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Case Report

T- ACUTE LYMPHOBLASTIC LEUKEMIA IN AN ADOLESCENT BOY WITH HBE THALASSEMIA

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ABSTRACT
Thalassemias are a group of congenital anaemias that have in common the deficient synthesis of one or more of the globin subunits of the normal haemoglobins (Hb). Hb variant HbE is the most common abnormal haemoglobin of Southeast Asia including Northeast India. HbE phenotype is a milder form with patients usually being asymptomatic. Malignancies as a complication of thalassemia is known but association of leukemia is rare. The case study of an adolescent boy with HbE thalassemia homozygous diagnosed with T- Acute lymphoblastic leukemia at his adolescence is presented here due to the rarity and diagnostic importance of the case.

Keywords: *Thalassemia, Leukemia, Malignancy*

INTRODUCTION
Thalassemias are a group of congenital anemias that have in common the deficient synthesis of one or more of the globin subunits of the normal haemoglobins (Hb) (Caterina and Galanello, 2004) . The primary defect is usually quantitative consisting of reduced or absent synthesis of normal globin chain. But there are mutations resulting in structural variants produced at a reduced rate like haemoglobin E (HbE). HbE is the most common abnormal haemoglobin of Southeast Asia (Chandrashekar and Soni, 2011). It is common in the North Eastern states of India and has a carrier frequency as high as 50% in some areas (Ministry of Health and Family Welfare, 2018). Asymptomatic persons are HbE heterozygotes and are clinically normal with minimal hematologic changes. Patients who are homozygous for HbE are also usually asymptomatic but mild anemia is usually present and few patients are symptomatic. The clinical spectrum of the disease is very heterogeneous.

CASE
A nineteen year old male, resident of West Bengal, India presented to medicine clinic with complaints of generalized weakness and fever for 3 months and loss of appetite and weight loss of 3 kgs in 1 month. He had been a well boy prior to 3 months. Bowel and bladder habits were normal. He takes non vegetarian diet and is a non smoker and non alcoholic. As preliminary investigations done outside showed anemia of 7.8gm/dl, he was referred to our centre for further management. Physical examination revealed pallor and mild hepatosplenomegaly. Laboratory evaluation showed haemoglobin 6.8 g/dL, red blood cell count (RBC) 2.54 $x10^6/mm^3$, total leukocyte count (TLC) of $4,400/mm^3$, lymphocytes 66.7% and reduced platelet counts $55,000/mm^3$. Peripheral blood film showed anisopoikilocytosis with predominantly microcytic hypochromic RBCs having uneven hemoglobin distribution, 25 nucleated RBCs per 100 WBCs were seen, with thrombocytopenia. With this picture further investigation to rule out or confirm hemoglobinopathies was suggested. Hb variant analysis was done using Bio-Rad D10 ^{TM} heamoglobin system, United States with D-10 ^{TM} dual HbA_2/ F/ A_{1c} program. The chromatogram showed Hb A: 20 %, Hb A2: 86.2 %, Hb F 1.7 %. Hence, the diagnosis of HbE homozygous was made with a suggestion for mutation studies with parent and sibling testing. After 5 days interval, repeat blood count showed Hb of 5.1g/dL, RBC count of 1.93 $x10^6/mm^3$, TLC of 2,900/ mm^3, platelet count of 28,000/ mm^3. In view of clinical and hematological picture, bone marrow studies were done. Bone marrow aspirate showed absent fragments and the random smear showed 21% blasts resembling lymphoblasts (Fig. 1a). Flowcytometry

was not done as the marrow cells were very scanty and diluted. Bone marrow biopsy showed atypical cell proliferation (Fig. 1b) having increased nuclear cytoplasmic ratio, scant cytoplasm, inconspicuous nucleoli with suppression of erythroid series. By immunohistochemistry the atypical cells were positive for CD45 (Fig. 1c), CD3 (Fig. 1d) and negative for myeloperoxidase, glycophorin, CD34, CD20 and CD117 favoring the diagnosis of Acute T lymphoblastic leukemia (T-ALL).

