

Glanzmann's thrombasthenia during pregnancy complicated by large subchorionic hematoma managed with antifibrinolytics, human leukocyte antigen-matched platelet transfusion, and primary cesarean delivery: a case report



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A 29-year-old primipara with Glanzmann's thrombasthenia presented for prenatal care at 8 weeks of gestation. Pregnancy remained uncomplicated until 22 weeks of gestation when a subchorionic hematoma, measuring 5.8 × 4.1 × 6.7 cm, was diagnosed and managed outpatient. At 28 weeks of gestation, the subchorionic hematoma was significantly expanding to 11 × 13 × 3.7 cm (~30% of the placental surface). The patient was admitted for antepartum surveillance and steroid treatment. Fetal and maternal status were reassuring. At 36 weeks of gestation, there was active extravasation from the subchorionic hematoma, prompting interdisciplinary discussion with neonatal intensive care unit, blood bank, pharmacy, anesthesia, hematology, and the patient regarding her options. Immediate delivery risked platelet sensitization because of unavailable human leukocyte antigen-matched platelets. The patient opted for medical management with aminocaproic acid. At 37 weeks of gestation, she underwent a scheduled cesarean delivery. Human leukocyte antigen-matched platelets and additional aminocaproic acid were administered preoperatively. Intrapartum hemorrhage of 1200cc was controlled with uterotonics in addition to the above measures. Antifibrinolytics were continued. The neonate had an uncomplicated postpartum course. The patient had symptomatic anemia on postoperative day 1, which prompted red blood cell transfusion. Discharge was delayed until postoperative day 6 to further monitor her bleeding; oral antifibrinolytics were continued for 2 weeks. This case adds to the growing use of adjuvant medications, including antifibrinolytics such as aminocaproic acid and tranexamic acid, to reduce the reliance on platelet transfusion. This is critical for maintaining a favorable response to platelet transfusions and minimizing the risk of fetal neonatal alloimmune thrombocytopenia in current and subsequent pregnancies among women with lifelong bleeding disorders.

Keywords: aminocaproic acid, case report, Glanzmann's thrombasthenia, pregnancy, subchorionic hematoma

Glanzmann's thrombasthenia (GT), from *thrombasthenie* (weak

platelets), is an inherited autosomal recessive platelet disorder.¹ It is characterized by a deficiency of the $\alpha_{IIb}\beta_3$ integrin glycoprotein (chromosome 17) on the platelet membrane which is necessary for function.² There are 3 subtypes of GT; type I and type II are quantitative defects, with type I being the most severe, and type III is a qualitative defect. The estimated prevalence of 1 per 1 million is more pronounced in certain ethnic groups (including those from Jordan, Iraq, France, and South India) or groups with consanguinity.³

GT patients have normal platelet counts but increased bleeding time.⁴ Flow cytometry (glycoprotein IIb/IIIa complex) is the gold standard for diagnosis.^{4,5} Patients generally present in infancy or early childhood with mucosal bleeding (frequent bruising, petechiae, epistaxis, gingival or gastrointestinal bleeding, hematuria, or vaginal bleeding).³

Pregnancy increases platelet aggregation and levels of platelet stimulating factors.⁴ Despite these changes, the underlying platelet defect of GT still renders patients at high risk for hemorrhage. The standard first-line therapy for severe bleeding in GT is platelet transfusion. However, minimizing recurrent platelet exposure is important because 15% to 20% of GT patients eventually become refractory to transfusion because of alloimmunization.^{6,7} In addition, autoantibodies to platelets may also cause fetal or neonatal alloimmune thrombocytopenia (FNAIT) in current and subsequent pregnancies.⁷ In GT patients, the use of recombinant factor VIIa and antifibrinolytics, such as tranexamic acid (TXA) and aminocaproic acid (ACA), has increasingly demonstrated favorable outcomes and reduced transfusion requirements outside of pregnancy.⁴ This case reports the use of antifibrinolytics for the

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management of antepartum bleeding in a GT patient.

