

Case Report of the Management of a Pregnant Patient with Glanzmann's Thrombasthenia: a Multidisciplinary Approach

Kalpana Tyagaraj*, Christina Dgheim, Linda Wong and Benson George

Department of Anesthesiology, Medical Center, 4802, 10th Avenue, Brooklyn, NY 11219

*Corresponding author

Kalpana Tyagaraj, MD, 718-283-1753, Maimonides Medical Center, Department of Anesthesiology, 4802 10th Avenue, Brooklyn, NY 11219, E-mail: kalpana_tyagaraj@msn.com

Submitted: 09 Oct 2018; Accepted: 19 Oct 2018; Published: 01 Nov 2018

Abstract

Glanzmann's thrombasthenia (GT) is a rare, inherited platelet disorder which predisposes a patient for potentially life threatening hemorrhagic episodes. We present a G2P1, 35 year old female with a diagnosis of GT undergoing an elective repeat cesarean section at 38 weeks gestation. A clear understanding of the pathophysiology of GT and familiarity with all the appropriate modalities of therapy to achieve hemostasis is critical for the optimal perioperative management of this patient to have favorable outcomes. A multi-specialty collaborative approach involving many healthcare providers was used to formulate a care plan for the peri-operative management of this parturient.

Keywords: Glanzmann's Thrombasthenia, Pregnancy, Platelet Dysfunction, Cesarean Section, Single Donor Platelet Transfusion

Introduction

Glanzmann's Thrombasthenia (GT) is a rare, autosomal recessive platelet disorder [1]. The incidence of morbidity and mortality associated with Glanzmann's thrombasthenia is largely unknown, although it is estimated that on in a million worldwide have GT [2].

The defect is manifested by several abnormalities of the glycoprotein (GP) IIb-IIIa complex on the surface of the platelet membrane [3]. The GPIIb-IIIa complex is essential for platelet aggregation and provides the the receptor for VWF and fibrinogen, therefore allowing the formation of a hemostatic plug [3]. Without this, the platelet plug never forms leading to vascular injury, easy bruising and excessive bleeding [4]. Uniquely, patients have normal platelet counts but exhibit very abnormal platelet function [1].

The GPIIb-IIIa complex also is a storage site for fibrinogen which allows for clot retraction therefore these patients have decreased levels of fibrinogen and abnormalities in clot retraction [2].

Two forms of GT have been described: Type 1 is the severe form in which less than 5% of normal GPIIb-IIIa exists and no clot retraction occurs; and Type 2 is the milder form where clot formation may occur and their platelet contains either 5% to 20% of normal GpIIb/IIIa [5].

Classification of Glanzmann's Thrombasthenia

Type I	<5% of normal GPIIb-IIIa
Type II	5-20% of normal GPIIb-IIIa
Variant	adequate levels GPIIb-IIIa but non-functioning

Clinical presentation of patients with the disorder includes symptoms like purpura, epistaxis, gingival hemorrhage, menorrhagia and mucocutaneous bleeding, manifesting as early as the neonatal period [4]. These patients are at an increased risk of severe bleeding during pregnancy, which can extend to 20 days in the postpartum period [2,4].

The laboratory studies show prolonged bleeding time with absent or decreased clot retraction [5]. Platelet count and coagulation studies are normal [5]. Fibrinogen levels are often decreased [4]. Light transmission aggregometry is the gold standard of diagnosis, here a patient platelet sample fails to aggregate when any agonist is added that enhances platelet aggregation [5]. Other modalities of diagnosis include a platelet function assay and flow cytometry [3]. The best way to diagnose GT is through genetic mutation analysis [2].

There remains no accepted or universally available monitor of platelet function [1]. Bleeding time and platelet aggregometry have been used but prove difficult to follow clinically [1]. A study by Monte used Thrombelastograph® analysis to demonstrate various aspects of coagulation. As expected clot strength (α) was poor as compared to normal pregnant women at similar gestation. It showed a transient increase in clot strength after platelet transfusion, which lasted about 2 hours.

Written consent was obtained from the patient or patient's family for the publication of the case report.

