Case Report

Glanzmann's Thrombasthenia In Pregnancy; A Case and Review of The Literature

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Abstract

We present an unusual case in which a primigravida patient with Glanzmann's thrombasthenia underwent uneventful pregnancy but unfortunately fetus died due to fetal ascites and heart problem. The patient received 10 units of single donor platelets, DDA VP, recombinant factor VII, Tranexamic acid and huge doses of oxytocin during delivery and in the postpartum period. In addition, we review the literature pertaining to pregnancy and Glanzmann's thrombasthenia with an emphasis on intrapartum prophylactic management. Ethical approval for the article was obtained from the hospital ethical committee.

Key Words: Ectopia cordis, omphalocele, pentalogy of Cantrell, thoraco-abdominal wall defect

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Introduction

Glanzmann's Thrombasthenia is a rare autosomal recessive bleeding disorder resulting from a quantitative deficiency or a functional abnormality of the major platelet membrane integrin receptor: glycoprotein IIb – IIIa complex or "GP2B – 3A". The deficient complex normally mediates platelet aggregation by binding adhesive proteins, which form bridges between activated cells.[1] Thrombasthenic platelets are severely deficient in the glycoprotein IIb – IIIa complex content or function and fail to aggregate and form the haemostatic plug at the site of vessel injury.[1] Pregnancy and delivery are rare in these patients and have been associated with a high risk of severe haemorrhage.[2] Despite normal platelet count, morphology, prothrombin, and activated thromboplastin times, Glanzmann's Thrombasthenia is characterized by a prolonged bleeding time and a severe haemorrhagic mucocutaneous diathesis.

Case Report

A 31 year old, the woman was followed during her first gestation. The patient was known to have Glanzmann's Thrombasthenia since childhood. Her condition has been diagnosed following severe epistaxis and menorrhagia. Prior to pregnancy she had been anaemic with relatively heavy periods. She had a positive familial history for this condition. The patient's pre – pregnancy haematologic workup demonstrated in Table I.

Table I: Pre – Pregnancy Haematologic Work Up

Haemoglobin	9.4g/dl
Haematocrit	25.2%
WBC	$7x10^9$/Litre
Platelet count	148 x 10^9/Litre
Prothrombin time	13 sec
APTT	25 sec
Bleeding time	> 18 min
Blood group	O Rh (-)
HbsAg	Negative
Serology	Negative
Rubella	Non - Immune

She was admitted to hospital at 9th week of gestation with bleeding per vaginum. During her stay in hospital she received 6 units of single donor platelets. Transvaginal ultrasonography showed a single viable fetus with CRL of 9 weeks. Her prenatal course was

uneventful and the patient had another ultrasound at 22 weeks of gestation, demonstrating a singleton fetus with normal appearing anatomy. She was again admitted through, Accident and Emergency with haematuria, abdominal pain and ecchymosis. She was put on I/V Ritrodrine 50mg in 500ml Ringer Lactate and was given 2 doses of Dexamethasone, 12mg I/M 12 hours apart and I/V Tranexamic acid 1gm 8 hourly. Transvaginal ultrasonography showed a live fetus of 32 weeks gestation and excessive amniotic fluid and with massive fetal ascites. Diagnosis of hydrops fetalis was made. The patient had multiple antibodies against HLA antigens, specifically platelet glycoprotein IIb – IIIa, and also had a high titre of anti – D1: 1024. Haematology and neonatology consultation was done. The decision was made for emergency LSCS and the patient and her husband were counseled about possible complications during delivery and postpartum period. They were informed about the possible poor outcome of the baby.

The same day the patient took her own decision and left the hospital against medical advice. After two days she visited obstetric accident and emergency with a complaint of no fetal movements. Ultrasonography was done which showed no fetal heart pulsation with massive fetal ascites. The patient was counseled for vaginal delivery and the induction was carried on with vaginal prostaglandins. She had smooth vaginal breech delivery of a macerated female infant weighing 2000 grams. Episiotomy was avoided and 1° tear was sutured. Placenta and membranes were delivered completely. Placental pathology was unremarkable and the weight was 846 gm with 3 vessels. During delivery the patient received 16µgm of DDA VP in 20cc normal saline I/V over 20 minutes. Tranexamic acid 1 gm I/V 6 hourly for 24 hours. Recombinant factor VII was given when cervix was fully dilated. 2 units of single donor platelets were given when cervix was eight cms dilated. After delivery oxytocin was given I/V continuously for 2 consecutive days in a total dose of 60 IU on the first and 40 units on the second and third and postpartum blood loss were estimated at approximately 1500 ml. A vaginal pack was placed and removed the following day. The patient's immediate post-delivery Haemoglobin = 7.4 g/dl. Subsequently 2 additional units of packed red blood cells and 2 units of platelets were administrated and followed by a rise in Haemoglobin to 9 g/dl, Hematocrit = 23.5% and platelets 200 x 10^9/L. The patient's postpartum course was normal. She received Rubella vaccination and Depo – Provera 150mg I/M for contraception. The patient was discharged on the fourth day in a satisfactory condition. She was given the appointment of 2 weeks in postnatal and Haematology clinic.

