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Glanzmann thrombasthenia in pregnancy: Optimising maternal and fetal outcomes

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Abstract

Glanzmann thrombasthenia is a rare autosomal recessive haemorrhagic disorder. The risks of miscarriage, antepartum and postpartum haemorrhage, and neonatal complications are all increased in individuals presenting with the disease in pregnancy. Some individuals may develop antibodies to platelet glycoproteins; the presence of these antibodies is a rare cause of neonatal alloimmune thrombocytopenia and potential intracranial haemorrhage. Multidisciplinary care is paramount for ensuring optimal fetal and maternal outcomes in such cases. We report a case of neonatal alloimmune thrombocytopenia secondary to maternal Glanzmann thrombasthenia in pregnancy.

Keywords

High-risk pregnancy, haemorrhage, haematology, maternal-fetal medicine, neonatal alloimmune thrombocytopenia, Glanzmann thrombasthenia

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Case

A 38-year-old South Indian primigravida (IVF pregnancy) with Glanzmann thrombasthenia booked into our obstetric service with a BMI of 30. She had a history of two early miscarriages. She was diagnosed with type 1 Glanzmann thrombasthenia at the age of 12 and was a carrier of a Glycoprotein IIIa missense mutation which resulted in a life-long absence of the IIb–IIIa platelet glycoprotein on the platelet surface. This deficiency confers abnormal primary haemostasis and a bleeding phenotype. Her partner was non-consaguinous and as such paternal genotyping was not performed.

Her medical history included a previous myomectomy (uterine cavity not breached), chronic hypertension and hypothyroidism.

During pregnancy, she developed two obstetric issues: gestational diabetes (stable on treatment with Metformin) and intrauterine growth restriction.

The patient was regularly reviewed by the Haematology and Maternal Medicine teams. She presented to the Emergency Department in the first trimester with epistaxis and haematuria. As expected in this disorder, the maternal platelet count was normal throughout pregnancy ($161–254 \times 10^9$/L), and at booking testing for platelet-specific antibodies was negative. Testing for platelet-specific antibodies was carried out every four to six weeks, and she tested positive for anti Human Platelet Antigen (HPA) IIb–IIIa antibodies at 29 weeks, with titres of 1 in 8. A multidisciplinary meeting between the Haematology, Obstetric and Anaesthetic teams was arranged for 32 weeks. It was felt that instrumental delivery should be avoided due to the risk of NAIT and intracranial haemorrhage, and the mother was counselled regarding this risk. The safest mode of delivery for the baby was deemed to be by caesarean section due to the combination of intrauterine growth restriction and potential risk of neonatal alloimmune thrombocytopenia (NAIT); timing would be dictated by fetal growth, but a desire to early delivery was encouraged, given the late complications reported in such cases. A general anaesthetic was planned due to the risk of bleeding with regional anaesthesia. A clear plan was made for haemostasis and postpartum monitoring in the Obstetric HDU.

The fetus was noted to be small at the anomaly scan. No structural or placental abnormalities were noted. Regular scans were arranged in order to monitor fetal growth and identify the development of intracranial haemorrhage. Her final scan at 35 + 3 weeks showed consistent growth, normal liquor volume and Dopplers and an estimated fetal weight of 1729 g. Delivery was arranged for 36 weeks, by elective caesarean section, and intramuscular steroids were administered beforehand.

Prior to her caesarean, HLA-matched platelets were given to reduce the risk of bleeding given the maternal poor platelet function characteristic of Glanzmann thrombasthenia. Novoseven was also administered due to the presence of maternal anti-HPA antibodies, which can reduce the efficacy of platelet transfusions. The caesarean was technically difficult, with multiple adhesions. Estimated blood loss was 1.5 litres; she received four units of HLA-matched platelets, a further dose of Novoseven, 487 ml of blood via cell salvage and tranexamic acid. NSAID use was avoided. She was transfused with a further unit of blood and platelets on day 1 post-operatively. She was discharged home on day 7 postoperatively with a two week supply of tranexamic acid.

