Pediatric Anesthesia and Critical Care Journal 2015;3(2):140-144
doi:10.14587/paccj.2015.27

PACCJ

Perioperative care of an adolescent with platelet storage pool disorder

K. M. Miller[1], J. M. Ruda[2], J. D. Tobias[3]

[1]The Ohio State University College of Medicine, Columbus, Ohio, USA
[2]Department of Otolaryngology and Head and Neck Surgery, Nationwide Children's Hospital and The Ohio State University, Columbus, Ohio, USA
[3]Department of Anesthesiology & Pain Medicine, Nationwide Children's Hospital and the Ohio State University, Columbus, Ohio, USA

Corresponding author: [1,2]J.D. Tobias, Department of Anesthesiology & Pain Medicine, Nationwide Children's Hospital, Columbus, Ohio, USA. Email: Joseph.Tobias@Nationwidechildrens.org

Key points

1. Platelet storage pool defect resulting from deficient delta granules leads to a bleeding tendency due to decreased secondary platelet aggregation related to the decreased release of ADP and other molecules that lead to the secondary aggregation of platelets.
2. Options to prevent or control surgical bleeding include DDAVP, antifibrinolytic agents, and the use of platelet transfusions.
3. Regional anesthetic techniques are generally contraindicated making general anesthesia necessary for the majority of surgical procedures.
4. Avoidance of medications (non-steroidal anti-inflammatory agents) that affect platelet function is mandatory.

Abstract

Bleeding due to platelet dysfunction can result from quantitative or qualitative disorders. Qualitative disorders may affect any of the many steps involved in platelet adhesion, activation, and aggregation. We present an adolescent with a qualitative platelet disorder storage pool defect, which results in abnormalities of secondary platelet aggregation and the potential for excessive bleeding following minor trauma or a surgical procedure. The normal function of platelets and their role in coagulation is reviewed, qualitative platelet disorders discussed, and the perioperative treatment of such patients presented.

Keywords: Platelet storage pool deficiency, platelet dysfunction, desmopressin, antifibrinolytic agent.

Introduction

Normal function of the coagulation cascade involves both a cellular (platelet) and a protein (coagulation factor) component. In the normal state, coagulation begins almost immediately following injury to a blood vessel as there is damage to the endothelium with exposure of tissue factor. The endothelial damage results in activation of platelets and the initiation of the coagulation cascade with binding of tissue factor to plasma Factor VII, which ultimately leads to fibrin formation. Additional coagulation factors or clotting factors beyond Factor VII respond in a complex cascade to form fibrin strands, which strengthen the platelet plug. Defects in any step of the process may lead to bleeding dyscrasias, which may present spontaneously or following incidental or surgical trauma. Although routine monitoring of coagu-

lation function is not generally necessary prior to surgical procedures, patients with a personal or family history of bleeding or bruising may warrant further investigation.[1] We present a 17-year-old with a history of a platelet storage pool defect who presented for adenotonsillectomy. The normal function of platelets is reviewed, the pathophysiology of functional platelet disorders presented, and perioperative care of such patients discussed.

Case report

Institutional Review Board approval for publication is not required for single case reports at Nationwide Children's Hospital (Columbus, Ohio). A 17-yr-old, 63.1 kg adolescent presented for adenotonsillectomy and inferior turbinate coblation/out-fracture due to recurrent tonsillitis and chronic nasal obstruction from inferior turbinate hypertrophy. His past medical history was significant for a diagnosis of platelet storage pool deficiency, asthma, recurrent tonsillitis and Ehlers-Danlos syndrome type III. When one of his siblings was diagnosed with a platelet storage pool deficiency, his mother expressed concern that he too could have the deficiency as he had frequent episodes of epistaxis and easy bruising. The diagnosis was confirmed by transmission electron microscopy, which demonstrated that platelets from his peripheral blood had an average of 3.11 delta granules per platelet, indicating a mild delta granule storage pool deficiency. Prior to the diagnosis, the patient had experienced an unusual amount of bleeding during both his circumcision and a groin injury requiring stitches. The family history was negative for adverse anesthetic reactions and was positive for a vague history of bleeding disorders on his maternal side. The patient was held *nil per os* for 6 hours prior to surgery. On arrival to the pre-anesthesia holding area, in consultation with our pediatric hematology consultant, a peripheral intravenous cannula was placed. Desmopressin (19 µg) was administered intravenously over 1 hour. Following this, he was transported to the operating room and standard monitors were placed. Premedication was provided by midazolam (2 mg). Anesthesia was induced with propofol (3 mg/kg), lidocaine (60 mg), dexmedetomidine (20 µg), and fentanyl (100 µg). Endotracheal intubation was facilitated by providing neuromuscular blockade with succinylcholine (100 mg). Maintenance anesthesia included sevoflurane in air/oxygen titrated to maintain the bispectral index at 40-60 to ensure amnesia. Neuromuscular blockade for the procedure was provided by rocuronium (20 mg). No intraoperative complications were reported. Total estimated blood loss was 10 mL. Fluids administered included 700 mL of Lactated Ringers. Prophylactic anti-emetic therapy included ondansetron (8 mg) and dexamethasone (4 mg). Postoperative analgesia was provided by hydromorphone (1 mg) and acetaminophen (1000 mg). After the procedure, residual neuromuscular blockade was reversed with neostigmine and glycopyrrolate. The patient's trachea was extubated in the operating room and he was transported to the post-anesthesia care unit (PACU). The remainder of his perioperative stay was uncomplicated. Postoperative pain was managed with oral hydrocodone-acetaminophen. The antifibrinolytic, ε-aminocaproic acid (Amicar®) (3,250 mg), was administered by mouth every 6 hours. Two additional doses of desmopressin (19 µ) were administered during the initial 24 hour postoperative period after rechecking his basic blood chemistries including sodium, BUN, calcium, creatinine, potassium, chloride, and carbon dioxide, all which were within normal ranges. His total perioperative stay was 33 hours. He was discharged with hydrocodone-acetaminophen for pain, oxymetazoline 0.05% nasal spray as needed for nosebleeds and ε-aminocaproic acid to complete a 10-day course. His postoperative course was unremarkable.

