A Case Report of Hypertriglyceridemia-Thalassemia Syndrome

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Abstract :

Thalassemia major is a severe hereditary haemolytic anaemia and is usually associated with normal serum lipid profile. But there are few reports in the literature that hypertriglyceridemia can have an idiopathic association with Beta-thalassemia major. We report a case of hypertriglyceridemia associated with Beta-thalassemia major, i.e. Hypertriglyceridemia-Thalassemia syndrome in a six month old female baby. The presence of severe hypertriglyceridemia in this child which rapidly resolved after transfusion, probably suggests a self limited mechanism which may not require therapy.

Keywords : Hypertriglyceridemia, Thalassemia

Introduction : Thalassemia refers to a group of genetic disorders of globin chain production in which there is an imbalance between the α-globin and β-globin chain production. β-Thalassemia syndromes result from a decrease in β-globin chains, which results in a relative excess of α-globin chains. Beta-Thalassemia refers to the absence of production of the β-globin.(1)

Thalassemia's consist of inherited defects in the rate of synthesis of one or more of the globin chains of hemoglobin.(2) Beta-thalassemia is a condition of impaired production of beta globin chains to a varying degree, leading to a relative excess of alpha globin chains, which precipitate within the cell.(3) The resultant anemia, hemolysis, and ineffective erythropoiesis form the fundamental pathology for clinical manifestations of Beta-thalassemia. High levels of triglycerides (TG) i.e. Hypertriglyceridemia is rarely associated with thalassemia major. Thalassemia itself results in increased risk of thromboembolic episodes. Hypertriglyceridemia predisposes the risk of atherosclerotic episodes. A very few cases reported in India as Hypertriglyceridemia-Thalassemia syndrome, an entity with this distinctive association.

Case report : A 4-month-old female baby, the second child of consanguineous parents was referred to us from a local hospital with complaints of pallor and irritability. She was delivered by full term normal delivery at a Private Hospital. Birth weight was 2.5kg and following no any post natal complications. She was exclusively breastfed and immunized for age. Later, parents noticed yellowish discoloration of skin with increased irritability. For the same, they took the child to local hospital and from there referred to our hospital for further investigations and management.

On physical examination, she had significant pallor, mild jaundice, and hepatosplenomegaly. Weight (6kg) and height (62cm) which is $>50^{th}$ percentile for age and sex with a head circumference at the 75^{th} percentile. There was no skin rash, oedema, lymphadenopathy, ascites or bleeding manifestations.

A complete blood count showed a WBC 18 x 103 /μL, Hb 4.7g /dL, HCT 12%, MCV 81.6fL, MCH 32.0pg, MCHC 39. 2g/dL and platelet count 430×l03/μL. Reticulocyte count was 3.8% and serum LDH was 1330 U/L. Peripheral blood shows marked anisopoikilocytosis with marked microcytic hypochromic cells, pencil cells, polychromatophils, macrocytes and few RBC seen.

Fig1: Hb electrophoresis report of the patient showing HbF levels 73.7%

Test Description	Value(s)	Unit	Reference Range	Method
HB ELECTROPHORESIS				
HbA	8.0	%	80 - 90	High Performance Liquid Chromatography (HPLC)
HbA2	1.3	%	2 - 3.5	
Hb F	LA1c/CHb - 73.7	%	0 - 4.0	
Hb 'D' Window	00	%	00	
Hb 'S' Window	00	%	00	
Hb 'C' Window	00	%	00	
P1	00	%		
P2	00	%		
P3	1.7	%		
Unknown 1	-	%	-	
Unknown 2	-	%	-	
unknown 3	-	%	-	

Remark: HbF is high for the age. It is suggestive of beta thalassemia homozygous or double heterozygous for beta thalassemia and delta beta thalassemia. Kindly repeat the test after 1 year of age and confirm doing parental screening and DNA analysis.

Patient Hb	HbA2 Level	HbF Level
Heterozygous B-Thalassemia	4-8 %	1-5 %
Homozygous B-Thalassemia	Normal or Increased	80-100 %
Heterozygous HPFH*	+ 1-5 %	10-20 %
Homozygous HPFH*	Absent	Absent

* Hereditary Persistence of Fetal Hemoglobin

END OF REPORT

The Hb electrophoresis was done. **(Fig1)** The result obtained was Hb A5%, HbF 73.7% and HbA 21.3%, suggestive of Beta-thalassemia homozygous or double heterozygous for Beta-thalassemia and Delta Beta-thalassemia. At the time of first visit patient was transfused two times and discharged with the advice of follow up for Hb electrophoresis and blood transfusion. On next visit at the age of 6th month of life, a child came with the same complaints of pallor and icterus. On investigation, WBC was 24.9 x 103, Hb 6.6g/dl, serum was noted to be grossly lipaemic. **(Fig2)** Hence, a serum lipid profile was obtained, the fasting triglyceride level was 1449 mg/dl i.e hypertriglyceridemia.[1] Total cholesterol and other lipid fractions were normal. Signs of hypertriglyceridemia like tonsillar hypertrophy, corneal arcusor and xanthomas were absent in the baby. Both parents blood counts and smears showed microcytic hypochromic anaemia with polychromasia and occasional target cells and their serum lipid fractions were within normal limits. After transfusion, the lipid levels were done. The patient was having triglyceride levels of 532mg/dl, almost 1/3rd of the pre-transfusion value. High Performance Liquid Chromatography (HPLC) carried out in EDTA blood samples of baby and parents confirmed baby as beta-thalassemia major and both parents as thalassemia minor trait.