The baby weighed 1700 g at birth, and the platelet count was 33 on the cord blood sample. This dropped to 16 on day four of life, and the baby received intravenous platelets and immunoglobulins, in order to reduce the immune-mediated clearance of circulating platelets. The baby's count was 40×10^9/L on discharge. A cranial ultrasound performed on day 0 of life showed no evidence of intracranial bleeding.

The mother will require preconception counselling for subsequent pregnancies, as the risk of a future fetus with NAIT is greater than 75%.[1] In such cases, non-invasive treatment with intravenous immunoglobulins can be administered in the antenatal period. Management of subsequent pregnancies should be multidisciplinary, between Haematology, Fetal and Maternal Medicine teams, and she will require regular monitoring of IIb–IIIa antibodies.

Literature review

Glanzmann thrombasthenia is an autosomal recessive haemorrhagic disorder, first described in 1918. It has an estimated prevalence of less than 1 in 1,000,000 and predominates among certain ethnic groups, such as Southern Indians, as with our patient.[2] It is caused by a deficiency or dysfunction of glycoprotein IIb–IIIa receptors on platelets, which are required for platelet aggregation.

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Males and females are equally affected, with an increased incidence in families with consanguinity. The gene encoding glycoprotein IIb–IIIa is carried on chromosome 17; there are currently 38 known mutations in glycoprotein IIb and 25 in glycoprotein IIIa.[3]

The disease can be classified as follows: type 1 (individuals have less than 5% of normal GP IIb–IIIa levels), type 2 (10-20% of normal GP IIb–IIIa levels) and type 3 (levels of GP IIb–IIIa are normal but there is functional inactivity).[3] Our patient had type 1 disease.

Individuals typically present in infancy and childhood with haemorrhagic complications, varying from minimal bruising to severe and frequent haemorrhage. The most common manifestations are mucocutaneous and include epistaxis, purpura, gingival haemorrhage and menorrhagia.[4] Less common sites of haemorrhage are the gastrointestinal and genitourinary tracts. Heterozygotes tend to be asymptomatic.[5] Our patient presented with menorrhagia and recurrent epistaxis.

The disease is diagnosed by demonstrating absent platelet aggregation in response to physiological stimuli. Individuals have a normal platelet count and morphology. The absence of platelet GP IIb-IIIa can be demonstrated using monoclonal antibodies and flow cytometry.[6]

Localised bleeding can be managed using multiple methods; epistaxis is managed by cauterisation or nasal packing, while menorrhagia may be managed with tranexamic acid or hormonal methods such as the combined oral contraceptive pill.

The first line of management for severe haemorrhage is platelet transfusion. Approximately 15–30% of individuals become refractory to transfusion and a significant proportion develop antibodies against GP IIb–IIIa or HLA.[7] DDAVP has been postulated to shorten bleeding time in individuals with type 2 Glanzmann's, but efficacy has not been proven.[8]

Recombinant factor VIIa concentrate (Novoseven®) is increasingly being used in patients who are refractory to platelet transfusions or have antibodies. It enhances the deposition of deficient platelets on the subendothelial matrix to increase clot stability. It carries an approximate 4% risk of thromboembolism in general, but in Glanzmann thrombasthenia patients the risk is unknown.[9]

Plasmapheresis, using Protein-A sephorose to restore platelet efficiency, has been used to remove antibodies in these patients. It is, however, only available in a small number of specialist centres and is incongruous with routine care.[10]

Pregnancy in individuals with Glanzmann Thrombasthenia carries multiple risks. The risks of antepartum, peripartum and postpartum haemorrhage are all increased. Postpartum haemorrhage is frequently severe, and may occur up to 20 days following delivery.[11] To date, severe postpartum haemorrhage in these individuals has been treated effectively using large doses of uterotonics, plasmapheresis followed by platelet transfusions and recombinant factor VIIa.[12,13] One case report cited the use of oral prednisolone to treat secondary PPH.[3]

