Scholars Journal of Applied Medical Sciences (SJAMS) **ISSN 2320-6691 (Online)**
Sch. J. App. Med. Sci., 2014; 2(6D):3097-3098 **ISSN 2347-954X (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublishers.com **DOI:** 10.36347/sjams.2014.v02i06.052

Case Report

Compound Heterozygous Beta Thalassemia with Heredietary Persistence of Fetal Haemoglobin: A Rare Haematological Combination and Different Spectrum of Thalassemia

Jaivinder Yadav[1], Deepak Sharma[2*], Hanish Bajaj Mittal[1], Suman Yadav[3], Sweta Shastri[4], Aakash Pandita[2]
[1]Pt. B.D Sharma, PGIMS, Rohtak, Haryana, India
[2]Department of Neonatology, Fernandez Hospital, Hyderabad, India
[3]Department of Anatomy, University College of Medical Sciences, Delhi, India
[4]ACPM Medical College, Dhule, Maharashtra, India

***Corresponding author**
Deepak Sharma
Email: dr.deepak.rohtak@gmail.com

Abstract: 5 year old male child presented with progressive abdominal distention, pallor, and growth failure since the age of 9 months. The foe did not respond to hematinic and required one blood transfusion for anemia. Liver and spleen were enlarged on abdominal exam. Peripheral smear showed features of haemolytic anemia and neonatal red blood cells. HPLC studies of patient revealed that father was a carrier for hereditary persistence of fetal hemoglobin (HPFH) and the mother was thalassemia trait. The child was compounded heterozygous for beta thalassemia and HPFH which resulted in relatively minor clinical severity as compared to beta thalassemia major.
Keywords: Beta Thalassemia, Fetal hemoglobin

INTRODUCTION

Beta thalassemia with HPFH is a rare disease with a clinical presentation different from thalassemia major and HPFH. It explains the variable clinical presentation of beta thalassemia when it is co-inherited with other haemoglobinopathies. This example highlights one of the rarest colors of the beta thalassemia clinical spectrum.

CASE REPORT

A five year old male child, born to non-consanguineous couple presented to us in the outpatient department with complaints of progressive abdominal distension, pallor and failure to thrive since age of 9 months. The child had easy fatigability with restriction of physical activity. The patient was started on hematinic suspecting nutritional anemia. He did not respond to hematinicand required one blood transfusion for anemia. There was no history of constipation, vomiting, jaundice, developmental delay, repeated infections, and family history of such illness.For detailed physical examination child was in respiratory distress with signs of congestive heart failure in the form of gallop rhythm, bilateral crepitations and pedal edema. Height and weight were below -3 standard deviation as per the WHO growth charts (94cm and 10kg). There was severe pallor, axillary lymphadenopathy was also present. Abdomen examination reviled hepatosplenomegaly with liver palpable 9 cm below costal margin with a span of 13 cm, firm in consistency, sharp border, non-tender and moving with respiration and a firm spleen of 13cm with sharp margins, present below the left costal margin. The laboratory investigation done showed hemoglobin of 4.2 mg/dl, total white blood cell count- 106700/UL, Platlet-130, 000, MCV-65fl (Normal range: 80-100 FL), MCH-22 pg/cell (normal range 27-31 pg/cell) and MCHC of 28 g/DL (Normal range: 32-36 g/DL) which was suggestive of microcyitc hypochromic anemia.Giemsa stained peripheral smear examination showed severe anisopoikilocytosis, microcytes, hypochromia, tear drop cells, fragmented cells and mark cells. The nRBC were seen in ratio of 460/100 WBC. The iron works were within normal bounds. The viral markers (Hepatitis B, C and HIV) were non-responsive. The 2D Echocardiography showed dilated left ventricle with global hypokinesia and ejection fraction of 40%. In holding on suspicion of thalassemia as provisional diagnosis hemoglobin electrophoresis using High performance liquid chromatography (HPLC) of the couple and patient was planned. The peripheral smear and HPLC of Mother showed Hb 12.4g/dl ; RBC Count of 4.36X 10^{12} /L, MCV of 78.9fl; MCH of 28.4pg; HPLC showed HbA- 94% and HbA2-3.6%. The HPLC of father showed Hb of 11g/dl; RBC Count of 4.03X10^{12}/L, MCV of 85fl; MCH of 31pg

and HPLC showed HbA-79% , HbA2-2.5% and HbF-19.4%. The HPLC of index case showed HbA-4%, HbA2-2.8% and HbF-92%. Molecular studies were planned, but were not usable in our institute and were not in the private lab due to fiscal restraints.The child was managed with packed red blood cell transfusion in small aliquots. The general condition improved todecrease in respiratory distress, improved oral intake and maintaining saturation of oxygen. Injectable furosemide was given for congestive cardiac failure.The child was discharged on day 7 and planned to follow in hematology OPD.