Fig2 : Picture showing milky serum of the patient after separation

After all necessary hematological and biochemical investigations, the baby was diagnosed as Beta-thalassemia major associated with hypertriglyceridemia and both parents as thalassemia minor. The child is on regular follow-up with red cell transfusion therapy for the past 1 year and her serum triglyceride level has returned to normal level during follow-up evaluation. A written consent was obtained from the parents for writing the case report.

Discussion: Beta-thalassemia major is an inherited haemolytic anaemia usually presenting within the first year of life with pallor, failure to thrive, hepatos-plenomegaly and a positive family history. Beta-thalassemia's are caused by various point mutations or deletions in the beta globin gene on chromosome 11, leading to diminished (beta+) or absent (beta 0) production of the beta chains of haemoglobin resulting in ineffective erythropoiesis. In Beta thalassemia major, the major red cell haemoglobin is HbF and the red cells completely lack HbA whereas in beta thalassemia major, HbF levels are generally normal or slightly increased. HbA2 level is normal or low in Beta-thalassemia homozygotes and it is elevated (4 to 8%) in Beta-thalassemia minor. About ten percent of the total world thalassemics are born every year in India.[3] Patients with thalassemia major usually present after six months of life with severe anaemia, failure to thrive, jaundice, hepatos-plenomegaly or poor weight gain and require follow-up with regular red blood cell transfusions. Our case presented with pallor, jaundice, hepatos-plenomegaly at four months of age with microcytic hypochromic indices and marked the

degree of anisopoikilocytosis on peripheral blood smear and with HbF levels of 73.7 % on HPLC.

Severe hypertriglyceridemia has been rarely reported in infants with thalassemia major, an association known as Hypertriglyceridemia – Thalassemia syndrome.[4] The pathogenesis of this rare association is not clear. It is important to recognize this rare association for the proper diagnosis and subsequent management of infants with thalassemia, especially in are as with low prevalence of thalassemia.

There are few case reports from North and West India pointing this association but there is no much data available on this from Kerala.[5] Children in these reports presented at an age ranging from five months to two years; this case presented at six months of age. In our case, serum lipid fractions of parents were normal and associated findings like tonsillar hypertrophy, corneal arcus, tendon and tuberous xanthomas were absent excluding primary hypertriglyceridemia. Secondary hypertriglyceridemia is observed in children in association with diabetes mellitus, obesity, nephrotic syndrome and uraemia which were ruled out by proper history and appropriate investigations.[6]

This case is presented here as hypertriglyceridemia can have an impact on the prognosis of thalassemic children by adding on to its morbidity by increasing the risk of developing early atherosclerosis and related complications. Follow-up for spontaneous resolution is also advised suggesting a self- limited mechanism which may not require therapy.[7]

The high levels of TG in these patients are associated with oxidative stress and a higher risk of acute pancreatitis and coronary diseases. Early recognition is thus essential. In our patient, the levels reduced after a transfusion therapy similar to previous reports.

Conclusion : Screening of all children with thalassemia and other haemolytic anemias is strongly suggested to exclude underlying hypertriglyceridemia-thalassemia syndrome and such children should be followed-up more cautiously for proper management. The high levels of TG in these patients are associated with oxidative stress and a higher risk of acute pancreatitis and coronary diseases. Being a self-limiting condition, Hypertriglyceridemia-Thalassemia syndrome does not require any specific intervention. The only intervention to be done is dietary advice with a low-fat diet and a follow-up lipid profile.

References :

1. Michael R.Debaun.MelissaJ.Vinchinsky P. Thalassemia Syndromes.Elsevier publication , 20th edition 462.10.
2. SrinivasanSR, SharmaC, FosterTA, BerensonGS. Longitudinal changes of serum lipid and apoB levels in a newborn-infant cohort. Metabolism.1982;31:167-71.
3. Bashyam MD, BashyamL, SavithriGR, GopikrishnaM, SangalV, DeviAR. Molecular geneticanalyses of beta-thalassemiain South India reveals rare mutations in the beta-globin gene. J Hum Genet.2004;49:408–13.
4. Rao AV, Bai KI, RamanujiahD.Hypertriglyceridemia in thalassemia major. J Indian Med Assoc.1972;59:15-17.
5. Gajanand T, Garg VK, Agrawal R, Chahar CK. Idiopathic hypertriglyceridemia associatedwiththalassemiamajor.Novel ScienceInternationalJournalofMedicalScience.2012;1(7):232-34.
6. Khera R, Singh M, GoelG, Gupta P, Singh T, Dubey AP. Hypertriglyceridemiathalassemiasyndrome:areportof4cases. Indian J Hematol Blood Transf.2014;30(supp1):288-91.
7. Das L, Samprathi M, Shukla U, Debapriya B, Rashmi Ranjan D. Hypertriglyceridemia thalassemia syndrome: common disease, uncommon association. Indian J Pediatr. 2016;83(7):720-22.