Case Report

Pre-operative course

A 35 year old G2P1001 female who was diagnosed with GT during her first pregnancy presents for elective cesarean section at 38 weeks gestation. Patient had a past medical history significant for frequent gum bleeds and nose bleeds as well as multiple transfusions as a child.

During her first pregnancy, she received 1 unit of HLA matched platelets and one unit of single donor platelets, during an otherwise uneventful Cesarean section. In the past, she was treated with aminocaproic acid for her excessive nose and gum bleeding. Tranexamic acid was also successfully used for the control of menorrhagia.

A multi-disciplinary team consisting of the hematologist, primary care physician, obstetrician, director of blood bank and the anesthesiology was available throughout this pregnancy for her care and planning of the delivery. One month prior to the planned elective Cesarean delivery, she was optimized with intravenous and oral iron, B12 and pre-natal vitamins therapy. Pre-operative labs values are as follows: hemoglobin 10.8, hemotocrit 32 and platelets 224K. The type and screen showed O-blood with antibodies to C and D red blood cell antigens in low titers (likely from previous transfusions) and blood bank personnel were not concerned with the likelihood of hemolysis. Patient was treated with Rho (D) immune globulins per guidelines.

In preparation, we obtained both aminocaproic acid (pregnancy category C) and tranexamic acid (pregnancy category B) to be kept on standby. One unit of HLA matched platelets for transfusion prior to cesarean section was arranged (this was obtained from an outside facility and required 48 hours of notice). The plan was to administer single donor platelets if the patient needed surgery emergently or bled excessively intra-operatively. If uncontrolled bleeding were to occur despite adequate platelet resuscitation, the plan was to administer recombinant factor VII, which was obtained. The patient was evaluated by the anesthesia team weeks prior and was in full understanding that general anesthesia was the plan for her c-section. A right antecubital 7 french rapid infusion catheter (RIC) catheter and 18 gauge IV catheter were placed in the upper extremities

Intra-operative course

HLA matched platelets were transfused en route to the operating room. In the OR, standard ASA monitors were placed. Patient was prepped and draped by the surgical team. General anesthesia was induced by rapid sequence induction with cricoid pressure using 200 mg of propofol and 120 mg of succinylcholine. Endotracheal intubation was done under direct laryngoscopy with size 7 endotracheal tube uneventfully. Spontaneous gum bleeding was noted during intubation and decision was made to give a 5 gram loading dose of aminocaproic acid and infusion was started at 1 gram per hour. Propofol infusion at 75 mcg/kg/hr was initiated to minimize inhalational anesthetic requirements and uterine relaxation. Sevoflurane was used at 0.4% MAC with 50% nitrous oxide. Rocuronium was administered after return of TOF. Operation proceeded and baby was delivered 4 minutes after the skin incision with APGAR scores of 8 and 9. Oxytocin infusion was started. Midazolam 2 mg, fentanyl 100 mcgs and morphine 2.5mg were given. Surgeon confirmed good uterine tone and proceeded to close. Excessive oozing was observed upon closure of the fascia and decision was made to give one unit of single donor platelets. Final estimated blood loss was 1500 ml and 2500 ml of crystalloids was administered. After closure, patient was reversed with appropriate doses of neostigmine and glycopyrolate and extubated successfully and transferred to the post-anesthesia care unit (PACU).

Post-operative course

The patient was monitored in PACU and she remained hemodynamically stable without signs of abnormal bleeding. CBC was drawn 4 hours post-operatively and the results are as follows:

HB 9.4 HCT 28 platelets 117K. Patient was transferred to postpartum floor. The remaining hospital course was uneventful and daily CBC's were monitored. She was discharged on 3rd postoperative day.

About one month after discharge our patient returned to the ER complaining of severe vaginal bleeding for three days. Her HB/HCT was 5.6/17. She required multiple transfusions of packed red blood cells, platelets (both single donor and HLA matched). The team attempted aminocaproic acid and conjugated estrogen without resolution of bleeding. She eventually required IR guided uterine artery embolization. Bleeding subsequently subsided and patient remained stable and was discharged.