Differential Diagnosis

- Storage disorder (Gaucher's disease and Nieman Pick disease)
- Haemolytic Anaemia
- Portal hypertension.
- Thalassaemia major

DISCUSSION

Beta thalassemia present with a spectrum of clinical features depending on the beta gene mutations and co-inheritance with other haemoglobinopathies. Increased HbF level in adulthood can be due to congenital and acquired conditions. Heterozygous HPFH have an HbF level between10-35% and have benign course [1]. When these people tie to another bearer of the beta globin mutation, the expression in offspring carrying a compound heterozygous genotype vary widely. Molecular studies provide more honest penetration of different clinical manifestations in these scenarios, but unfortunately it could not be executed due to financial constraints in our example.

Our case presented with clinical characteristics similar to thalassemia intermedia with growth failure, hepatosplenomegaly and transfusion requirement which were significantly lower in comparison to thalassemia major [2, 3]. There is scarcity of such types of instances in literature with very few cases reported till now. Thein *et al*. [4] described an Asian Indian family with a non-deletion form of hereditary persistence of fetal haemoglobin (HPFH) and beta zero thalassemia. The patient was homozygous beta zero thalassemia had an unusually mild form of the disease, which was attributed to the co-inheritance of HPFH [4].

Similarly Josef Prchal *et al*. [5] reported two adult Black siblings who were diagnosed with homozygous b thalassemia with severe deficiency of β chain production, but clinically had mild symptoms and almost with normal hemoglobin. On further investigating they reported father with the typical hematological findings of β thalassemia trait and mother with elevated Hb F level (42.2%) [5].

Mary Anne Tan Jin Ai *et al*. [6] reported Mild Beta-Thalassemia intermedia caused by compound Heterozygosity for Gγ(Aγδ β)o/ β-Thalassemia and molecular characterization of the defect in four Chinese families. The presence of Hb F high levels can be caused by several genetic factors. E.g., deletions and point mutations in the beta gene cluster, and the main QTLs (Quantitative trait loci): the XmnI polymorphism (-158 C / T) (rs7482144) on chromosome 11, the HMIP locus on chromosome 6 and the SNPs present in the BCL11A gene on chromosome 2 hence a genetic an analysis must be done. The gene for heterocellular HPFH is nonallelic to the beta-globin locus and it acts as a modifier of the homozygous beta-thalassemia phenotype by increasing fetal haemoglobin production and thus diminishing the pathophysiological and clinical consequences of the thalassemia defect.

CONCLUSION

In conclusion co-inheritance of HPFH with beta thalassemia reduces the severity of disease and complications but these patients may present later in life presenting with a diagnostic challenge to the treating physicians.

Learning Points/Take Home Messages

- Patient with HPFH and beta thalassemia have a milder clinical phenotype in comparison to thalassemia major and present later in life.
- These patients should be kept in follow up and haemogram should be repeated periodically to prevent such complications developed in our case.
- HPLC and Molecular studies in patient, sibling and parents are essential to clinch the diagnosis and prevention in subsequent pregnancies.

REFERENCES

1. Lim WF, Muniandi L, George E, Sathar J, Teh LK, Lai MI; HbF in HbE/β-thalassemia: A clinical and laboratory correlation. Hematology. 2014 Sep 22.
2. Uda M, Galanello R, Sanna S, Lettre G, Sankaran VG, Chen W *et al*.; Genome-wide association study shows BCL11A associated with peristent fetal hemoglobin and amelioration of the phenotype of beta-thalassemia. Proc Natl Acad Sci USA, 2008; 105(5):1620-1605.
3. Balgir RS; The burden of haemoglobinopathies in India and the challenges ahead. Curr Sci., 2000; 79(11): 1536–15347.
4. Thein SL, Weatherall DJ; A non-deletion hereditary persistence of fetal hemoglobin (HPFH) determinant not linked to the beta-globin gene complex. Prog Clin Biol Res., 1989; 316B: 97-111.
5. Prchal J, Stamatoyannopoulos G; Two siblings with unusually mild homozygous beta-thalassemia: a didactic example of the effect of a nonallelic modifier gene of the expressivity of a monogenic disorder. Am J Med Genet., 1981; 10(3): 291-300.
6. Tan Jin Ai MA, Yap SF, Tan KL, Wong YC, Wee YC, Kok JL.; Mild Beta-Thalassemia intermedia caused by compound heterozygosity for G(A)o/-thalassemia and molecular characterization of the defect in four Chinese families. Acta Haematol., 2003;109(4): 169-175.