

B-Thalassaemia : A Case Report

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Abstract

A case report of B-thalassaemia intermedia was diagnosed in a 22 years old Nepalese women on the basis of the investigations of blood, bone marrow, haemoglobin electrophoresis and X-rays with clinical findings.

Introduction

Thalassaemia is a congenital hemolytic anaemia with an inherited impairment of hemoglobin synthesis in which there is partial or complete failure to synthesize a specific type of globin chain. The severe transfusion dependant form of it is designated as

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B - thalassaemia major and the less severe form i. e. microcytic constitutional anaemia as *Thalassaemia intermedia* and milder conditions as *Thalassaemia minor*⁷. Though previously called Mediterranean anaemia, it is now realised that it had wide-spread geographical distribution occurring in the Middle-east, India, in Negroes, Thailand and South-east Asia including Nepal. This is the first case where besides the *clinical* findings and detailed investigations including hemoglobin, red cell indices, morphology of the blood smear, Cello-gel electrophoresis for HbA₂ and quantitative alkali denaturation test for Hb-F, bone marrow and various biochemical examinations including X-rays were done and the diagnosis of B-Thalassaemia intermedia was made.

Case Report

Miss JKS, 22 years presented with weakness and dizziness of 20 years duration. Fever and pain right chest and left hypochondrium of 7 days duration. She had similar illness from her childhood for which she received blood transfusions along with Iron and folic acid supplements several times in the past. She was the youngest among her healthy looking eleven brothers and sisters from her two mothers. Regarding her personal history, she was menstruating regularly. On her general physical examination, she was of average built, but anaemic, pale with icteric sclera. There was no lymphadenopathy. On her systemic examination, liver was just palpable and spleen was enlarged by four fingers which was non-tender. On auscultation of heart, there was soft systolic murmur without radiation.

Laboratory Investigations

1. Routine urine test : Albumin traces and pus cells 4 - 5/HPF.
2. Routine Stool test : Normal.
3. Routine Blood test: Hb- 3.8 g %, RBC 1,860,000/cmm., WBC - 2,000/cmm , DC-N47, L53, BT-8 min., CT-7min., Platelets- 230,000/cmm.
4. Peripheral Blood smear : Revealed microcytic hypochromic anaemia along with anisocytosis, poikilocytosis and target cells.
5. Red cell indices : MCV- 60 μ^3 (Normal 82-92 μ^3)
MCHC- 30% (Normal 32-36%)
PCV- 12% (Normal 37-47%)
6. RBC Fragility test : Initial hemolysis -0.46% (Normal 0.44-0.40%)
Complete hemolysis -0.24% (Normal 0.32-0.18%)
7. Bone marrow examination : Erythroid hyperplasia with reduced megakaryocytes. M:E:1.25:1 and iron staining strongly positive.
8. Hb- electrophoresis using Cello-gel : HbA₂ - 20% (Normal 2.3 - 3.8%)
9. Quantitative Alkali denaturation test for Hb-F: 9.4% (Normal less than 4%)

10. X-ray Skull and Extremities showed Hair-brush appearance with widening of diploic spaces and cortical thinning respectively.
11. Serum Triglycerides - 2.6 mmol/L (Normal 0.45-1.58 mmol/L).
12. Liver function test :- Bilirubin - T-34 mmol / L (Normal 3.5-20.5 mmol/L), D-19 mmol/L (Normal less than 7 mmol/L).

Discussion

There are case reports of suspected thalassaemia in Nepal. Only one survey was performed in 1972 among Sherpas and one case of B - Thalassaemia was diagnosed in 129 subjects. In the same year, screening test for Thalassaemia at Bir Hospital, Kathmandu was carried out. During which 11 cases of Thalassaemia have been diagnosed, 3 of which were Thalassaemia major. Similarity in Biratnagar 4% of 99 subjects had evidence of thalassaemia⁶. However these cases were diagnosed on the basis of clinical findings and basic hematological studies.

