CASE REPORT

Myeloproliferative Disorder Type Chronic Myeloid Leucemia – Eosinophilic Form

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Chronic eosinophilic leucemia (CEL) is a very rare form of leucemia in the western world. Adequate response is seldomly achieved after treatment with corticosteroids, interferon-alfa (INF-alfa) and medications containing hydroxi-urea (Litalir). The study presents a patient with CEL with no initial therapeutic response to the use of corticosteroids, INF-alfa and hydroxi-urea, and with neither clinical nor hematological response. After setting a diagnosis of CEL, patient was ordinated Imatinib (Glivec tabs) in a daily dose of 200 mg. Two days afterwards there was an evident withdrawal of subjective and clinical symptoms of disease, and the complete blood count showed significant amendment. Key words: chronic eosinophilic leucemia, imatinib (Gleevec).

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1. INTRODUCTION

Hypereosinophilic syndrome is a state of permanent overproduction of eosinophils. The value of more than 0.50x10^9/L eosinophil granulocytes in the blood is a clear sign of this disease. During the last years variants of clonal damage of eosinophil cell branch, atypic myeloproliferative variants and damage of T-lymphocytes creating IL-5 have been discovered. Clinically, the disease is characterized by eosinophilic infiltration and infiltration of liberated mediators. Hypereosinophilic syndromes with the 4q12 deletion are more likely to be presented as chronic eosinophilic leucemia (1, 2).

Chronic eosinophilic leukemia (CEL) is a rare type of leucemia in the western world. Although it can be diagnosed in all ages, this type of leucemia is most frequent in patients 25 to 60 years of age. The disease is more frequent in male population, and the prognosis is the same in both male and female (3).

The symptoms of CEL is tiredness, weakness and signs of increased metabolism: increased sweating, high temperature and weight loss (4). The disease is diagnosed casually in asymptomatic phase with signs of leucocytosis, eosinophilia or splenomegaly (5). Splenomegaly is evident in 90% of cases where the spleen can be mildly enlarged or occupy the whole left hemiabdomen (6). Liver is usually slightly enlarged. Patient can be pale because of anaemia and hemorrhagic syndrome can be present due to increased or decreased platelet count. Signs of uric diatesis can also be evident. Disease is also characterized by multiple organ damage due to eosinophilic infiltration and liberated mediators.

Diagnosis of CEL is made by increased eosinophil count of more than 0.50x10^9/L, cytogenetic abnormalities with the 4q12 deletion and the presence of FIP1L1-PDGFR – alfa gene, which is a tirosin kinase activator (7). Patients with CEL should be treated with imatinib (Gleevec) in a daily dose of 100-400 mg.

2. CASE REPORT

A patient of 26 years of age was hospitalized in February 2010 in the Department of Hematology, Oncology and Radiotherapy due to fever and high temperature (39.5°C). The patient showed evident signs of sweating, right knee and elbow swelling, loss of appetite and general weakness and dizziness. Clinical signs included fever, palor, intense sweating, splenomegaly and medium hepatomegaly.

In the complete blood count there was evident leucocytosis 40,64x10^9/L due to eosinophilia 11,90x10^9/L, anaemia with erythrocytes 1,97x10^12/L, hemoglobin level 59g/L, and thrombocytopenia 78x10^9/L. Sedimentation was 115/150 during both hours and multiple elevation of CRP level in blood 59,4mg/L. In peripheral blood smear there was enormously large number of myeloid elements, with the domination of segmented eosinophil and neutro-
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Myelogram (sternum) also gave evidence of increased white blood cells count with the domination of mature segmented eosinophil and neutrophil granulocytes as well as an increased number of myelocytes, promyelocytes and metamyelocytes accompanied by rare myeloblasts and a very decreased number of platelets, which also point to myeloproliferative disorder. Biopsy of bone marrow showed average cellularity of about 90% with 10:1 proportion of myeloid to erythroid cell branch. All forms of maturation were observed in the myeloid cell branch with about 5% of blasts and numerous myelocytes with the domination of mature forms including a large number of displastic eosinophils. Immunohistochemistry (IHH) tainting for identification of CD3 and CD20 proved presence of individual regular small lymphocytes. Morphological characteristics and IHH findings of analysed sample point to hypercellular bone marrow with the proliferation of mature myelopoiesis forms which is a definite proof of chronic myeloproliferative disease with the domination of eosinophils. The absence of other causes of eosinophilia also point to chronic eosinophilic leukemia. Immunophenotypisation by flow cytometry showed that 93% of cells in the sample represented the population of SS/CD45 granulocytes, while there was total absence of weakly positive cells with low SS that would represent blast forms.