Case Report

A 29-year-old primipara with type I GT presented for prenatal care at 8 weeks of gestation without complications until a subchorionic hematoma (SCH), measuring $6.7 \times 5.8 \times 4.1$ cm (Figure 1), was diagnosed at 22 weeks and 2 days of gestation. She was managed as an outpatient, with serial weekly ultrasound examinations. The SCH significantly expanded to $13 \times 11 \times 3.7$ cm (~30% of the placental surface) at 28 weeks of gestation. She was admitted for antepartum surveillance and steroid treatment. Fetal and maternal status were reassuring. Hematology was already consulted. Antiplatelet antibodies were negative and her admission laboratory test results were unremarkable, as noted in the Table. Factor VIIa was reserved in the event of a major hemorrhage. The American Red Cross was contacted to assure the availability of human leukocyte antigen (HLA)-matched platelets. Delivery after 34 weeks of gestation was discussed with the patient given the chronic nature of her abruption and hematoma, but she declined and opted for expectant management until term.

At 36 weeks and 2 days of gestation, there was active extravasation and increased size of the SCH, measuring $17.4 \times 10.5 \times 7.8$ cm (Figure 2) (Supplemental Video). This prompted interdisciplinary discussion with maternal-fetal medicine (delivering provider) and neonatology specialists, the blood bank, pharmacy, anesthesia and hematology specialists, and the patient regarding her options. The team concluded that immediate delivery had a risk for platelet sensitization because the HLA-matched donor was out of town and thus unavailable. The patient opted for medical management. Oral ACA, on formulary at the hospital, was initiated at 4000 mg every 6 hours; the hematoma was stable in size without evidence of extravasation on repeat ultrasound examination every 3 to 4 days.

HLA-matched apheresis platelets were reserved and collected the day

before the patient's planned delivery at 37 weeks and 6 days of gestation. Despite being offered a trial of labor and counseled about the risks and benefits of abdominal surgery in the setting of platelet dysfunction or coagulopathy, the patient requested a primary cesarean delivery to mitigate the perceived risk of fetal complications. She underwent cesarean delivery with general anesthesia (because of the risk of unpredictable spinal hematoma in patients with platelet disorders). Preoperatively her platelet count was $132,000/\mu\text{L}$ and hemoglobin level 12.8 g/dL. An infusion of ACA at 1 g per hour was initiated 24 hours before surgery. She received a pack of single-donor, HLA-matched platelets 1 hour before surgery. She delivered a 3090-g male neonate with an Apgar score of 8 and 9 at 1 and 5 minutes, respectively. A ruptured retroplacental hematoma was noted on gross examination. Intrapartum hemorrhage of 1200cc was controlled with oxytocin, methergine, ACA infusion, and 1 additional platelet transfusion from the same donor. Immediately after delivery, the patient's platelet count decreased to $108,000/\mu\text{L}$, and her hemoglobin level was 6.5 g/dL; she received 2 units of packed red blood cells at this time. On postoperative day 1, symptomatic anemia prompted transfusion of 2 additional units of packed red blood cells. On postoperative day 2, the platelet count was $120,000/\mu\text{L}$ and hemoglobin level 10 g/dL. Although it was reserved in case of significant hemorrhage, she did not require factor VIIa. ACA was continued, and she was transitioned to oral ACA, once tolerating a diet. Discharge was delayed until postoperative day 6 to further monitor her bleeding; oral TXA of 1000 mg 4 times a day was continued on discharge to complete a total of 14 days of postpartum antifibrinolytic therapy.