The basic defect in B-Thalassaemia is the globin chain imbalance with excessive production of α -chains, precipitation of the α -chains and a severe degree of ineffective erythropoiesis⁷. The affected individuals inherit only one B-chain gene from each parent. Thus these individuals are either heterozygotes, homozygotes. Statistically, one quarter of the offspring of two heterozygotes (B-Thalassaemia trait) will have the homozygous state i. e. B-Thalassaemia major. The deficiency of B-chain productions lead to a large excess α - chains within the developing red cells. These free excess α - chains have decreased solubility and will form insoluble aggregates or inclusion bodies within the RBC precursors in the bone marrow. They bring about abnormalities in the permeability as well as entrapment and destruction of RBC by macrophages in mononuclear phagocytic system which is characterised by both intramedullary erythroid destruction and shortening of the life span of circulating RBC that emerge from the bone marrow. Thus, these patients have characteristic parameters of both ineffective erythropoiesis and peripheral hemolysis⁸. These characteristic parameters were present in our patient in the form of anaemia, hyperbilirubinemia, reduced red cell count and erythroid hyperplasia with normoblastic erythropoiesis.

Globin component of hemoglobin comprises of non-identical polypeptide chains (α , β , γ or ϵ), out of the normal adult Haemoglobin, 97% is HbA ($\alpha_2\beta_2$ i. e. 2 α & 2 β). Similarly, about 2.5% of adult Hb is HbA₂ ($\alpha_2\alpha_2$ i. e. 2 α and 2 α) whereas the amount of Hb-F ($\alpha_2\gamma_2$ i. e. 2 α and 2 γ) at birth varies from 50 to nearly 100% which declines during the first 2 to 3 months of life and becomes negligible i. e. less than 1% in the adulthood⁵. Using Cellogel electrophoresis and singer's Alkali denaturation test, our patient is found to have increased HbA₂ and Hb-F of 20 and 9.4% respectively.

There is nearly always some degree of splenomegaly and often hepatomegaly which is due to the constant bombardment of the reticuloendothelial elements of these organs

by abnormal red cells. Progressive splenomegaly causes pooling of red cells with hemodilutional anaemia, increase in the plasma volume and some shortening of the red cell survival. Abdominal discomfort may be due to splenomegaly⁷. There was hepatosplenomegaly causing discomfort in our patient.

Cardiomegaly and a variety of murmurs presumably due to hyperdynamic circulation may be seen. Engle in 1954 described 2 major clinical forms of cardiac complications causing death in adolescents i. e. cardiac arrhythmias and congestive cardiac failure. It is due to deleterious effects of iron in the myocardium⁷. In our patient, only soft systolic murmur without radiation was present due to hyperdynamic circulation.

One of the most important and consistent hematological findings is abnormality of the morphological appearances of the red cells, which include marked anisocytosis and a variable number of target cells. Anaemia is typically microcytic hypochromic with hemoglobin persistently below 9-10 g%. Red cell indices like MCV, MCHC and PCV low⁷. Osmotic Fragility tests reveals increased resistance to hemolysis². These are compatible with the findings in our patient.

Bone marrow examination showed marked erythroid hyperplasia and staining for Iron showed an abundance in the reticuloendothelial cells and also in the red cell precursors⁷. Erythroid hyperplasia and positive Iron staining were present in our case as well.

X-ray reveals typical findings of hemolytic anaemia. There is widening of diploic spaces which are due to overgrowth of hemopoietic tissue whereas the Hair-brush appearance is probably a compensatory phenomenon to support to diploic space in the presence of a weakened atrophic or thinned outer table⁴. Usually the bones are found to be osteoporotic¹. X-ray findings of our patient revealed the bony changes of hemolytic anaemia.

There may be non-specific raised serum lipid profile in this disease⁷. Raised serum triglycerides in our patient is consistent with this finding.

Mild degree of jaundice may be present² which is true in our study case, having icteric sclera with raised bilirubin.

Conclusion

A case report of B-Thalassaemia intermedia in Nepal is presented. Though occasional case reports of B-Thalassaemia from Nepal are reported but these cases were reported mainly on clinical findings and some hematological investigations or X-ray findings. Hemoglobin electrophoresis, Fetal hemoglobin estimations, bone marrow studies are the major investigations required beside the above mentioned investigations to diagnose a B-Thalassaemia. This case report on the basis of detailed investigations and clinical findings support the view that Thalassaemia is seen in Nepalese population.

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