet counts started to rising slowly. After 2 weeks Imatinib therapy, WBC counts decreased to 1,800/μl thus, we discontinued Imatinib temporarily and after 4 weeks when WBC counts reached above 3,000/μl, we restarted it. 2 months after discharge he was visited in clinic. Dyspnea, wheezing, fever and night sweating had been resolved completely.WBC diff, Hemoglobin level and platelet counts had been normalized and hepatosplenomegaly had been disappeared in physical examination and also in abdominal sonography thus, we started to taper of prednisolone and continued Imatinib 100 mg daily for him.

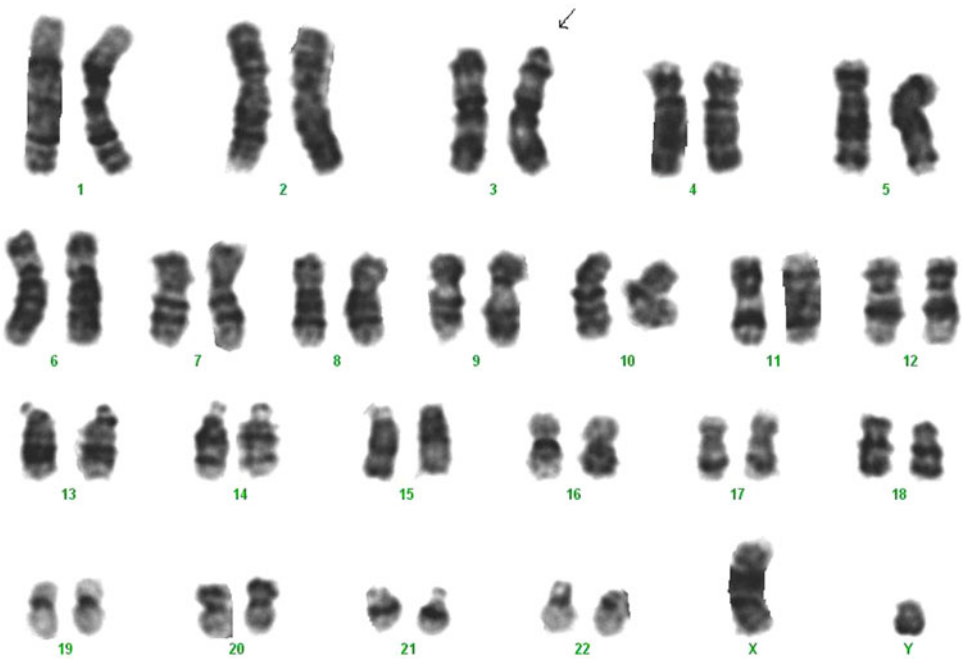

Fig. 1 *Arrow* showes inversion of chromosome 3 (p25, p26)

Results

In this 53-year-old male with IHES we found chromosomal mosaicism for inversion of chromosome 3(p25, p26) in cytogenetic study of bone marrow aspiration. He was presented with long standing fever, night sweating, episodic dyspnea and wheezing. He had huge splenomegaly and unexplained severe eosinophilia (WBC = 35×10^3/μl, 45% neutrophil, 45% eosinophils, 5% monocytes, 5% lymphocytes). All of symptoms and signs of disease and also eosinophilia resolved slowly after administration of Imatinib combined with short course of prednisolone. Now after 7 months he has free of disease with normal CBC diff and normal sizes of liver and spleen in abdominal ultrasonography.

Discussion

Deletion in Chromosome 4q12 which leads to fusion of two genes: FIP1-Like1 (FIP1L1) and PDGFR Alpha is the most common chromosomal abnormality in IHES. [5].

Bigoni et al. [6], performed cytogenetic study on six patients with IHES. They detected 3q deletion in one case; 5q31 deletion was detected in one case. No chromosomal abnormalities were found in remaining four cases. Jacob et al. [7] , reported a case of rapidly fatal HES with 49, XYY, t (3; 5), +8, +mar. Malbrain et al. [8], reported 46, XY, t (5; 9) (q32; q33) in a 49 year/o male with IHES. Marco et al. [9], reported cytogenetic abnormality 46, XY, t (7; 12) (q11; p11) in a case of IHES.

Imatinib is more effective in IHES patients with FIP1L1-PDGFR than in those without it [10].

In this case of IHES which presented with unexplained hypereosinophilia, dyspnea, wheezing, fever, night sweat, hepatosplenomegaly and mononeuritis multiplex, we found chromosomal mosaicism for inversion of chromosome 3(p25, p26). He achieved complete remission about 2 months after starting Imatinib (100 mg/day) and short course of prednisolone (50 mg/daily). Now after 7 months, he is taking Imatinib 100 mg/day and is free of all signs and symptoms with normal CBC diff and eosinophil counts.

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Conflict of interest The authors declare that there are no conflicts of interests.

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