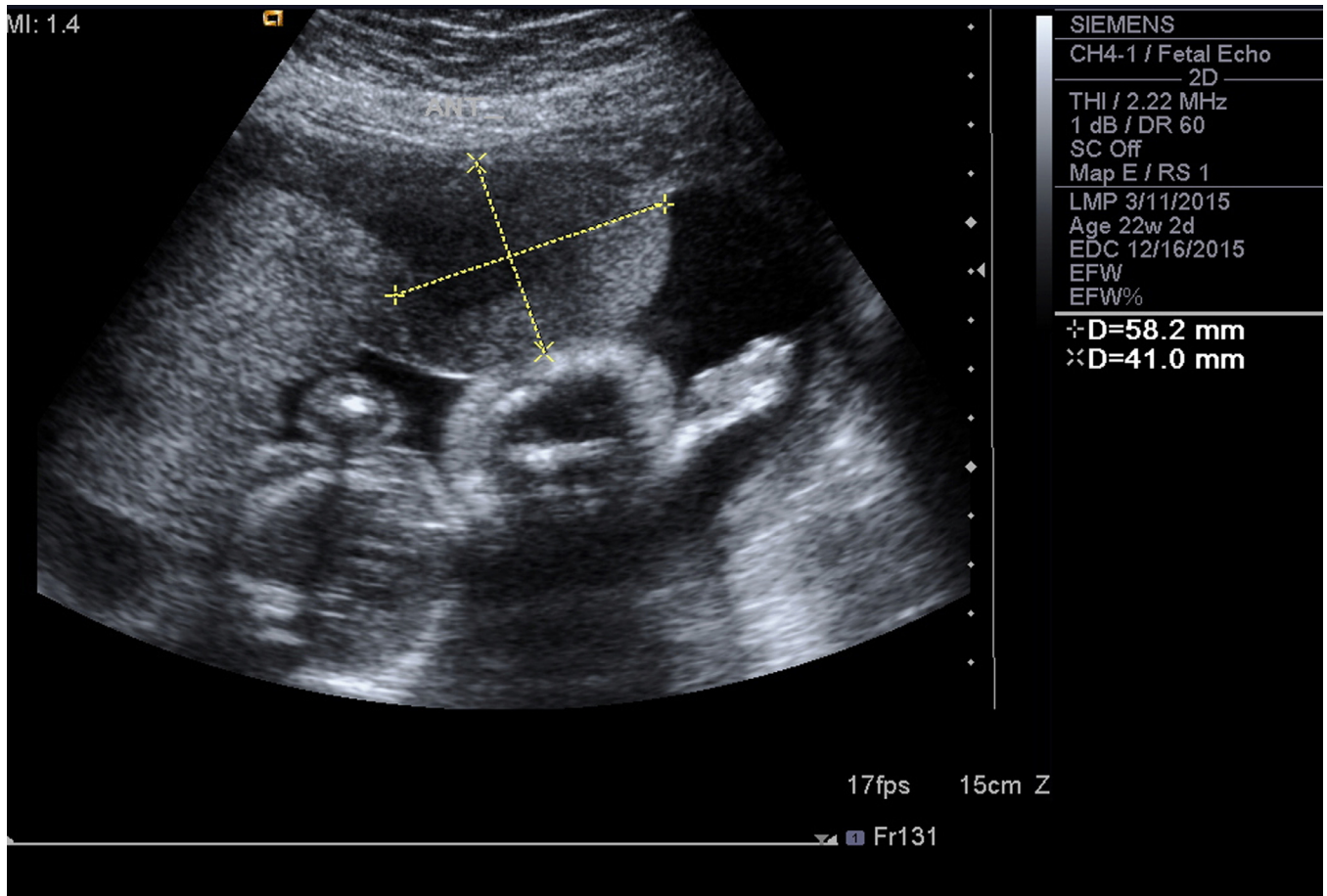
The neonate had an uncomplicated postpartum course and a normal platelet count of $264,000/\mu\text{L}$ on the first day of life. Placental pathology demonstrated a third-trimester placenta, measuring 508 g and $15 \times 15 \times 3$ cm, with mild meconium staining, few calcifications, and no other anomalies noted.

Comment

There are fewer than 100 cases of GT in pregnancy cited in literature.^{1,8} None of these cases describe the management of antepartum obstetrical bleeding using antifibrinolytics. In a systematic review of 40 cases of GT in pregnancy,⁹ antepartum bleeding was noted in about half of the cases that reported on the prenatal period. Most of the bleeding was not obstetrical in nature and included the following: 42% epistaxis, 28% urinary tract, 14% gingival, and only 14% vaginal bleeding (2 patients).⁸ None of the cases reported placental hematomas. Most cases of nonobstetrical bleeding resolved spontaneously; only some cases of epistaxis required platelet therapy. Both of the patients with vaginal bleeding were given multiple transfusions of HLA-matched platelets; 1 patient had a term neonate without issues, and the other had an intrauterine fetal demise at 31 weeks of gestation secondary to intracranial hemorrhage from FNAIT.²

Use of TXA has become ubiquitous for the treatment of postpartum hemorrhage, as supported by the World Health Organization recommendations and the World Maternal Antifibrinolytic Trial.^{10,11} Data on antifibrinolytics during pregnancy are limited to several studies from more than a decade ago, despite bleeding being associated with a 3 to 4 times increased risk of perinatal mortality.⁹ TXA during pregnancy has been used for vaginal bleeding, placental abruption, placenta previa, and before delivery.⁹ Twelve patients with vaginal bleeding (at 24–36 weeks of gestation) received 1 g of oral TXA 3 times a day, for 7 days or until delivery (in cases of persistent bleeding). All patients had stabilization of vaginal bleeding.¹² In a placental abruption cohort, 73 patients were treated, with only 6 patients in the antepartum period. These 6 patients had a mean gestational age of 30.2 weeks and received 1 g of oral TXA 4 times a day for an average of 5.8 weeks. There were no neonatal or thrombotic complications in this cohort.¹³ There were 2 pulmonary emboli in a retrospective cohort of 256 women with unspecified bleeding