Discussion

Platelets, an essential component in blood coagulation, are produced from megakaryocytes, which comprise approximately 0.05-0.1 percent of bone marrow cells. The fragmentation and release of platelets from the megakarocytes is controlled by the hormone, thrombopoietin.

The maturation time of platelets is approximately 4-5 days. They range in size from 2-4 μm with the normal concentration in blood varying from 150,000 to 400,000 cells per μl of blood.[2]

As platelets circulate within the vasculature, endothelial injury results in platelet activation and their adherence to the site of injury. This initial adhesion to the endothelium at the site of injury involves von Willebrand factor (vWF) and the platelet surface protein glycoprotein Ib. The platelet-endothelium interaction causes a transformational change in the shape of the platelet leading to the secondary aggregation of other platelets through platelet surface receptors known as glycoprotein IIb-IIIa thereby initiating the coagulation cascade. When platelets are activated, they release numerous molecules from cytoplasmic granules. These granules are classified according to the molecules released.[3] Alpha granules contain numerous growth factors including insulin-like growth factor 1, TGF-α, TGF-β, platelet-derived growth factors, platelet factor 4 as well as factor V, fibronectin, and von Willebrand factor. Dense granules, also known as delta granules, secrete very small molecules including adenosine triphosphate (ATP), adenosine diphosphate (ADP), guanosine diphosphate (GDP), serotonin (5-HT), calcium, and magnesium.[4] Gamma granules are similar to lysosomes and contain several hydrolytic enzymes. Lambda granules contain molecules involved in clot resorption, which are needed during the later stages of vessel repair.

Disorders of platelet function can result from quantitative or qualitative disorders.[4-6] Qualitative disorders may affect any of the many steps involved in platelet adhesion, activation, and aggregation (table 1). Our patient had an inherited qualitative platelet disorder (storage pool defect) related to deficient delta granules, which would result in decreased secondary platelet aggregation due to decreased release of ADP and other molecules that lead to the secondary aggregation of platelets. This deficiency would predispose to excessive bleeding which may occur spontaneously or following minor trauma or a surgical procedure. For these patients, there is a range of bleeding tendencies from mild to severe based on the severity of the deficiency. As was the case with our patient, daily therapy is not generally required as bleeding generally occurs only with traumatic or surgical injury. However, these patients should avoid contact sports, be vaccinated against hepatitis A and B, and are advised not to take non-steroidal anti-inflammatory drugs.[7]

In patients presenting for any type of surgical procedure where there is a risk of bleeding, proper functioning of the hematologic system is essential in order to promote a safe and successful perioperative stay. A personal and family coagulation and bleeding history is essential during the preoperative evaluation. Excessive bleeding may occur spontaneously or following a relatively minor traumatic event or surgical procedure such as circumcision. Routine evaluation of coagulation function is generally not recommended in the absence of a family or personal history suggestive of a bleeding tendency.[1] For patients with a previously diagnosed disorder, preoperative laboratory evaluations and the development of a plan between the surgeon, anesthesiologist, and hematologist are essential. As indicated, laboratory testing including prothrombin time (PT), activated partial thromboplastin (aPTT), platelet count, and platelet function analysis can be performed to provide to assess the patient's hemostatic function.[8] The primary issues related to perioperative care include the perioperative administration of medications to augment the coagulation process, the administration of blood products or factors to correct the coagulation defect, and a relative contraindication to the use of regional anesthesia given the potential for bleeding. As such, general anesthesia is generally recommended for surgical procedures.

