Case Report- Pregnancy in Beta Thalassemia Major or Cooley's Anemia

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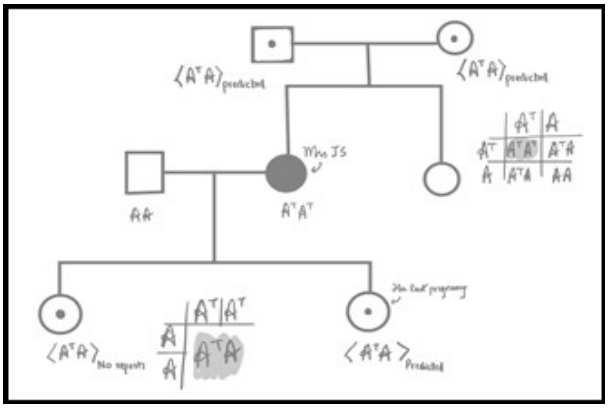
Abstract

CASE

A 33 y/o, homemaker, of Banpur, Khordha, of low SE status presented in her third pregnancy (GRAVIDA 3 PARA 1 LIVING 1 ABORTIONS 1) at POG- 39 weeks 6 days (Corresponding to 10 weeks scan) for safe confinement. She was perceiving fetal movements well. Her LMP- 27/04/2022; EDD- 04/02/2022. Her previous 3 Cycles-regular/ 3 days/ 28-32 day-cycles/ no passage of clots/ no dysmenorrhoea. No H/O OCPs or Lactational Amenorrhoea. In the present pregnancy, she had her Antenatal checkup done outside, regularly. This was a Spontaneous Conception. There is no Folic Acid intake Preconceptionally. No H/O ECG, ECHO Preconceptionally. In 1ST TRIMESTER- patient had taken Folic Acid regularly; Dating scan done at 10 weeks; NT Scan not done; No H/O fever, rashes, UTI, Hyperemesis, bleeding PV. In 2ND TRIMESTER- Anomaly Scan done- No Congenital anomalies detected; patient started having Quickening around 20 weeks and was taking ONLY Calcium taken regularly. Both doses of Tetanus Toxoid were taken at 4 weeks gap. There is H/O Dyspnoea- HB- 5.8 g/dL and ECG- normal- H/O 2 PRBC transfusions at 5 months POG. OGTT not done; FBS- 90 mg/dL. There was no H/O UTI, high BP, pedal edema, bleeding PV. In 3RD TRIMESTER- the patient had 1 ep of chest pain and dyspnoea at 39 weeks POG- HB- 6.6 g/dL (ECG not available). She was transfused 1 PRBC (a second PRBC transfusion had to be stopped due to onset of chills and rigors). There is no h/o bleeding or leaking PV, abdominal pain.

The patient has been married for 9 years (Non Consanguineous). Her first pregnancy was 6 years back, for which Cesarean Section was done, in view of CephaloPelvic Disproportion. Beta Thalassemia Major was first detected in that pregnancy. There were no Blood Transfusions. A term, baby girl of birth weight- 2.5kg was born alive and healthy. The baby was found to be asymptomatic but positive for Beta-Thalassemia trait. She conceived 1 year back again but spontaneously aborted at 1 & ½ months gestation. Suction and Evacuation was not done.

She is not a known case of Chronic Hypertension, Type 2 Diabetes Mellitus, Bronchial Asthma, Thyroid abnormalities. She has no history of undergoing Splenectomy. There is no H/O Recurrent Abortions in the family; No H/O Hemoglobinopathies; No H/O HTN, Type 2 DM, Cardiac Disease. Husband tested negative for Beta-Thalassemia.



On examination, the patient was conscious and well oriented to time place and person. She was of moderate built but undernourished (BMI- 22.21 kg/m2). She had moderate Pallor and mild Icterus and Pedal Edema upto below knees. Her blood pressure readings were high at the time of admission (150/90 mmHg) but was otherwise vitally stable. She had "Chipmunk Facies"- Depressed Nasal Bridge; Elevated Malar Prominence; Protruding Maxilla and her SternoCostal Joints were prominent.

Bilaterally her breasts were soft, nontender, no flattening of nipples was noted. No Thyromegaly was noted. No abnormalities were noted on Respiratory and CardioVascular Examination. On Abdominal Examination**,** Modified Pfannenstiel scar and Linea Nigra were noted. On palpation, AbdominoPelvic Grips- Uterus was of Term size, relaxed, fetus in longitudinal Lie with cephalic presentation with head X! palpable and no scar tenderness was noted. On Auscultation- FHR- 150 bpm.

