Glanzmann’s Thrombasthenia In Pregnancy

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**Designation**: Fellow, NTR UHS

**Hospital**: Fernandez Hospital, Hyderabad

**Date of Presentation**: 08.04.2017
Case

- 22 Yrs Mrs X,
- Married life 2015, NCM, Primigravida, Spontaneous conception.
- Obstetric history: spontaneous conception
- Booked with us at 33 weeks of gestational age
- ANC till now at outside nursing home.
History of Present Pregnancy

- **1st trimester**: took folic acid, viability scan done, missed NT and genetic screening
- **2nd trimester**: took iron, calcium supplementation, received tetanus prophylaxis
- **TIFFA done outside** – Normal
Further

- 3rd trimester: referred to our hospital in view of platelet disorders.
- Detected to have chronic anemia, evaluated for the same, HPLC normal.
- Growth scan at 33 weeks - FGR baby with normal doppler - weekly fetal surveillance done.
- Received 2 doses of steroid injections, planned to induce at 37 weeks.
Past Medical History

- Glanzmans thrombosthenia since 2012, Not on any medications.
- H/O menorrhagia since menarche
- H/O epistaxis, trauma related bruises
- Prolonged APTT in 2007. Factor 8 and 9 - normal,
- Counseled for genetic testing, not done.
- Loose patella syndrome (2005), h/o recurrent knee joint problem,
- Family history: 2 cousins in family having haemophilia, siblings not tested for hemorrhagic disorder.
- Allergies: none
Examination

- BMI-23.67, BP-120/80mmHg, pulse 96/min, grade 1 pallor present, no edema, icterus, cyanosis, clubbing.
- Respiratory and CVS - normal.
- P/A-fundal height -30 weeks, SFH corresponds to 30 weeks of gestation
- Cephalic presentation, FHR + regular 140/min, uterus relaxed.
Examination

- Investigations: B+, all antenatal investigations including HPLC normal.
- HAEMOGRAM, coagulation profile
- Admission history; admitted on 13/02/2017 in view of FGR for induction of labour.
## Investigations

<table>
<thead>
<tr>
<th>14 FEB</th>
<th>13 FEB</th>
<th>11 FEB</th>
<th>16 JAN (33 WKS)</th>
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<tbody>
<tr>
<td>HB</td>
<td>7.6</td>
<td>8.63</td>
<td>9.83</td>
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<tr>
<td>PCV</td>
<td>22.8</td>
<td>25.9</td>
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<tr>
<td>RBC</td>
<td>2.63</td>
<td>3.01</td>
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<tr>
<td>RDW</td>
<td>18.3</td>
<td>18.0</td>
<td>17.3</td>
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<tr>
<td>WBC</td>
<td>13500</td>
<td>19800</td>
<td>12600</td>
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<tr>
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<tr>
<td>ISI</td>
<td>1.28</td>
<td>1.28</td>
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<tr>
<td>INR</td>
<td>0.99</td>
<td>0.99</td>
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Management - Before starting IOL

- 3 SDP donors were screened and kept ready
- 1 SDP just before delivery/one if excess bleeding
- 4 PRBC, 6 RDPS, 6 FFP were reserved
- Injection tranexa 1 gm tid stat if excess bleeding p/v followed by 500 mg tid.
- Induced with CRB followed which ARM was done.
Intrapartum care

- Active stage of labor on 14/02/2017 at 11.55 hr.
- 1 SDP transfused at 8 cm dialatation,
- Delivered baby boy weighing 2.4 kg with normal APGAR and cord ABG at around 17.44 hrs with intact perineum.
- Regional anesthesia / im injections avoided.
- Post partum period uneventful, post delivery evaluated for chronic anemia, advised serum ferritin, B12 levels - normal.
- Discharged on day 3 - oral iron therapy
Platelet functional disorders

- Deficiency: Glanzmann thrombasthenia
  - GpIIb-IIIa complex
- ADP induces conformational change
- Fibrinogen
- Platelet
- GpIIb
- Endothelium
- Subendothelium

Deficiency: Bernard-Soulier syndrome

Deficiency: von Willebrand disease
Glanzmann's Thrombasthenia

- Rare autosomal recessive disorder
- Lack of glycoprotein 2b-3a complex in platelet membrane
- Platelets aggregation is severely impaired – no thrombus formation
- Normal platelet counts but exhibit very abnormal platelet function
- Major mucocutaneous bleeding
- High risk of PPH.
- Type 1 (severe): <5% of normal GPIIb-IIIa levels.
- Type 2 (less severe): 10-20% of normal GPIIb-IIIa levels.
- Type 3 (variant): normal levels of GPIIb-IIIa, but functionally inactive.
- The clinical severity of Glanzmann's Thrombasthenia does not correlate with the sub-type.
Diagnosis