Perioperatively, there are 3 basic treatments for patients with platelet storage pool disorders: 1) l-deamino-8-d-arginine vasopressin or desmopressin (DDAVP), 2) ε-antifibrinolytic agents including aminocaproic acid, and 3) platelet transfusions.[8] The treatment options will

depend not only on the patient's response, but also the magnitude of the surgical procedure and the potential risk and consequences of bleeding. Patients with mild disease should be treated with DDAVP, instead of blood products. DDAVP can be administered intravenously, subcutaneously or intranasally although the intravenous route is generally chosen for perioperative care. Dosing recommendations include 0.3 μg/kg administered over 60 minutes to avoid hemodynamic effects including hypotension.[9] DDAVP can effectively reverse the platelet storage pool defects by increasing the release of von Willebrand factor antigen and Factor VIII from endothelial cells thereby increasing platelet aggregation.[10,11] No effect is noted on the actual platelet count, merely their function. For minor surgical procedures, desmopressin can limit the need for allogeneic blood products and the associated risk to the patient. Mild adverse effects include tachycardia, headache, cutaneous flushing, and fluid retention. More adverse effects include hypotension, hyponatremia, and seizures. Hyponatremia occurs most commonly in patients receiving hypotonic intravenous or oral fluids. Given these concerns, serum sodium levels and osmolality should be monitored if multiple doses are administered. Despite the augmentation of platelet function, the incidence of thrombotic complications is rare.

Anti-fibrinolytic agents, including ε-aminocaproic acid or tranexamic acid, may also be effective in preventing bleeding, specifically in oral and otolaryngology surgery due to the high concentration of proteolytic enzymes that are present in the saliva. These two agents prevent clot degradation by binding to the lysine residue of plasminogen and blocking its conversion to plasmin which acts to degrade fibrin.[12] Both agents are available in intravenous and oral formulations. The most common side effects of the anti-fibrinolytic drugs are gastrointestinal symptoms including nausea or diarrhea. These symptoms typically resolve with dose reduction. There have also been rare reports of thrombotic events. However, none of these published reports were in pediatric-aged patients. In patients with severe platelet storage pool disorders or during major surgical procedures or trauma, additional therapies may be needed in addition to DDAVP and antifibrinolytic agents. In such patients, the use of allogeneic blood products including platelet transfusions may be required.[13-15]

In summary, when preparing patients with platelet storage pool disorders for perioperative care, the options to prevent or control bleeding include DDAVP, the antifibrinolytic agents, and the use of platelet transfusions. In patients with mild to moderate disease, bleeding can usually be prevented by meticulous surgical technique and the adjuvant use of DDAVP and an anti-fibrinolytic agent. Given the potential for bleeding, regional anesthetic techniques are generally contraindicated making general anesthesia necessary for the majority of surgical procedures. Adequate vascular access should be obtained to allow for the administration of blood and blood products as needed. Strict attention to the potential effects of medications on platelet function is suggested. The use of non-steroidal anti-inflammatory agents is contraindicated given their potent effect on platelet function. Postoperative monitoring to ensure adequate hemostasis and absence of bleeding complications may be indicated.

References

1. Burk CD, Cohen AR, Miller L, Handler SD. Preoperative history and coagulation screening in children undergoing tonsillectomy. Pediatrics 1992; 89:691-5.
2. Machlus KR, Thon JN, Italiano JE. Interpreting the developmental dance of the megakaryocyte: A review of the cellular and molecular processes mediating platelet formation. Br J Haematol 2014;165:227-36.
3. Whitehart S. Platelet granules: Surprise packages. Blood 2011;118:1190-1.
4. Krishnegowda M, Rajashekaraiah V. Platelet disorders: An overview. Blood Coagul Fibrinolysis 2015;26:479-91.
5. Orfanakis A, DeLoughery T. Patients with disorders of thrombosis and hemostasis. Med Clin N Am 2013;97:1161-80.
6. White JG. Inherited abnormalities of the platelet membrane and secretory granules. Hum Pathol 1987;18:123-39.
7. Alamelu J, Liesner R. Modern management of severe platelet function disorders. Br J Haematol 2010;149:813-23.
8. Hume HA, Limoges P. Perioperative blood transfusion therapy in pediatric patients. Amer J Therap 2002;9:396-405.
9. Özgönenel B, Rajpurkar M, Lusher JM. How do you treat bleeding disorders with desmopressin? Postgraduate Med J 2007;83:159-63.
10. Sakariassen KS, Cattaneo M, van der Berg A, et al. DDAVP enhances platelet adherence and platelet aggregate growth on human artery subendothelium. Blood 1984;64:229-36.
11. Rao AK, Ghosh S, Sun L, Yang X, Disa J, Pickens P, Polansky M. Mechanisms of platelet dysfunction and response to DDAVP in patients with congenital platelet function defects. A double-blind placebo-controlled trial. Thromb Haemost 1995;74:1071-8.
12. Ortmann E, Besser MW, Klein AA. Antifibrinolytic agents in current anaesthetic practice. Br J Anaesth 2013;111:549-63.

O'Brien, S H.: Common management issues in pediatric patients with mild bleeding disorders. Semin Thromb Hemost 2012;38:720-6.

Seligsohn U. Treatment of inherited platelet disorders. Haemophilia 2012;18:161-5.

Martlew VJ. Perioperative management of patients with coagulation disorders. Br J Anaesth 2000;84:446-55.