Intensive Care Management of a Parturient with Glanzmann's Thrombasthenia: A Case Report

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Abstract: Twenty-nine years old primigravida with a diagnosis of type 1 Glanzmann's thrombasthenia planned for labour induction was admitted to Intensive Care Unit for close observation, pain management and correction of any anticipated bleeding.

Keywords: Glanzmann's thrombasthenia, Pregnancy, Hemorrhage, Thrombocytopenia.

INTRODUCTION

Glanzmann's thrombasthenia (GT) was first described by the Swiss pediatrician Eduard Glanzmann in 1918 as a hereditary hemorrhagic thrombasthenia.[1] A prolonged bleeding time and an isolated, rather than clumped, appearance of platelets on a peripheral blood smear were early diagnostic criteria. In 1956, Braunsteiner and Pakesch reviewed disorders of platelet function and described thrombasthenia as an inherited disease characterized by platelets of normal size that failed to spread onto a surface and did not support clot retraction.[2] The diagnostic features of GT including the absence of platelet aggregation as the primary feature were clearly established in 1964 by the classic report on 15 French patients by Caen et al.[3] Those patients with absent platelet aggregation and absent clot retraction were subsequently termed as having type I disease (less than 5% of normal glycoprotein IIb–IIIa levels); those with absent aggregation but residual clot retraction, type II disease (10-20% of normal glycoprotein IIb–IIIa levels); and type 3 (levels of glycoprotein IIb–IIIa are normal but there is functional inactivity); while variant disease was first established in 1987.[4]

Glanzmann's thrombasthenia is considered a rare disease, the exact incidence has been difficult to calculate, but is estimated at one in 1,000,000, with an autosomal recessive inheritance, males and females are affected equally with an increased incidence in families with consanguinity.[5]

In this report we described the peripartum management of a 29y primigravida with type 1 Glanzmann's thrombasthenia planned for labour induction in intensive care unit.

CASE REPORT

A known case of type 1 Glanzmann's thrombasthenia, 29 years old, 67 Kg body weight, 160 cm height (BMI=26.2 kg/m^2) and 38 weeks pregnant primigravida planned for asthma patient with irrelevant other medical history. No past history of surgical interventions and not known history of drug allergy. While her husband was non-consanguineous, her father and mother were consanguineous, with no family history of the same condition.

Her basal laboratory investigations included: Hemoglobin (Hb) 12 g/L with platelet count of 147×10^9/L. Prothrombin time (PT) 0.58 second with activated partial thromboplastin time (APTT) 25.2 seconds (ratio: 0.58 and 0.8 prospectively). Blood film showed unremarkable WBCs and platelet morphology with normocytic normochromic RBCs. Blood group A+ve with negative AB screen.

Platelet aggregation test revealed no aggregation response upon the addition of adenosine diphosphate (ADP), collagen, epinephrine and arachidonic acid. There was only aggregation response upon addition of ristocetin. As the patient has normal platelet count and abnormal aggregation response to the previously mentioned aggregation agents, so this picture is consistent with Glanzmann's thrombasthenia.

Plan for delivery: A multidisciplinary team of hematologists, obstetricians, neonatologists and anesthesiologists were involved in the care of the patient, and a regimen for perioperative care was implemented for safe mother and foetal outcome. A clear plan was made for hemostasis and postpartum monitoring in ICU. Vaginal delivery is preferred unless contraindicated from an obstetric point of view, ventouse extraction and high forceps are contraindicated, foetal scalp monitoring and blood sampling should be avoided as the foetus is at risk of bleeding.

Decision for induction of labour was taken by obstetricians, prostaglandin E2 (propess 10 mg vaginal delivery system) was inserted. Intravenous immunoglobulin (IVIG) 0.6 g/kg (40g=8 vials) and intravenous tranexamic acid (1g/8 hrs) was started as guided by hematologists.

For labour analgesia, the patient was kept on remifentanil Intravenous Patient-Controlled Analgesia (IV-PCA) in separate IV access with the following parameters; (20ug/ml); bolus started at 20ug increased up to50 ug,

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lockout time 2 min. During all the time she was kept under complete monitoring including respiratory rate, heart rate,invasive blood pressure, oxygen saturation, urine output and Cardiotocography (CTG).

During the third stage of labour; recombinant factor VIIa concentrate (NovoSeven) was given by intravenous bolus injection at a dose of 90ug/kg (6mg). The average blood loss was around 800 ml and the patient received 6 units of Human leucocyte antigen (HLA) matched platelets. Episiotomy repair in layers with good hemostasis was done; one vaginal pack was inserted and was removed after 6 hrs, the uterus contracted with no vaginal bleeding.