Discussion

Pregnancy and delivery in patients with GT is rare and associated with a high risk of severe hemorrhage [5]. Different modalities have been used for the management of GT but basic practices including good surgical homeostasis and oxytocin infusions as an integral part of carries essential [2].

Prophylactic platelet transfusion is a widely accepted treatment in the prevention of postpartum hemorrhage [1]. Patients receiving no prophylactic platelet transfusions were more likely to experience postpartum hemorrhage than patients who were given platelets (63% vs 38% incidence) [2]. Repeated platelet transfusions however predispose to the development of antiplatelet antibodies, resulting in a variable response to subsequent platelet transfusions [3]. These patients should be monitored for antibodies to platelets frequently [1]. Single donor HLA matched platelets if available are preferred to minimize risk of antibodies exposure [1]. In our case, a good response to platelet transfusion was observed but in many cases, platelet transfusion may not help at all [1]. Gamma globulin infusion on night previous to surgery and antibody removal by plasmapheresis are the modalities described to dampen this antiplatelet response to platelet transfusions.

Recombinant factor VII acts on platelets in the absence of tissue factor, to activate factors IX and X, thus enhancing thrombin generation [6]. The increased production of thrombin may then provide a strong signal for the recruitment of other platelets [5]. Treatment with rFVII is well tolerated generally, although it is very expensive and Factor VII has not been shown to be as effective in prevention of PPH as prophylactic platelet transfusion [7]. The possibility of thrombotic events also is a risk with the use of rFVII. In the cases described by Kale, the use of rFVII was used as a last resort as a life saving measure.

Anti-fibrinolytic therapy such as aminocaproic acid and tranexamic acid may resolve mild to moderate bleeding and work particularly well for mucocutaneous bleeding and have been found to be useful and safe [2].

Several case reports have suggested allogeneic matched bone marrow transplantation to be the definitive therapy in patients not responding to platelet transfusions with recurrent bleeding leading to successful resolution of bleeding episodes [2].

Our understanding of this disease has improved and various peripartum treatments are described to limit associated obstetric hemorrhage; however, there remains no consensus regarding the best management of hemorrhage in patients with GT [5].

Author Contribution

Case Report conception and design: Kalpana Tyagaraj, MD
Acquisition of data: Christina Dgheim, DO
Drafting of manuscript: Christina Dgheim, DO
Critical revision: Benson George, MD and Linda Wong, MD

The above mentioned authors declare that there is no conflict of interest regarding the publication of this paper.

Financial Disclosures: None

References

1. Monte S, Lyons G (2002) Peripartum management of a patient with Glanzmann's thrombasthenia using Thrombelastograph®. Br. J. Anaesth 88: 734-738.
2. Solh T, Botsford A, Solh M (2015) Glanzmann's Thrombasthenia: pathogenesis, diagnosis, and current and emerging treatment options. J. of Blood Med 6: 219-227.
3. Kashyap R, Kriplani A, Saxena R, D. Takkar Dr. V. P. Choudhry, et al. (1997) Pregnancy in a patient of Glanzmann's thrombasthenia with antiplatelet antibodies. J Obstet Gynaecol Res 23: 247-250.
4. Magudapathi, Chandrakala, Suthanthira Kannan (2014) "Glanzmann's Thrombasthenia Complicating Pregnancy." Journal of Obstetrics and Gynaecology of India 64: 3-5.
5. Neena M, Chanana C. Deka D (2006) Pregnancy in a patient with Glanzmann's thrombasthenia. Indian J Med Sci 60: 111-113.
6. Shamsi TS, Hossain N, Soomro N, Hasan JA, Noorani M et al. (2005) Use of recombinant factor VIIa for massive postpartum haemorrhage: case series and review of literature. J Pak Med Assoc 55: 512-515.
7. Kale A, Bayhan G, Yalinkaya A, Yayla M (2004) The use of recombinant factor VIIa in a primigravida with Glanzmann's thrombasthenia during delivery. J Perinat Med 32: 456-458.

Copyright: ©2018 : Kalpana Tyagaraj, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.