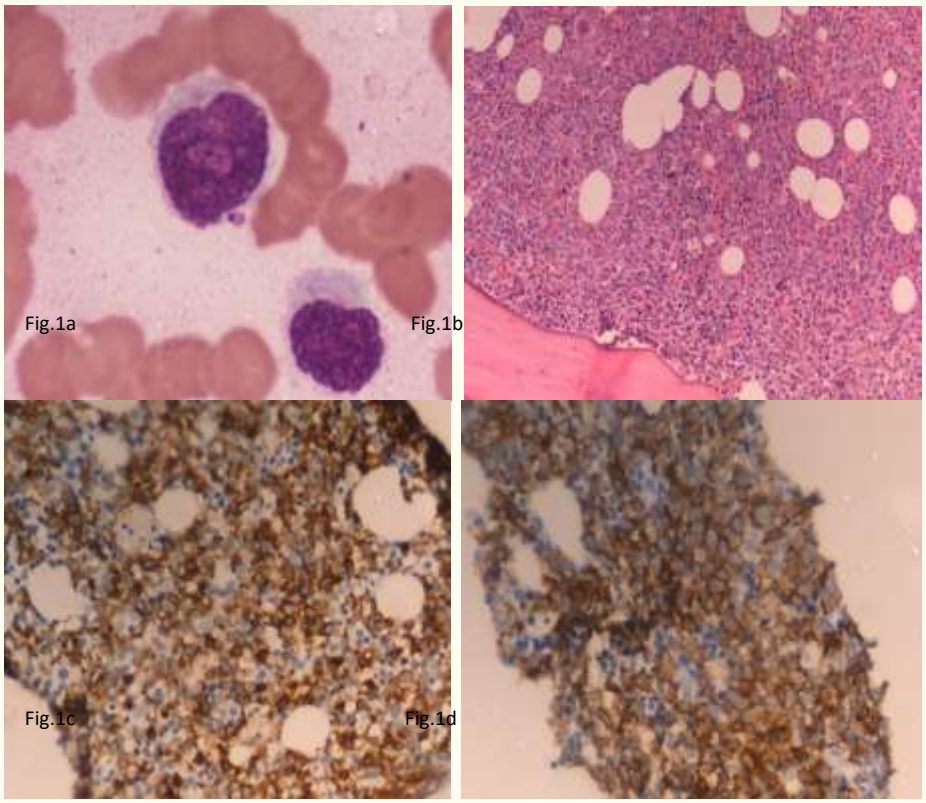

Fig 1a: Bone marrow aspirate, Blast (Leishman stain, 100x) Fig.1b: Bone marrow biopsy showing atypical cell proliferation (Hematoxylin and eosin, 40x) Fig.1c: CD45 positivity in atypical cells (40x) Fig.1d: CD3 positivity in atypical cells (40x)

DISCUSSION

Extensive literature search revealed reports regarding malignancies with beta thalassemia major and beta thalassemia intermedia in a large cohort study. The incidence of malignancy ranges from 0.002- 0.054 % (Karimi *et al.,* 2009). There are rare case reports stating beta thalassemia major complicated with lymphoma, beta thalassemia intermedia with AML (Alavi *et al.,* 2013). Naderi et al. had reported two cases of ALL with beta thalassemia major. In our centre we had reported ALL in HbE alpha thalassemia co existing in a child at presentation (Rajendran *et al.,* 2015). Immune imbalance, generations of free radical due to iron overload and recurrent infections in these patients are hypothesized as causes of leukemia development in these patients. In our index case the adolescent patient who had HbE homozygous and who had been otherwise normal, deteriorated due to the new occurrence of T- ALL. But in our patient we did not find any of the above said co-relations. The occurrence of leukemia may be similar to the general population. In an asymptomatic patient with hemoglobinopathy, when there is clinical or haematologic variation, evaluation of the patient for any malignant conditions need to be undertaken instead of repeated transfusion.

CONCLUSION

This case is presented for the rarity of T-ALL that occurred in a previously asymptomatic adolescent boy with HbE thalassemic syndrome. The possibility of leukemia is to be kept in mind when new symptoms like thrombocytopenia develop in patients with thalassemic syndromes.

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