FIGURE 1
Transabdominal ultrasound image of inferior edge of placenta



At 22 weeks and 2 days of gestation with subchorionic hematoma measuring $6.7 \times 5.8 \times 4.1$ cm. Image obtained at satellite clinic.

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disorders, but this was not significant when compared with the 4 cases of venous thrombosis (3 pulmonary emboli and 1 deep vein thrombosis) in the control group of 1846 patients (0.7% vs 0.2%, respectively; odds ratio, 3.6; 95% confidence interval, 0.7–17.8).¹⁴ One Russian randomized controlled trial, referenced in other reports, demonstrated a significant decrease in antepartum bleeding but has not been independently verified.⁹

TXA and ACA, both synthetic lysine analogs, are competitive inhibitors of plasminogen.¹³ Multiple studies with animal models and case reports in humans have demonstrated consistent

TABLE
Admission laboratory test results

Lab	Result
Hemoglobin	12.2 g/dL
Platelets	159 k/ μ L
aPTT	28 s
PT/INR	9.9/0.91 s
Platelet antibodies	IgG and IgM negative
Fibrinogen	356 mg/dL

aPTT, activated partial thromboplastin time; Ig, immunoglobulin; INR, international normalized ratio; PT, prothrombin time.

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FIGURE 2
Transabdominal ultrasound image of inferior edge of placenta



At 36 weeks and 2 days of gestation with subchorionic hematoma measuring $17.4 \times 10.5 \times 7.8$ cm and active extravasation, characterized by swirling and motion within the clot, with no leakage outside the defined hematoma. At this time appropriate-for-gestational-age fetus, with normal umbilical artery dopplers performed (Supplemental Video 1).

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transfer across the placenta.⁹ The half-life of TXA is about 1 to 1.5 hours and the fetal concentration of TXA is similar to maternal levels at delivery.¹³ TXA is noted to be 10 times more potent than ACA.¹⁵ Less data are available on the use of ACA in pregnancy, but a series of studies on its use in 92 patients during threatened abortion failed to demonstrate any risks to the fetus or mother.¹⁶ There remains no general recommendation on when to use antifibrinolytics for bleeding in pregnancy.¹⁷

Immediate concerns about maternal hemodynamic stability were balanced with the longitudinal sequelae of frequent platelet transfusions. Historically, the standard of care for bleeding in GT was platelet transfusion, but there are increasing data to support the use of antifibrinolytics for minor bleeding and

recombinant factor VIIa for major bleeding.^{3–5,18,19}

GT patients are susceptible to delayed postpartum hemorrhage, with a median time of 10 days, but up to 12 weeks postpartum.⁸ Antifibrinolytics are recommended for 2 weeks postpartum.⁵ TXA has not been demonstrated in breast milk and is compatible with lactation.⁹ No data are available for the effects of ACA on lactation.¹⁶

The strengths of this report stem from providing patient and provider perspectives on the successful management of bleeding in the antepartum and postpartum periods with antifibrinolytics in patients with underlying platelet disorders. Reproductive-aged women with GT theoretically have increased lifetime risks of

platelet sensitization. Therefore, medical management with TXA or ACA allows prolongation of pregnancy and prevention of platelet antibody formation, which lead to maternal and neonatal risks. The study is limited by its nature as a case report.

Conclusion

Successful management of chronic placental abruption, subchorionic hematoma, and postpartum hemorrhage with antifibrinolytics is possible for patients with underlying platelet disorders, specifically GT. ACA was used to control antenatal retroplacental hemorrhage and avoid recurrent platelet transfusions, which have been associated with FNAIT and fetal death. The neonate was delivered at term via cesarean

delivery with favorable outcomes for both mother and neonate. Both platelet transfusions were single-donor, HLA-matched, and avoided until delivery. ■

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.xagr.2021.100031](https://doi.org/10.1016/j.xagr.2021.100031).

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