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A RARE CASE OF BETA THALASSEMIA MAJOR WITH NO REQUIREMENT OF BLOOD TRANSFUSION

Internal Medicine

Dr. Raj Sachde 3rd Year Resident Of Internal Medicine, P.d.u. Medical College
Dr. Manal Vithalani Intern, P.d.u. Medical College

ABSTRACT

Beta thalassemia major is a severe inherited blood disorder typically requiring lifelong blood transfusions for survival. We present a rare case of a 22-year-old female diagnosed with beta thalassemia major who, unusually, has not required any blood transfusions throughout her life. Clinical examination and laboratory investigations confirmed the diagnosis of beta thalassemia major based on presence of anaemia, ineffective erythropoiesis, and characteristic genetic testing revealing homozygosity for beta globin gene mutations. Despite the absence of regular transfusions, the patient's clinical course has been remarkable, characterized by compensatory mechanisms likely involving enhanced erythropoiesis and iron metabolism adaptations. This case challenges conventional management paradigms and underscores the variability in disease presentation and management strategies in beta thalassemia major. Further research is warranted to elucidate the underlying mechanisms and identify potential therapeutic implications for similar cases.

KEYWORDS

INTRODUCTION

Beta thalassemia major is a well-known genetic disorder characterized by severe hemolytic anaemia necessitating regular blood transfusions for survival. It results from mutations affecting the beta globin gene, leading to absent or markedly reduced synthesis of beta globin chains. The standard management paradigm involves lifelong transfusions to alleviate anaemia and mitigate associated complications, including growth retardation, skeletal deformities, and organ dysfunction due to iron overload. It's worldwide prevalence rate is 1 in 100,000 births, whereas in India it's prevalence rate is 1 in 3,000 births.

Case Report

A 22-year-old female presented to the Internal Medicine OPD of Civil Hospital Rajkot, with complaints of fatigue which was gradual in onset, on and off since last 6 months, which was relieved on resting, it was not associated with dizziness, anorexia, joint pain or abnormal blood loss; she also had dyspnea on exertion since last 3 months, which was non-progressive in nature, not associated with change in position or time of day, relieved on resting. She has no history of chest pain, breathlessness, perspiration, palpitation, feeling of tightening of chest, pedal edema, cough, cold, fever, haemoptysis, dizziness, altered sensorium or recent drug intake. She had regular menstruation, which lasted for 4-5 days, in a cycle of 28 days with moderate blood loss. Regular bowel and bladder movements, adequate sleep of 7-8 hours. Her last menstrual period was on 29th April 2024. Neither does the patient nor does her family have a history of tuberculosis, diabetes mellitus, hypertension, hospitalization or blood transfusion. Her parents have thalassemia minor. Patient has no addictions.

On Examination

Temperature – normal
Pulse – 92/minute
Blood pressure – 110/70 mm Hg
Respiratory rate – 12 to 14/minute
SpO_2 – 98% on room air

Patient was examined in natural light with adequate exposure. It showed presence of pallor in palpebral conjunctiva, no icterus, cyanosis, edema, lymphadenopathy, clubbing noted. Abdominal examination was normal, no any organomegaly noted on deep palpation. Remaining systems were normal on examination.

Investigations

Haemoglobin – 8.8 gm/dl
RBC count – 3.80 million/cumm
WBC count – 8700 cells/cumm
Platelet count – 1.29 lacs/cumm
Hematocrit – 28.0%
MCV – 73.7fl
Mentzers index –19.4
RDW – 42.8%
LDH level – 145 U/L
Serum iron – 61 mcg/dl
She has normal renal and liver function tests.
Abdominal USG did not show any splenomegaly or hepatomegaly,

Patient was referred to hematologist for anaemia workup. Haemoglobin electrophoresis showed:
HbA2 – 1.5%
HbF – 91.2%
HbAO – 7.3%
HbS and HbD – absent

Following this, genetic workup was done to differentiate between delta beta thalassemia, hereditary persistence of fetal haemoglobin, and beta thalassemia major. Genetic analysis showed NM_000518.5(HBB):c. 92+5G>C , hence showing presence of beta thalassemia major in this patient.