Discussion

Over 500 cases of thrombasthenia have been reported in the world literature. The incidence is more in families with consanguinity.[3]

The gene for GP IIb –IIIa is carried on chromosome 17 in humans so it affects male and female equally. The molecular characterization of Glanzmann's Thrombasthenia in patients and their families has permitted DNA – based carrier detection to be done.[4] 1TGA2B and 1TGAB3 gene mutations associated with Glanzmann's Thrombasthenia have been observed.[5]

Acquired thrombasthenia due to Glycoprotein IIb – IIIa platelet antibodies has been shown in several conditions.[6]

Clinical presentation of patients with Glanzmann's Thrombasthenia includes haemorrhagic symptoms mainly purpura, epistaxis, gingival haemorrhage and menorrhagia. Laboratory criteria for the diagnosis of this condition include normal platelet count, normal platelet morphology as shown in figure I, prolonged bleeding time, absent or severely diminished platelet aggregation in response to adenosine phosphate and other agonists, normal platelet aggregation by ristocetin, and normal plasma coagulation studies.[7]

Although literature regarding Glanzmann's Thrombasthenia in obstetrics is limited, most reports have associated this unusual condition with a high risk of severe peripartum and postpartum haemorrhage. Reflecting on the rarity and the potential severity of this condition, an array of various intrapartum management modalities have been suggested to decrease obstetrical associated haemorrhage in pregnant patients with Glanzmann's Thrombasthenia.

The only theory to prevent bleeding in Glanzmann's Thrombasthenia is platelet transfusion. In spite of multiple antibodies against specifically platelet glycoprotein IIb – IIIa, our patient received a total of 10 units of single donor platelets during pregnancy, intrapartum and postpartum period. There was no massive postpartum vaginal bleeding. Other authors[2] support our view to give platelets during delivery and they reviewed 64 patients and stated that although glycoprotein IIb – IIIa on transfused platelets is "strongly immunogenic", it is uncommon that these patients develop more iso – antibodies. Accordingly, these authors advocate that platelet transfusion be

continued until the patient is discharged. Another authors[8] state that infusion of platelet concentrates is "almost always" associated with the production of antibodies against the glycoprotein IIb – IIIa complex. In addition, to platelets we also used high dose of oxytocin during delivery and postnatal period, and found no haemorrhagic complications.

Based on available information, the optimal delivery route is unclear. Maternal outcomes and estimated blood loss have been similar in patients delivered vaginally and by caesarean section.[7] Thus, we believe that a trial of labour is warranted in the absence of the usual obstetric indications for caesarean delivery. In our patient, there was an obstetric indication and we decided to do emergency LSCS but unfortunately patient left the hospital against medical advice, other authors[2] reviewed six patients who had caesarean deliveries, none of the patient suffered excessive bleeding as long as platelet transfusions were continued until healing was complete. Therefore, it appears that caesarean delivery should be withheld for currently accepted obstetrical indications.

Vivier et al[9] performed plasmapheresis and platelet transfusions in a massively allo – immunized patient with Glanzmann's Thrombasthenia. Patient bleeding time improved, caesarean section was performed with less blood loss. In addition to platelets and immunotherapy, patient had been treated with antifibrinolytic therapy (Tranexamic acid or aminocaproic acid and DDAVP). We used both these modalities in our patient with no more haemorrhagic complications.

The latest modality being used to correct postpartum haemorrhage in these patients is recombinant factor VIIa.[10] Potential future therapeutic measures for patients with Glanzmann's Thrombasthenia include in – utero bone marrow transplantation or gene correction which could cure the disease before birth.

Conclusion

Our case and review of literature pertaining to pregnancy and Glanzmann's Thrombasthenia support that these patients are prone to peripartum and postpartum haemorrhage. The transfusion of single donor platelet transfusion appears prudent and may assist management of these rare patients who may present with life threatening haemorrhage.

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