The main fetal risk arises from the presence of maternal HPA antibodies to platelet glycoproteins, classically IIb–IIIa in Glanzmann thrombasthenia. Our patient may have developed these antibodies when receiving platelet transfusions in the past while undergoing abdominal myomectomy or surgical management of miscarriage, as these platelets may have not have been HPA-matched. However, it is noted that in this case early in pregnancy, such antibodies were not detected, and hence are likely to have developed during exposure of fetal platelets. Maternal antibodies can cross the placenta, causing fetal thrombocytopenia, with a risk of subsequent fetal intracranial haemorrhage. Leticee et al. published a case series of eight women with type 1 Glanzmann thrombasthenia and GP IIb–IIIa antibodies. Of the eight babies, two died in utero secondary to intracranial haemorrhage, two babies were born with severe thrombocytopenia – one of whom died on day 2 of life and in the other four cases no bleeding was reported.[14]

In conclusion, managing pregnancy in individuals with Glanzmann thrombasthenia poses multiple challenges for both the mother and fetus. There is currently no reliable maternal parameter that can accurately predict fetal status or likelihood of NAIT. Management must be multidisciplinary, between Obstetric, Haematology and Anaesthetic teams, and preconception counselling is essential in order to ensure optimal maternal and fetal outcomes.

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Ethical approval

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Guarantor

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Contributorship

Ayona Wijemanne, Ingrid Watt Coote and Steve Austin cared for the patient and wrote the manuscript.

References

1. Dunsmore K. Intravenous immunoglobulin G therapy in fetal and neonatal alloimmune thrombocytopenia. *BioDrugs* 1997; 8: 265–272.
2. Nurden A. Glanzmann's thrombasthenia. *Orphanet J Rare Dis* 2006; 1: 10.
3. Madgudapathi C, Kannan S and Giri D. Glanzmann's thrombasthenia complicating pregnancy. *J Clin Case Rep* 2012; 2: 142.
4. Sebastiano C, Bromberg M, Breen K and Hurford MT. Glanzmann's thrombasthenia: report of a case and review of the literature. *Int J Clin Exp Pathol* 2010; 3: 443–447.
5. George JN, Caen JP and Nurden AT. Glanzmann's thrombasthenia: the spectrum of clinical disease. *Blood* 1990; 75: 1383–1395.
6. Malhotra N, et al. Pregnancy in a patient of Glanzmanns Thombasthenia. *Indian J Med Sci* 2006; 60: 3.
7. Laursen B and Jacobsen S. Transfusion problems in patients with Glanzmann's thrombasthenia. *Eur J Haematol* 1992; 49: 143–144.
8. Lethagen S and Nilson IM. DDAVP-induced enhancement of platelet retention: its dependence on platelet-von Willebrand Factor and the platelet receptor GPIIb/IIIa. *Eur J Haematol* 1992; 42: 7–13.
9. Kale A, Bayhan G, Yalinkaya A, et al. The use of recombinant factor VIIa in a primigravida with Glanzmann's thrombasthenia during delivery. *J Perinat Med* 2004; 32: 456–458.
10. Nurden AT, Pillois X and Wilcox DA. Glanzmann thrombasthenia: state of the art and future directions. *Semin Thromb Hemost* 2013; 39: 642–655.
11. Siddiq S, Clark A and Mumford A. A systematic review of the management and outcomes of pregnancy in Glanzmann's thrombasthenia. *Haemophilia* 2011; 17: e858–e869.
12. Sherer DM and Lerner R. Glanzmann's thrombasthenia in pregnancy: a case and review of the literature. *Am J Perinatol* 1999; 16: 297–301.
13. Shamsi TS, Hossain N, Soomro N, et al. Use of recombinant factor VIIa for massive postpartum haemhorrage: case series and review of literature. *J Pak Med Assoc* 2005; 55: 512–515.
14. Leticee N, Kaplan C and Lemery D. Pregnancy in mother with Glanzmann's thrombasthenia and isoantibody against GPIIb-IIIa: is there a foetal risk? *Euro J Obstet Gynecol Reprod Bio* 2005; 121: 139–142.