Finally patient was diagnosed with beta thalassemia major but she has not required any blood transfusion till date since her birth.

Management

Our patient is currently on hematinics. She is explained her optimal diet which comprises of foods rich in iron and multivitamins.Unlike our patient, patients of beta thalassemia major require blood transfusions with iron chelators. Drugs like thalidomide and hydroxyurea are prescribed.'

Our patient is explained the necessity of genetic counseling and genetic workup of the potential husband. She is advised to consult her doctors regarding this when she decides to marry.

Transfusion of whole blood or packed red cells maybe given if required in stressful conditions.

Targeted therapies: hematopoieic stem cell transplantation (HSCT), cord blood transplantation from a related donor, or autologous HSCT with gene therapy.

Surveillance: complete blood count every 3–4 weeks and with illnesses.

DISCUSSION

The level of HbF in our patient is the reason behind no requirement of blood transfusions till date. HbF is being produced naturally in this patient, which is not possible without presence of gene mutations and this merits a discussion of the controls of HbF gene silencing.

An upstream super-enhancer called the β-globin locus control region (LCR) binds erythroid-specific and ubiquitous transcription factors. The β - globin gene switching which occurs at around 6 months of

postnatal life, happens by silencing, first of HBE and then of HBG2 and HBG1, which favors the interaction of the LCR with HBB. There are two possibilities in our patient. Firstly, HBG2 or HBG1 is upregulated by rarepoint mutations in their promoters, leading to expression of the linked HBB getting downregulated. Second possibility is that deletions of the HBB promoter remove competition for the LCR, increasing the expression of HBG2, HBG1, and HBD. The transcription factors BCL11A (2p16) and ZBTB7A (19p13) are potent silencers of the HbF genes which are responsible for the switch from HbF to HbA. Mutations in these binding sites abolish the normal silencing of the HbF genes.

REFERENCES

1. Musallam KM, Rivella S, Vichinsky E, Rachmilewitz EA. Non-transfusion-dependent thalassemias. Haematologica. 2013 Jun;98(6):833-44. doi: 10.3324/haematol.2012.066845. PMID: 23729725; PMCID: PMC3669437.
2. Galanello R. Recent advances in the molecular understanding of non-transfusion-dependent thalassemia. Blood Rev. 2012 Apr;26 Suppl 1:S7-S11. doi: 10.1016/S0268-960X(12)70004-8. PMID: 22631043.
3. Sankaran VG, Menne TF, Xu J, Akie TE, Lettre G, Van Handel B, Mikkola HK, Hirschhorn JN, Cantor AB, Orkin SH. Human fetal hemoglobin expression is regulated by the developmental stage-specific repressor BCL11A. Science. 2008 Dec 19;322(5909):1839-42. doi: 10.1126/science.1165409. Epub 2008 Dec 4. PMID: 19056937.
4. Liu N, Xu S, Yao Q, Zhu Q, Kai Y, Hsu JY, Sakon P, Pinello L, Yuan GC, Bauer DE, Orkin SH. Transcription factor competition at the γ-globin promoters controls hemoglobin switching. Nat Genet. 2021 Apr;53(4):511-520. doi: 10.1038/s41588-021-00798-y. Epub 2021 Mar 1. Erratum in: Nat Genet. 2021 Apr;53(4):586. doi: 10.1038/s41588-021-00834-x. PMID: 33649594; PMCID: PMC8038971.
5. Liu N, Hargreaves VV, Zhu Q, Kurland JV, Hong J, Kim W, Sher F, Macias-Trevino C, Rogers JM, Kurita R, Nakamura Y, Yuan GC, Bauer DE, Xu J, Bulyk ML, Orkin SH. Direct Promoter Repression by BCL11A Controls the Fetal to Adult Hemoglobin Switch. Cell. 2018 Apr 5;173(2):430-442.e17. doi: 10.1016/j.cell.2018.03.016. Epub 2018 Mar 29. PMID: 29606353; PMCID: PMC5889339.