The results of cytogenetic examination on 20 metaphase mitosis of stimulated T-lymphocytes from the sample of peripheral blood showed neither structural nor numerical changes in the karyotype. These findings confirmed normal male karyotype (46XY). Cytogenetic examination using RT PCR showed absence of BCR/ABL gene expression. Molecular-genetic RT-PCR test in the sample c-DNA showed fusion gene of interstitial deletion 4q12, or in other words gene fusion of FIP1L1-PDGFR-alfa. Echocardiographic findings of heart were in order and no elements of hypereosinophilic syndrome was found.

Radiographic CT analysis of chest, abdomen and low pelvis showed signs of hepatosplenomegaly and a single lymph node with diameter of 15mm in right axilla. No eosinophilic infiltration of organs was observed. Based on all performed results of clinical examinations, the conclusion was that we dealt with chronic myeloproliferative disease CML-eosinophilic form.

Before the setting of diagnosis the patient was treated with blood products (erythrocytes and platelets) and corticosteroids with the supportive therapy of antibiotics, antivirotics and antifungal medications. The resistance to corticosteroids developed rapidly, so we used Interferon-alfa (INF-alfa) s.c. in the dose of 3 million i.j. three times weekly. During the administration of INF-alfa patient received transfusion of erythrocytes and platelets, and showed signs of high temperature, while the complete blood count parameters made no significant progression. Treatment with medications containing hydroxi-urea (Litalir) also showed no satisfactory response.

After making definite diagnosis of CEL, patient was administered imatinib (Gleevec) in a daily dose of 200 mg. After two days there was an evident withdrawal of subjective and clinical symptoms of disease, and total blood count

**Figure 1. Blood marrow of the patient HE, 40x2**

**Figure 2. Blood marrow of the patient HE, 100x6**

**Figure 3. Spleen of the patient, HE, 40x**

**Figure 4. Spleen of the patient, HE, 100x**
showed significant amendment of all parameters, including increase in number of platelets, leucocytes and their differential formula, erythrocytes and hemoglobin. Sedimentation and CRP also showed signs of normalisation.

Patient was reliesed home with maximal quality of life with the recommendation of regular hematologist control. Six months afterwards, a molecular–genetic analysis of peripheral blood sample confirmed no presence of previously identified fusion gene transcript FIP1L1-PDGFR-alfa. It was concluded that the disease was brought into molecular remission, and parameters of blood count were in referent values.: leucocytes: 5,73x10⁹/L; erythrocytes: 5,13x10¹²; hemoglobin: 155g/L; platelets: 164x10⁹. Clinical findings were in order, and patient was with the maximal quality of life.

3. DISCUSSION

Imatinib is a very promising first line therapy and a therapy of choice for patients with chronic eosinophilic leukemia. Its application results in a longlasting response in patients who responded weakly to prior forms of therapy. Our case suggests that the application of imatinib (Gleevec) is a very succesfull form of therapy in patients with CEL, especially those refractory to corticosteroids and INF-alfa. In this population of patients imatinib (Gleevec) showed high efficacy, leading to significant reduction of disease in peripheral blood, bone marrow and other sites, making a great benefit for patients (8).

REFERENCES