Grade 3 SPLENOMEGALY (3 cm past-UMBILICUS) was better appreciated post-partum.

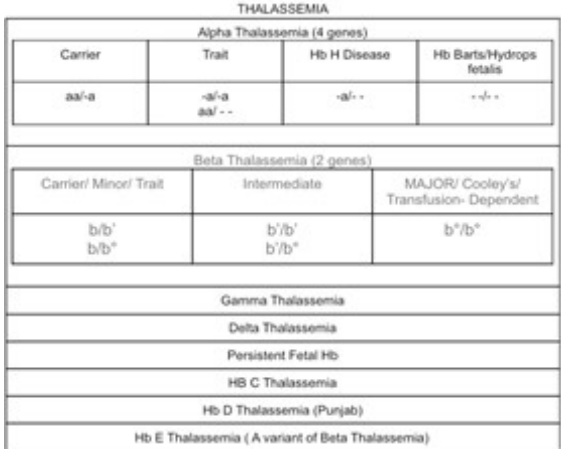
Following tests were performed- [At Admission- from outside] Blood Group-O POSITIVE; (26/01/2023)- Hb-6.6 g/dL (Underwent 1 PRBC transfusion after this); (30/06/2022)- TSH- 4.48 micro IU/mL; (29/06/2022)- FBS- 90 mg/dL; (25/12/2022) USG at 34 weeks POG- SLIUF/ BREECH/ Placenta- Fundal-Anterior, grade II/ AFI- 12 cm/ EFW- 2.420 kg/ FHR- 128 bpm. [After Admission- hospital based]- Blood Group with Extended Phenotyping- O POSITIVE, Cap C +, small e + ; ICT +ve, DCT -ve; CBC- Hb- 6.03 g/dL- RBC Indices s/o Microcytic Hypochromic Anemia; TRBC- 3.28 x 10^6/mm3; TLC- 6.79 x 10^3/mm3; TPC- 0.65 x 10^5/mm3 (at admission); Peripheral Smear- Anisopoikilocytosis ++, TARGET CELLS +, Tear Drop Cells +, Fragmented RBCs +, Nucleated RBCs. Repeat CBC (after 2 PRBC transfusion) - Hb- 8.5 g/dL; Reticulocytes- 6%; TLC- 9.13 x 10^3/mm3; TPC- 0.68 x 10^5/mm3. HIV/HBsAg/HCV- NR, anti HepA and Hep E- negative. PT, APTT, INR- Within Normal Limits (WNL); RFT, S Electrolytes- WNL. LFT- Direct Bilirubin - 1.52 mg/dL; AST-52 IU/L; ALT-22 IU/L; ALP- 269 IU/L; LDH- 872 U/L**.** Urine Dipstick Negative; URINE RME- Proteins negative, Urobilinogen 1+. CTG- normal.

Following was her management- Tab LOBET 100 mg TDS with Blood Pressure charting 2 hourly; FHR monitored every ½ hourly; Vitals monitored- esp Pulse Rate and BP; Watched for Scar Tenderness. Multidisciplinary intervention was done- Cardiology- 2D-ECHO done- LVEF 50%, Global Hypokinesia, Mild Pulmonary Artery HTN, Pericardial effusion; Inj LASIX 10 mg iv BD and <1.5 L/day fluid restriction and to avoid volume overload. Hematology Consultation- 2 PRBC pre-op and 1 PRBC intra-op given. She was taken up for ELECTIVE LSCS with BTL- around 100 mL ascitic fluid was suctioned. A term, female baby, birth weight- 2.4 kg was delivered by vertex at 2:53 pm on 02/02/2023. Baby cried immediately after birth- shifted to the NICU for observation. Liquor was reduced and Thick Meconium stained. Placenta & Membranes delivered in toto. No PPH noted. Modified Pomeroy's Method for Bilateral Tubal Ligation. Postpartum, the patient was shifted to ICU for observation post-operatively. Repeat CBC- HB- 9.4; TLC- 9.73x

10^3/mm3; TPC- 0.65 x 10^5/mm3; Repeat LFT- Direct Bilirubin - 0.98 mg/dL. Tab FOLVITE 5mg once daily; Cap Lactoferrin once daily after food; Tab Vit B Complex- B1, B6, B12 twice daily.

