CLINICAL VIGNETTE

A Patient with Glanzmann Thrombasthenia Presenting for Emergency Eye Surgery

Peter G. Lee, MD and Elizabeth Tsai, MD

Case

A 30-year old male with past medical history of Glanzmann Thrombasthenia (GT) and left eye traumatic glaucoma presented to the emergency department with sudden onset of intense left eye pain and retro-orbital headache. His left eye pain quickly worsened with associated double vision and loss of color discrimination. The patient previously had undergone placement of a left eye Ahmed Glaucoma valve 20 years earlier after being struck with a baseball and developing traumatic glaucoma. Ophthalmology evaluated the patient and diagnosed acute angle closure glaucoma from possible aqueous misdirection versus complete blockage of the drainage site. He was subsequently scheduled for urgent pars planus vitrectomy with lensectomy of the left eye.

On interview, patient stated he was diagnosed as a child with Glanzmann Thrombasthenia and had always required hemostatic agents prior to surgical procedures. He received aminocaproic acid prior to his Ahmed Glaucoma Valve placement 20 years ago and more recently received recombinant activated human factor VII (rFVIIa) for wisdom teeth extractions. His only significant bleeding complication was an upper gastrointestinal bleed in the setting of aspirin use requiring multiple transfusions. He reported no other life-threatening bleeds. He commonly experienced less severe mucocutaneous bleeding from his gums and epistaxis.The patient was followed regularly by an outside Hematologist who prescribed aminocaproic acid 1 gram orally every 4 hours as needed for minor bleeding.

Physical exam was significant for mucosal bleeding from the gums but was otherwise unremarkable with no petechiae or ecchymoses noted. Vital signs were within normal limits and airway exam was Mallampati Class 3 with normal thyromental distance and neck range of motion.

Laboratory studies were significant for microcytic anemia, hemoglobin 10.5 grams/deciliter. Platelet concentration, and coagulation studies (prothrombin time, INR, partial thromboplastin time), were all within normal limits.

Preoperative hematology consultation was obtained for management of potential bleeding complications from patient's GT. Hematology recommended administration of rFVIIa, 90 micrograms/kilogram (mcg/kg) intravenously (IV) one hour prior to procedure given ongoing mucosal oozing from gums and urgent need for surgery. Alternatively, if rFVIIa was not available, tranexamic acid, 10 milligrams/kilogram (mg/kg) IV could be used prior to surgery. Post-procedural recommendation was tranexamic acid 10 mg/kg IV 2-4 hours post procedure with a subsequent dose of tranexamic acid 10 mg/kg IV 8 hours following first dose.

The patient was given rFVIIa 6mg IV in the preoperative holding area and then brought to the operating room and transferred to the operating room table with placement of standard anesthesia monitors. Supplemental oxygen was provided with a nasal cannula at 3 liters/minute. After routine surgical time out, patient was given midazolam 2 mg and fentanyl 100 mcg IV for moderate sedation. Opthalmology applied topical anesthesia 0.5% tetracaine, 2 drops, to the left eye and performed a sub-tenon block for surgical anesthesia with 1:1 mixture of 2% lidocaine and 0.75% bupivacaine, cataract extraction, synechiolysis, 23 gauge pars plana vitrectomy, and air fluid exchange of the left eye. Case duration was 85 minutes and a total of 6mg of midazolam and 300mcg of fentanyl was incrementally dosed during the case to maintain moderate IV sedation. Lactated ringer's 500ml IV was administered with estimated blood loss was 5ml.

Patient was taken to the post-anesthesia care unit where he was notably awake and alert with minimal pain in his left eye. Post-anesthesia care stay was unremarkable and he received tranexamic acid 10mg/kg IV 2 hours post-surgery and a repeat dose 8 hours later as recommended by Hematology. Post-operative day 1, he had corneal blood staining and persistent elevated intraocular pressure. Repeat surgery with anterior chamber washout to attempt to reestablish patency of Ahmed valve was discussed but ultimately decided against because of minimal expected benefit to patient's baseline poor vision and increased risk of complications with additional surgery to the affected eye. Left eye glaucoma was medically managed with eye drops and he was discharged home with outpatient follow up with Ophthalmology clinic.