Three hours after delivery of placenta, she received 5mg NovoSeven, then 3mg after 3 hrs, then another 3mg after 3 hrs more then was kept on 2mg every 6 hours for one day and IV tranexamic acid was continued 1g/8hrs for 3 days. Twelve hours after delivery she received another 6 units of HLA-matched platelets, no other blood products were needed.

Serial complete blood count (CBC), coagulation profile and Thromboelastography (TEG) were done before and after administration of each Recombinant factor VIIa concentrate and HLA-matched platelets, allowed us to make a qualitative assessment of the effect of platelets and recombinant factor VII.

Spontaneous vaginal delivery of a girl infant, weight 3.035 Kg, Apgar score 7 and 9 (at 1 and 5 min), was admitted to special care unit as the neonate might be at risk of thrombasthenia.

team expertise in inherited bleeding disorders, with access to staff that are able to provide treatment any time of day.[8]

Day 2 and 3 postpartum stay were uneventful, NovoSeven dose was reduced to 1mg twice a day with tranexamic acid continued 8 hourly. By day 4, the heart rate was 40/min., and Novoseven was stopped as it may be a precipitating factor of bradycardia. Serial electrocardiogram (ECG) and cardiac markers were unremarkable, cardiology consultation and bedside echocardiogram was done showed; ejection fraction (EF) 60%, bilateral ventricular dilatation, pulmonary artery systolic pressure (PASP) 35mmHg, with no significant valvular pathology. Discontinue NovoSeven improve the condition without medical intervention and cleared by cardiologist as no suspicious of cardiac disease. Table 1 showing the peripartum regimen of Intravenous immunoglobulin, Tranexamic acid, Recombinant factor VIIa concentrate and HLA-matched platelets received by the patient.

By day 5, patient was safely discharged from ICU to ward under supervision of the treating team; Hb was 10.6g/L with platelet count 89×10^9/L, PT 0.8 sec and APTT 25 sec. No postpartum hemorrhage occurred; her hospital stay was uneventful and she was discharged home 9 days postpartum on oral tranexamic acid 250mg three times a day. On discharge her Hb was 12.9 g/L with platelet count 144×10^9/L, PT 0.86 sec and APTT 24.5 sec. One week after discharge she was evaluated in Outpatient Department (OPD) by hematologist and obstetrician with no complaint, two weeks later tranexamic acid was stopped

Time	Drug	Dose
Induction of labour	Intravenous immunoglobulin	0.6 g/kg
	Tranexamic acid	1g/8hrs then Ig/8hrs/ 3 days
Third stage of labour	Recombinant factor VIIa concentrate	90ug/kg (6mg)
Delivery of the placenta	HLA-matched platelets	6 units
3hrs after placenta delivery	Recombinant factor VIIa concentrate	5mg
6hrs after placenta delivery	Recombinant factor VIIa concentrate	3mg
9hrs after placenta delivery	Recombinant factor VIIa concentrate	3mg
12hrs after placenta delivery	Recombinant factor VIIa concentrate	3mg then 2mg/6hrs/1day
	HLA-matched platelets	6 units
Day 2 and 3 ICU	Recombinant factor VIIa concentrate	1mg every 12 hrs

Table 1: Peripartum regimen of Intravenous immunoglobulin, Tranexamic acid, Recombinant factor VIIa concentrate and HLA-matched platelets received by the patient.

DISCUSSION

Glanzmann's thrombasthenia is an autosomal recessive hemorrhagic disorder; it is caused by a deficiency or dysfunction of glycoprotein IIb–IIIa receptors on platelets, which are required for platelet aggregation.[6] Clinicians should be aware that, around half the women with GT who are pregnant may not be aware of the diagnosis.[5] Counselling of the pregnancy associated risks and screening of the father in consanguineous families to identify at risk foetuses, is important.[7]

Pregnancy with GT and in particular, during delivery represents a high risk of severe hemorrhage and are best managed in a specialized center with a multidisciplinary

and last visit was one month later in hematology clinic, all the medications were stopped with no bleeding.