Discussion

Thalassemia is an Autosomal Recessive condition. It can be prenatally diagnosed by Chorionic Villus Sampling & Amniocentesis. Hemoglobin is made up of 2 alpha and 2 beta chains with Iron as core. In Beta Thalassemia Major or Cooley's Anemia, mutations of the beta globin genes cause impaired production of beta chains. The relative excess of alpha chains binds to RBC membranes and causes hemolysis. Hypochromic microcytic anemia- from a few months after birth requires life-long transfusions. Proportion of hemoglobin A2 is increased (>=3.5%).



Hemoglobin	Chains
Hb A	α2 β2
Hb A2	α2 δ2
Hb F	α2 γ2

Following are the RCOG (2014) Guidelines For Management Of Thalassemia In Pregnancy

PRECONCEPTUAL INTERVENTIONS- Good glycaemic control- for patients with established Diabetes Mellitus- HbA1c of 6.1%. Euthyroid pre pregnancy. ECHOcardiogram and ECG , T2* Cardiac MRI- to detect Iron Overload Cardiomyopathy or Cardiac Failure. USG- to detect cholelithiasis and evidence of liver cirrhosis due to iron overload or transfusion-related viral hepatitis. Endocrine and cardiac status, preferably prior to pregnancy.

Aggressive Iron chelation therapy- To reduce and optimize body iron burden and reduce end-organ damage preconceptionally

Once pregnant- Iron chelators DEFERASIROX & DEFERIPRONE -ideally discontinued 3 months prior conception. Desferrioxamine- short half-life & is safe for

infusion (even during ovulation induction therapy) (avoided in 1st trimester) Can be used safely after 20 weeks of gestation at low dose (20 mg/kg/day) at least 4–5 days a week). Folic acid (5 mg)- preconceptually to all women to prevent neural tube defects. If splenectomy -> *Pneumococcal & Hemophilus influenzae* vaccination and boosters are advised prior.

ANTENATAL CARE- Should be reviewed monthly until 28 weeks of gestation and fortnightly thereafter. If splenectomy -> Prophylactic dose of penicillin should be maintained during pregnancy (5U IV f/b 4 U 4 hourly). Women with diabetes should have monthly assessment of serum fructosamine. Thyroid function- during pregnancy in hypothyroid patients. Cardiac assessment at 28 weeks of gestation and thereafter as appropriate. Regular cardiology review during pregnancy as signs of cardiac decompensation are the primary indications for intervention with chelation therapy.

USG DURING PREGNANCY- Early scan at 7–9 weeks of gestation. Nuchal translucency Scan at 12- 14 weeks of gestation. Detailed anomaly scan at 18–20+6 weeks of gestation. Serial fetal biometry scans every 4 weeks from 24 weeks of gestation

BLOOD TRANSFUSION DURING PREGNANCY- Aiming for a pretransfusion hemoglobin of 10g/dL. Regular transfusions should be considered if there is worsening maternal anemia or evidence of FGR.

INTRAPARTUM CARE- In absence of diabetes and growth restriction, plans for delivery should be made for women without thalassaemia. Thalassaemia in itself is not an indication for cesarean section. Continuous intrapartum electronic fetal monitoring. Active management of the third stage of labor. Intravenous desferrioxamine 2 g over 24 hours should be administered during labor.

THROMBOPROPHYLAXIS- Women with a platelet count greater than 6 lakh/ mm3 should commence or continue taking low-dose aspirin (75 mg/day). Those who have undergone splenectomy and have a platelet count above 6 lakh/mm3 should be offered low-molecular-weight heparin thromboprophylaxis as well as low-dose aspirin (75 mg/day).

POSTPARTUM CARE- Women with thalassaemia should be considered at high risk for venous thromboembolism. Routine prophylaxis with heparin (Not advised during pregnancy) -upto 6 weeks postpartum. Iron chelation therapy should be resumed as soon as possible after delivery. Breastfeeding is safe and should be encouraged.

Conclusion

The aim of management of pregnancy in a Beta Thalassemia Major female is to avoid fluctuations in hemoglobin concentration and the cardiac workload**.** Hence, maintain Hb > 10 g/dL. Hence, transfusions are likely to be required. Expansion of the bone marrow, especially in those who are not regularly transfused leads to the Bone deformities & Osteopenia and Extramedullary Hematopoiesis. Repeated transfusions causes

breakdown of donor RBCs which causes iron overload which causes end organ damage; heart- cardiac dysfunction with ventricular pump failure and arrhythmias; liver- hepatic dysfunction/ jaundice; anterior pituitary- infertility; islet cells of the pancreas- diabetes; thyroid- hypothyroidism.

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