Discussion

Glanzmann thrombasthenia (GT) is a rare bleeding disorder caused by a quantitative or qualitative defect of platelet membrane glycoprotein IIb/IIIa, a fibrinogen receptor required for platelet aggregation.[1] Platelets fail to aggregate in response to stimuli because the receptor is missing or nonfunctional, resulting in disrupted platelet function and diminished clot

retraction.[2] This is clinically characterized by a lifelong bleeding tendency with an elevated risk of fatal bleeding episodes. The disease is hereditary, autosomal recessive inheritance or acquired through autoimmunization or alloimmunization. The estimated incidence is 1:1,000,000.[3]

Spontaneous and unpredictable bleeding episodes are the hallmark of the disease. The bleeding phenotype is heterogeneous, ranging from mild to severe. Although GT is classified according to platelet membrane αIIbβ3 protein levels (ie, types I, II, and variant), neither classification nor specific genetic mutation correlate with bleeding phenotype as the severity of bleeding may differ even among patients with the same genetic mutation.[4] Overall, GT is considered a severe bleeding disorder, and serious bleeding may be fatal, although overall the mortality rate in GT is relatively low.[5]

Diagnosis is based on presence of normal platelet count, prolonged bleeding time, prolonged platelet function analysis time, failure of platelets to aggregate on light transmission aggregometry, and/or confirmation of specific genetic mutations.[3]

Symptoms often manifest shortly after birth, and most cases are diagnosed before age 5 years. Common symptoms include epistaxis, gingival bleeding, purpura, ecchymoses, and menorrhagia. Severe bleeding after minor trauma or surgery may occur.[3]

Treatment is typically not required on a daily basis and only when necessary to control spontaneous bleeding episodes or prior to surgical procedures. First line treatment for mild to moderate bleeding episodes such as epistaxis or gingival bleeding is local treatment with compression, nasal packing, or topical thrombin. Second line treatment if local measures are inadequate are antifibrinolytics (ie: tranexamic acid) and are indicated for prophylaxis for minor surgical procedures. Third line treatment with platelet transfusion and/or rFVIIa is indicated if bleeding is severe or persists despite use of local measures and antifibrinolytics.[1]

Although platelet therapy is the current standard treatment for severe or refractory bleeding in GT, potential risks include allergic and immune reactions, blood-borne pathogen transmission, and immunization. If possible, HLA-matched platelets should be used to avoid platelet alloimmunization and subsequent therapeutic failure of platelet transfusion. If HLA-matched platelets are not available, patients should receive leukocyte-reduced platelets to reduce the rate of alloimmunization.[3]

Currently rFVIIa is approved for GT with refractoriness to platelet transfusions (with or without antibodies to platelets). However, data from the Glanzmann's Thrombasthenia Registry (a study of 218 GT patients) reveals that rFVIIa was frequently and effectively used off-label for nonsurgical and surgical bleeds regardless of platelet antibodies/refractoriness status.[1] At therapeutic concentrations, rFVIIa binds to activated platelets and directly activates Factor X to Factor Xa, resulting in thrombin generation. Thrombin converts fibrinogen to fibrin, enhances GT platelet adhesion and aggregation, and leads to primary hemostasis. Additionally, thrombin acts in stabilizing the clot by activating a fibrinolysis inhibitor which prevents clot lysis.[1] A study of rFVIIa in patients with severe hemophilia in the nonbleeding state, found mean terminal half-life of ~2.6 hours after a single 90 μg/kg dose.[6]

Surgery can be very challenging in patients with GT and requires close cooperation between the surgeons, hematologists, and anesthesiologists. Careful consideration of the appropriate perioperative bleeding prophylaxis and treatment must be considered in light of the planned surgery and patient's baseline medical condition. In the presented case, at the recommendation of our Hematology service, rFVIIa was effectively administered prior to the operation and tranexamic acid, an antifibrinolytic, was administered post operatively for bleeding prophylaxis. Potential bleeding complications from airway instrumentation and endotracheal intubation was avoided by performing the surgery with local anesthesia and IV sedation versus general endotracheal anesthesia. NSAIDs which are commonly used for postoperative analgesia were strictly avoided given their antiplatelet activity. If endotracheal intubation is necessary, video laryngoscopy should be considered to facilitate a non-traumatic laryngoscopy and intubation.

GT patients who are pregnant present additional challenges. They are at increased risk for intrapartum and postpartum hemorrhage and require bleeding prophylaxis with vaginal delivery.[3] Labor epidural and neuraxial anesthesia, the typical anesthesia for cesarean sections, should be avoided due to the increased risk neuraxial bleeding.

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