1. Prolonged bleeding time
2. Absent platelet aggregation to ADP, adrenaline, thrombin
3. Defective clot retraction
4. Flow cytometric studies demonstrating absence or reduction in glycoproteins
Absent Platelet Aggregation

The diagram shows the effect of different agonists (ADP, Collagen, Adrenaline) on the optical density of platelets. The graph compares normal platelets and Glanzmann’s thrombasthenia. The addition of agonists results in a decrease in optical density, indicating aggregation. The red lines represent Glanzmann’s thrombasthenia, showing no significant change in optical density compared to normal platelets.
Peripartum Management

- Presence of anti-platelets antibodies - platelets transfusion ineffective
- Regional anesthesia contraindicated if history of hemorrhage
- IV Gammaglobulin infusion on the night before surgery or 8-12 hrs before active labour.
Peripartum Management

- C.S - rapid sequence induction using thiopental and succinyl choline
- A bolus of oxytocin followed by infusion after delivery of baby.
- SDP just before delivery and if patient is bleeding after delivery too.
Other Modalities - Recombinant factor 7

- Serial thrombo elastograph before & after administration of each blood products for qualitative assessment of the effects of platelets.

- Recombinant factor 7 - acts on the platelets in the absence of tissue factor to activate factor 9 & 10, increases thrombin generation which provide strong signal for the recruitment of other platelets.

- Recombinant factor 7 - 2hrly for first 12 hrs, 3 hrly for next 12hrs then 4th hrly. Dose 90 microgm/kg.
Other Modalities

- Patients who cannot receive platelet transfusions because of alloimmunization or antibody formation to the absent platelet glycoprotein (e.g., Glanzmann thrombasthenia and Bernard-Soulier syndrome) may benefit from rFVIIa.

- Removal of antibodies by plasmapheresis, HLA matched platelets.
Bernard-Soulier Syndrome

- Rare autosomal recessive disorder
- Thrombocytopenia and clinically significant bleeding.
- Symptoms: Menorrhagia right from menarche
- Morphologically normal large platelets
- Defect in glycoprotein1b-5-9a responsible for platelet adhesion to collagen, essential first step in primary hemostasis.
Giant Platelet Syndrome

- **Diagnosis**
  1. Absence of platelets agglutination to ristocetin
  2. PS showing morphologically normal but large platelets.
Peripartum Management

- High risk of PPH
- Mode of delivery should be determined by obstetric indications
- It is unlikely that infant will be affected as this is a rare autosomal recessive disorder but the risk should be born in mind in case of consanguineous couple.
Von Willebrand Disease

- Complete or partial absence of, or defective vWF
- Adhesive protein that has important roles in platelet function and stability of factor 8
- Required for the binding of platelets to the sub-endothelium after vessel injury
- Deficiency leads to defect in primary hemostasis.
- Menorrhagia, epistaxis, bleeding after dental extraction, PPH.
- Severe forms causes reduced levels of factor 8 with hematoma and hemorrhosis.
Diagnosis

1. Prolonged APTT,
2. vWF, factor 8 levels reduced,
3. prolonged bleeding time
4. PFA -100-combined measure of platelets adhesion and aggregation
Diagnosis

Normally, bleeding stops because platelets stick together and start a clot.

With vWD, platelets don't stick together as they should.
Peripartum Management

- Pregnancy may lead to normalization of vWF and factor 8 levels-so no increased risk of APH.
- Postpartum levels rapidly fall - increased risk of primary & secondary PPH.
- Ascertain type of vWD pre pregnancy or early pregnancy.
Peripartum Management

- Aspirin / NSAIDs are avoided.
- Desmopressin infusion to increase vWF and factor 8 levels prior to procedures like delivery.
- For women who don't respond to FFP, plasma derived factor may be used to control or prevent severe bleeding.
Platelet functional disorders

Deficiency: Glanzmann thrombasthenia

Deficiency: Bernard-Soulier syndrome

GpIb-IIIa complex

ADP induces conformational change

Fibrinogen

GpIb

Platelet

Endothelium

Subendothelium

von Willebrand factor

Deficiency: von Willebrand disease
Adhesion: Platelet GpIb + vWF + Collagen

Secretion: TxA₂, ADP, Serotonin

Aggregation: Platelet GpIb/IIa + Fibrin

- Bernard-Soulier
  - Von Willebrand Disease

- Platelet Granule Abnormalities and Secretion Disorders
  - Glanzmann’s Thrombasthenia
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