Case Report

Acute Lymphoblastic Leukemia in a Patient with ß-Thalassemia Intermedius

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ABSTRACT

Occurrence of leukemia in thalassemia is a rare presentation. Here we report a case of thalassemia intermedius developing T cell acute lymphoblastic leukemia (ALL). He was diagnosed to have thalassemia intermedius at the age of 3 years. Since then he was receiving Folic acid regularly and blood transfusions as and when needed. At the age of 18 years he developed acute cervical lymphadenopathy and was found to have markedly raised leukocyte count ($117.53\times10^3/mm^3$), thrombocytopenia ($21000/mm^3$) and anemia (Hb-7.4 gm%). Peripheral smear examination revealed 80% blast cells. Bone marrow examination was suggestive of acute leukemia. Immunohistochemistry studies (IHC) showed tumour cells to be positive for CD 3 and terminal deoxynucleotidyl transferase (TdT). CD 34 was focally positive. Cells were negative for CD 20, CD 10 and myeloperoxidase (MPO) confirming the diagnosis of T cell ALL.

Key words : Thalassemia, Leukemia, Blood transfusion

Introduction -

ß-thalassemias are a group of inherited disorders that result from reduced or absent synthesis of â globulin chain. ß-thalassemia major as one of the main form of ß-thalassemia is the most severe form of the disorder. ß-thalassemia intermedius and ß-thalassemia minor has few symptoms. ß-thalassemia trait is asymptomatic. Those patients who are untreated or poorly transfused represent various clinical manifestations including stunted growth, pallor, jaundice and skeletal changes[1]. These patients develop new complications and association with other conditions including malignancy[2]. The immune imbalance is responsible for occurrence of different malignancies such as leukemias and lymphomas. In the condition like thalassemia multiple blood 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 of ß-thalassemia intermedius that manifested with T cell ALL.

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Case Report -

18 year old male patient presented for complaints of pallor, fatigue, stunted growth and recent onset of swellings in neck. He was diagnosed to have heterozygous thalassemia intermedius at the age of 3 years and was receiving Folic acid daily and blood transfusion as and when required. He developed swellings in neck from two weeks and was found to have increased total leukocyte count, anemia and thrombocytopenia with abnormal white cells on peripheral smear examination. The case was referred to this hospital for further investigations. On examination, he was markedly pale. He had haemolytic facies, stunted growth, lymphadenopathy in cervical and inguinal region and hepatospleenomegaly. He had no bleeding gums or purpuric spots. Cardiovascular and respiratory system was normal. Chest X ray showed presence of mediastinal lymph nodes and mild cardiomegaly ***(Figure1).*** 2-D echo examination revealed mild dilatation of RA and RV. Patent foramen ovale was observed. Laboratory investigations are enlisted in ***(Table 1)***. He had not received any chelating agents in past. Bone marrow examination was suggestive

of acute leukemia ***(Figure2)***. IHC studies revealed cells to be positive for CD3 and TdT. CD34 was focally positive. The cells were negative for CD10, CD20 and MPO.

Family history revealed that his father was diagnosed to have thalassemia minor and was asymptomatic. His mother had a normal Hb electrophoresis pattern. His elder brother was diagnosed to have heterozygous thalassemia intermedius and had anemia, stunted growth, bony changes and required blood transfusions intermittently and at present was doing well. Both children having thalassemia intermedius is rare. This may occur in a case of heterozygous ß-thalassemia. It is unlikely that mother has silent ß-thalassemia as that would have caused increased foetal Hb in both the kids.

Discussion -

In this article we report a case of ß-thalassemia intermedius with unusual co-existence of T cell ALL. The occurrence of this malignancy with thalassemia causes worsening of the disease condition and severity of anemia. The review of literature revealed some cases of malignancies with ß-thalassemia. The occurrence of leukemia with thalassemia is a rare event. Karmini etal. in a retrospective study of patients from 2002 to 2007 in 4 thalassemia centres in Iran found 4630 cases of thalassemia. 5 patients with ß-thalassemia were found to have lymphoma and 5 had leukemia. Proportion of patients with cancer was high in ß-Thalassemia intermedius. Worsening of anemia, spleenomegaly or lymphadenopathy should be motive for concern in thalassemia cases[4]. Nadari etal. reported ALL in two patients of â- thalassemia major[5].

One possibility that results in co-existence of thalassemia with malignancy may be the carcinogenic and toxic effects of excess iron resulting from multiple blood transfusions. Steven et al. found that risk of cancer was high in patients with elevated iron level[6].This patient had S. iron 125 µgm/dl and S. ferritin 1764.81 ngm/ml which is quite high. This report suggests that worsening of clinical condition in a patient of thalassemia needs to be looked for associated haematological malignancy.

Table 1 : Showing laboratory investigations. Figures in bracket indicate normal values

Haemoglobin	7.4 gm%
TLC	117.53X103/mm3
Blasts	80%
Neutrophils	08%
Lymphocytes	11%
Monocytes	01%
Platelets	21000/mm3
S.bilirubin	1.2 mg%
Hb F	0.8%
Hb electrophoresis	A+A2 pattern
Hb A2 fraction	4.6%
S.iron	125µgm/dl.(65-125)
TIBC	316µgm/dl.(250-450)
Transferin saturation	39.56%(14-50)
Ferritin	1764.81ngm/ml (21.81-274.66)

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Fig. 1 : **X-ray chest PA view showing mediastinal widening and mild cardiomegaly**

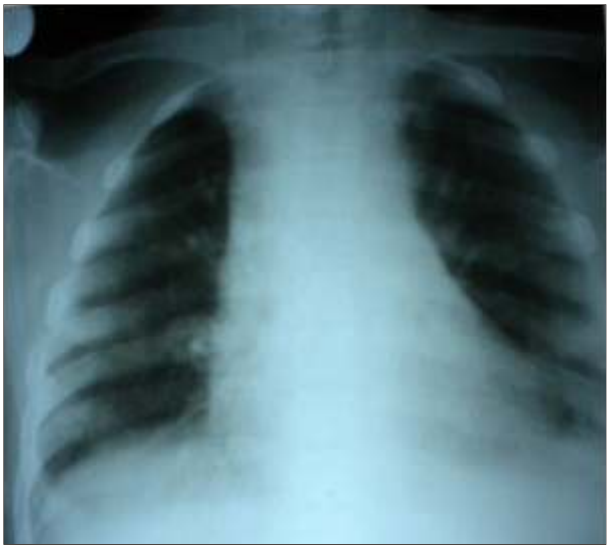

Fig. 2 **: Bone marrow full of blast cells suggestive of acute leukemia**