

Acute Lymphoblastic Leukemia in Two Patients with β -Thalassemia Major

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Article information	Abstract
Article history: Received: 23 Apr 2013 Accepted: 12 June 2013 Available online: 16 Dec 2013 ZJRMS 2014 Nov; 16(11): 50-51 Keywords: Thalassemia major Leukemia Transfusion	Occurrence of leukemia in thalassemia major is a rare presentation. Here we report two cases of thalassemic patients, developing acute lymphoblastic leukemia. The genetic analysis revealed that, female and male patients were homozygous for IVSI-6 and IVSI-5, respectively. Two years ago the female patient presented by a high leukocyte count (154,000 μ L) and male one also presented by 80,000 WBC/ μ L count 1 year ago. Microscopic examination of both patients revealed lymphoblasts that morphologically accommodate with ALL-L1 that were confirmed by photocyotometry.

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Introduction

β -thalassemias are a group of inherited blood disorders that result from reduced or absent synthesis of β globin chain. β -thalassemia major as a one of the main form of β -thalassemia is the most severe form of disorder. Those who untreated or poorly transfused represent various clinical manifestations including stunted growth, pallor, jaundice and skeletal changes [1]. These patients possible to develop new complications and associations with other conditions including malignancy [2]. The immune imbalance is responsible for occurrence of different malignancies such as leukemia and lymphomas. In the condition like thalassemia multiple transfusions cause excess iron accumulation and result in generating toxic oxygen free radicals and therefore immune system modification and stimulate growth of infectious organisms [3]. Here we report a case with β -thalassemia that manifest with B-cell lymphoblastic lymphoma (B-LBL).

Case Presentation

Here we described 2 patients, a 3.5 years old male and an 11 years old female patient that referred to pediatric physician and diagnosed as thalassemia major at 3 years and in the 6 month of life, respectively. Firm diagnosis of disease was made by molecular analysis that lead to demonstration of 2 homozygous mutations that in female patient was IVSI-6 and in male one it was IVSI-5. After diagnosis of thalassemia, both patients received regular blood transfusion that in female patient this treatment regimen was a hyper transfusion one. During period of transfusion therapy female patient received regular chelating therapy with deferoxamine (DFO) for more than 10 years but male one did not received any chelating therapy.

Two years ago, female patient referred to her physician by low grade fever, fatigue and marked pallor that in

laboratory evaluation a high leukocyte count (154,000/ μ L) was found. We also found one year ago in routine checked up of 3.5 years old male thalassemic patient an 80,000/ μ L white blood cell count with low platelet count (Table 1).

Table 1. Some findings of two patients with thalassemia

Sex	Patient	
	Male	Female
Age (yr)	3.5	11
WBC/ μ L	80,000	154,000
Lymphocyte (%)	90	85
Hemoglobin (g/dL)	6.5	9
Platelet/ μ L	45000	35000
CSF analysis	Normal	Normal
AST (U/L)	35	85
ALT (U/L)	22	94
Ferritin (ng/dL)	1150	1350
ALP (U/L)	150	425

Microscopic examination of both patients revealed round lymphoblast with high N/C ratio and non-observing nucleolus that morphologically accommodate with ALL-L1 (FAB classification). Immunophenotypic analysis revealed the lymphoblast with following phenotypes: CD10-positive, CD19-positive, CD20-positive and CD22-positive. The pathology revealed lymphoblastic leukemia, predominantly precursor B cell lymphoblastic leukemia. At time of diagnosis of leukemia both patients had splenomegaly that in female was mild and in male was moderate.

Discussion

In this article we report a case of β -thalassemia with unusual co-existence of B-cell lymphoblastic lymphoma (B-LBL). The occurrence of this malignancy with

thalassemia cause worsening of disease condition and severity of anemia.

The review of literature revealed some cases of malignancies occurring with β -thalassemia. The occurrence of thalassemia with leukemia is a rare event. Voskaridou et al. report a 32 years old man with thalassemia major whose leukocytosis and thrombocytosis were gradually increased and leading to a diagnosis of chronic myelogenous leukemia [4]. Lau et al. also reported an 8 year old Greek boy with thalassemia major and pulmonary tuberculosis that manifests with acute lymphoblastic leukemia after treatment of tuberculosis [5]. In other study, Zurlo et al. noted the malignancies as a forth cause of death after cardiac disease, infection and liver disease in thalassemia major patients. They also reported the death of 8 cases of thalassemia major patients with malignancies [6]. In another study Otrrock et al. described 25 years old patients with thalassemia and non-Hodgkin lymphoma and revealed that the patient required more blood transfusion [7].

One possibility that result in co-existence of thalassemia with malignancy is the carcinogenic and toxic effects of excess iron resulted from multiple transfusions. In the study of Steven et al. on 3,287 men and 5,269 women

between 1,971 to 1,975; 379 men developed cancer during study. Following investigations on iron profile of these patients revealed that risk of cancer in those with moderately elevated iron level was increase [8].

In our study the co existence of thalassemia with B-LPL cause to emphasize that the possibility of occurrence of malignancy in thalassemia major patients should be considered.

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Authors' Contributions

All authors had equal role in design, work, statistical analysis and manuscript writing.

Conflict of Interest

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