Management of the pregnant GT patients should start in the prenatal period through avoidance of medications that increase the risk of bleeding (Non-steroidal anti-inflammatories and aspirin).[9] Identification of HLA or glycoprotein IIb/IIIa antibodies during pregnancy, which are present in up to 70% of patients, is key for planning delivery5 and all women with GT should be monitored for platelet alloantibodies throughout pregnancy.[10]

Once induction of labour was initiated, the patient was maintained on remifentanil IV-PCA for labour analgesia. She received IVIG, tranexamic acid and rFVIIa was given in the 3rd stage of labour until the 3rd postpartum day and 6 units HLA-matched platelet was given during delivery of the placenta and another 6 units after 12 hours. Close

monitoring of CBC, PT, APTT and TEG were done to determine the need for replacement therapy and to make a qualitative assessment of the effect of platelets and recombinant factor VII.

In general, regional technique for labour analgesia is contraindicated and support with rFVIIa and antifibrinolytics is given for vaginal deliveries with the option of adding platelet transfusion for cesarean sections.[11] Other guidelines have advocated for the use of either platelet transfusions, or rFVIIa in com¬bination with an anti-fibrinolytic, as prophylaxis for vaginal delivery.[10] The use of rFVIIa as prophylaxis was documented in three pregnan¬cies, either alone or in combination with platelets, and did not prevent hemorrhage in those cases.[12] A gamma globulin infusion was given to the patient on the night before surgery in an attempt to dampen this antiplatelet response.[13] Recombinant factor VIIa concentrate enhances the deposition of deficient platelets on the subendothelial matrix to increase clot stability and is used in patients who are refractory to platelet transfusions or have antibodies.[14] Platelet transfusions are required not only prior to delivery, but sometimes should be continued for at least a week.[15] A systematic review performed by Siddiq and his colleagues (2011) revealed that hemorrhage during or after delivery in a woman suffering from GT is common and severe, and occurred up to 20 days postpartum.[16]

Platelet transfusion is the first line of management for severe hemorrhage but approximately 15–30% of individuals become refractory to transfusion and a significant proportion develop antibodies against glycoprotein IIb–IIIa or HLA.[6] Repeated platelet transfusions predispose to the development of antiplatelet antibodies, resulting in a variable response to subsequent platelet transfusions.[17] Severe postpartum haemorrhage in these individuals has been treated effectively using large doses of uterine tocolytics, plasmapheresis followed by platelet transfusions and recombinant factor VIIa.[18] Plasmapheresis has been used to remove antibodies in this patients.[19] If platelet transfusions are required, the most HLA-compatible platelet concentrates must be chosen in order to avoid platelet anti-HLA all immunization.[20] Vadasz et al (2015); documented maternal platelet alloan¬tibodies in 16 pregnancies, and plasma exchange successfully reduced the alloantibody titre in one case.[21] The main foetal risk arises from the presence of maternal Anti-human platelet antigen (HPA) to platelet glycoproteins, classically IIb–IIIa in Glanzmann's thrombasthenia.[6] Maternal antibodies can cross the placenta, causing foetal thrombocytopenia, with a risk of subsequent foetal intracranial haemorrhage.[22]

Sherer and Levner in 1991, wrote about a case of GT parturient suffered from postpartum hemorrhage for 3 weeks after intrapartum transfusions of 4 units platelet, another unit was transfused thereafter, the bleeding stopped.[23] A case report in 2012; by Madgudapathi and his colleagues cited the use of oral prednisolone to treat secondary postpartum haemorrhage.[24] Another case by Capuzzo et al; reported that secondary postpartum bleeding on day 14 of delivery was controlled with oxytocin, prostaglandins, methylergometrine and tranexamic acid, but bleeding was decreased after platelet transfusion.[25]

Four days after delivery, the patient developed sinus bradycardia (HR 40/min), after discussion with the cardiologist and the hematologist, Novoseven was stopped as it may be a precipitating factor. Bradycardia is an adverse event that was reported in 1% of the patients with hemophilia A or B that were treated with NovoSeven for bleeding episodes.[26] Several authors[27-29] did not reported the thromboembolic complications of Novoseven as a problem, while, a published 16-patient case series[30] revealed a 25% incidence of thromboembolic complications and O'Connell and colleagues[31] noted that the thromboembolic event was the probable cause of death in 72%.

CONCLUSION

A parturient with GT should be managed in a tertiary care centre which provides collaboration between obstetricians, hematologists and anesthesiologists. Due to the rare incidence and the ethical issues, there are no guidelines for the management of such case. Platelet transfusion as a prophylaxis, in combination with tranexamic acid and rFVIIa demonstrates the effective management; sinus bradycardia has been reported as an adverse event of rFVIIa.

Ethical Approval

An informed written consent was obtained from the patient for the publication.

Conflicts of Interest

The authors declare no conflicts of interest.

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