CASE REPORT

Glanzmann's Thrombasthenia Complicating Pregnancy

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Introduction

Glanzmann's thrombasthenia is an autosomal recessive hemorrhagic disorder characterized by a severe reduction in or the absence of platelet aggregation in response to multiple physiologic agonists. It is due to qualitative or quantitative abnormalities of platelet receptor GPIIb/IIIa required for platelet aggregation. Pregnancy is not uncommon because fertility is not affected, but an association is rare. Pregnancy poses a special mention in these patients because of increased risk of severe hemorrhage. Newborn thrombocytopenia is occasionally severe, but always transitory. We report a 21-year-old primigravida, who underwent vaginal delivery at term with IUGR and oligoamnios.

Case Report

A 21-year-old primigravida with Glanzmann's thrombasthenia presented to our antenatal clinic in the second

trimester of pregnancy. The diagnosis of Glanzmann's thrombasthenia was made during a work up done for puberty menorrhagia. The bleeding was controlled with tranexamic acid and progesterone. She never required platelet transfusions. She had a history of prolonged bleeding following injections or injuries during childhood. The patient's pregnancy work up was showing hemoglobin of 9.5 gm%, white cell count of 13,000/mm, platelet count 2.5 lakhs, aptt of 25/29; while bleeding time was >10 min, clot retraction time was absent.

She had a spontaneous conception as fertility is usually not compromised in these patients. All antenatal investigations including a detailed scan of the fetus were normal. Her antenatal course was uneventful in the first and second trimesters except for moderate anaemia for which she was on oral hematinics. She was diagnosed as IUGR and oligoamnios (EFW 2.26 kg, AFI 5 cm) at 37 weeks and induced with prostaglandins and monitored closely. She progressed to deliver vaginally a 2.240 kg female baby. The first stage lasted for 7 h 15 min. The second stage lasted for 25 min and two units of platelet rich plasma were transfused. Episiotomy was performed followed by instrumental delivery because of fetal bradycardia (6 min). There was no additional bruising or laceration of the perineum. The third stage was unevenful. Estimated blood loss was 250 ml. An oxytocin infusion of 20 units in 500 ml ringer lactate was started immediately following delivery of the anterior shoulder.

Patient had hematuria which settled on the second post natal day. Baby was in NICU for respiratory distress and

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phototherapy in view of hyperbilirubinemia—which on evaluation was found to be physiological and not a manifestation of Glanzmann's thrombasthenia. Patient's hemoglobin after 48 h was 8.2 gm%. Mother and baby were discharged on third postnatal day in good condition. During her follow up visit 15 days later, the patient had heavy vaginal bleeding, for which she was treated with tranexamic acid, and was resolved in 2 days.

Discussion

Glanzmann's thrombasthenia is a rare inherited bleeding disorder caused by a deficiency or dysfunction of the GPIIb–IIIa receptor on platelets. Glanzmann, a Swiss pediatrician, initially described thrombasthenia in 1918 when he noted purpuric bleeding in patients with normal platelet counts.

Over 500 cases of Glanzmann's thrombasthenia have been reported in the international literature. Although it predominates among certain ethnic groups (Arobs, Jordanian tribes, Iraqi Jews, French gypsies, and individuals from south India), an estimate of worldwide incidence and prevalence has not been reported. The incidence is more in families with consanguinity.

Death following bleeding is estimated at approximately 5–10m % mostly due to occurrence of severe unprovoked intracranial or gastro intestinal hemorrhages.

The gene for GPII–IIIa is carried on chromosome 17 in humans, and thus, it affects men and women equally. Many patients with identified mutations are compounded heterozygotes, being higher where consanguinity is common.

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So far, 38 mutations in GPIIb and 25 mutations in GPIIIa have been recorded. It is speculated that a 15;17 translocation characteristic of acute promyelocytic leukemia may interfere with GPIIb and GPIIIa genes, located at 17q21.32.

The molecular characterization of Glanzmann's thrombasthenia in patients and their families has permitted DNA-based carrier detection and prenatal diagnoses to be performed. Acquired thrombasthenia due to glycoprotein IIb–IIIa platelet antibodies has also been defined in several conditions.

Patients with GT are typically diagnosed in infancy or early childhood. However, it can also be diagnosed in adult. The most common clinical manifestations of Glanzmann's thrombasthenia are menorrhagia, easy bruising, purpura, epistaxis and gingival bleeding. Less common are gastrointestinal hemorrhage and hematuria. Hemarthrosis and

intracranial hemorrhages are rare. Carriers of Glanzmann thrombasthenia appear to be asymptomatic.

Glanzmann's thrombasthenia is classified into three types, depending on the level of GPIIb–IIIa present. The clinical manifestation does not depend on the severity.

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 goal of treatment is to control bleeding episodes.

Platelet transfusion is the standard therapy. However, approximately 15–30 % of patients become refractory to platelet transfusion or develops antibodies to GPIIb–IIIa and/or HLA antibodies.

Factor VII is indicated for the treatment of bleeding episodes and for the prevention of bleeding during surgery or invasive procedures in patients with Glanzmann's thrombasthenia with antibodies to GPIIb–IIIa and/or HLA, and with past or present refractoriness to platelet transfusions.

Desmopressin (DDAVP) has been tried in some patients with Glanzmann's Thrombasthenia and may shorten bleeding time in patients with type 2 only, but there is no notable clinical efficacy.

Oral contraceptives can regularize menstrual cycles and reduce the bleeding. This is sometimes recommended before a girl's first period, as hemorrhage is particularly severe at this time.

Immunoabsorption is the removal of antibodies to platelets by plasma exchange with the use of protein-A Sepharose columns which may transiently restore platelet efficacy. However this technique is not available everywhere, it is labor intensive and requires an adequate venous access. It is not effective in active bleeding as these process reqs.

Allogeneic marrow transplant has been reported in two patients with Glanzmann's thrombasthenia.

Other Treatments

Compression, gelatine sponge or gauze, antifibrinolytic agents such as tranexamic acid or topical thrombin can be used to control minor bleeds.

Conclusion

Pregnancy is rare in patients with Glanzmann's thrombasthenia, and pregnancy is life threatening for both mother and fetus [1]. Pregnant patient may develop bleeding

because of gynecologic or obstetric causes, and bleeding may occur during and after delivery and even during puerperium. There is lack of consensus regarding treatment of postpartum hemorrhage in patients with Glanzmann's thrombasthenia. Studies show that large doses of uterotonics prevent post-partum hemorrhage in the patient. Plasmapheresis followed by platelet transfusions have also been successfully used for prevention and treatment of intra and postpartum bleeding in cases of Glanzmann's disease as this reduces the number of antiplatelet antibodies making transfusions effective. The latest modality being used to correct postpartum hemorrhage in these patients is recombinant factor VIIa [2]. Oral prednisolone has also been used to treat secondary PPH in some centers [3].

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