Anesthetic Care of a Patient With Bernard-Soulier Syndrome for Posterior Spinal Fusion

Sushmitha S. Boppana, Brian Hall, Ashley Beaujon, Dmitry Tumin, Joseph D. Tobias

Abstract

Bernard-Soulier syndrome (BSS), a rare autosomal recessive disorder first identified in 1948, is characterized by excessive and prolonged bleeding due to thrombocytopenia and platelet dysfunction with increased platelet size and deformability. The primary defect in BSS involves the glycoprotein (GP) Ib-IX-V complex, which is important in initiating platelet aggregation and thrombosis after vascular injury by facilitating the adhesion of platelets to von Willebrand factor. The coagulation defect in BSS can lead to significant bleeding during traumatic injury or surgical intervention. We present a 17-year-old adolescent with BSS who presented for posterior spinal fusion for idiopathic scoliosis. Previous reports of peroperative care of patients with BSS are reviewed and options for anesthetic care including peroperative control of the coagulation defect are presented.

Keywords: Bernard-Soulier syndrome; Coagulation; Posterior spinal fusion; Platelet function

Introduction

Bernard-Soulier syndrome (BSS), a rare autosomal recessive disorder, was first identified in 1948 [1]. It is characterized by excessive and prolonged bleeding due to thrombocytopenia and platelet dysfunction with increased platelet size and deformability [2]. Patients with BSS have a defect in or complete lack of the key glycoprotein (GP) Ib-IX-V complex, normally found on the surface of platelets. The GPIb-IX-V is important in initiating platelet aggregation and thrombosis after vascular injury by facilitating the adhesion of platelets to von Willebrand Factor (vWF), which is exposed on the vascular subendothelium after blood vessel injury. The binding of GPIb-IX-V to vWF results in a decrease in velocity of platelets as they move past damaged vessel walls and is critical in the process of initiating thrombosis to repair damaged vasculature [2, 3]. In addition to mediating adhesion of platelets to the blood vessel wall at sites of vascular injury by binding vWF, the complex facilitates platelet activation at low concentrations of thrombin, which may have roles in the platelet formation and turnover given that BSS is associated with decreased number and abnormal size. The lack of or defect in the functioning of GPIb-IX-V results in a compromised ability to initiate platelet adhesion and aggregation resulting in a bleeding diathesis [4]. Diagnosis is confirmed by platelet function testing with lack of platelet aggregation in response to ristocetin. We present a 17-year-old adolescent with BSS who presented for posterior spinal fusion for idiopathic scoliosis. Previous reports of peroperative care of patients with BSS are reviewed and options for anesthetic care including correction of the coagulation defect are presented.

Case Report

Institutional Review Board approval is not required at Nationwide Children’s Hospital (Columbus, OH, USA) for the presentation of single case reports. The patient was a 17-year-old, 70.9 kg girl who presented for posterior spinal fusion to treat adolescent idiopathic scoliosis. Her past medical history was positive for BSS, diagnosed at 3 years of age on platelet function testing for presentation of easy bruising and excessive bleeding. She also had been diagnosed with Ehlers-Danlos syndrome, diagnosed at age of 9 years with genetic testing and idiopathic scoliosis. Due to the BSS, she has macrothrombocytopenia with a baseline platelet count in the 50,000 - 70,000/ mm³. Her past surgical history was positive for one orthodontic procedure that did not involve anesthesia and resulted in no complications. Although prior platelet transfusions had resulted in an inadequate increase in her platelet count, work-up for platelet specific antibodies was negative. Her medications at the time of surgery included tranexamic acid (1,300 mg PO TID) to control menstrual bleeding, celecoxib (100 mg...
Anesthesia and Bernard-Soulier Syndrome

PO BID) for menses-associated pain, an oral probiotic and a benzoyl peroxide 10% topical wash. Physical examination revealed a well-nourished and well-developed young woman in the 85th percentile for weight and 89th percentile for height. She denied any recent health concerns and her vital signs were unremarkable. Her airway examination revealed a Mallampati class I airway with a thyromental distance greater than three fingerbreadths. Her cardiorespiratory examination was unremarkable. She was eager to proceed as prior posterior spinal fusion (PSF) surgery, scheduled 3 months earlier, and was cancelled due to inadequate response to two platelet transfusions, resulting in a platelet count of 74,000/mm³, which did not meet the desired threshold of 100,000/mm³. Given the inadequate response to previous platelet transfusions, after hematology consultation, a plan was devised to further address these issues perioperatively and her surgical procedure was rescheduled. The platelet count the day prior to surgery was 72,000/mm³ and she received one unit of pheresed platelets, which increased her platelet count to 78,000/mm³. Other coagulation parameters including prothrombin time (PT), partial thromboplastin time (PTT) and international normalized ratio (INR) were within normal limits. Due to previous issues with a limited response to platelet transfusions, it was decided to monitor in vivo coagulation function using the rotational thromboelastogram (ROTEM®). The values were within normal limits except for a prolongation of the clot formation time (CFT). The patient was kept nil per os for 6 h before being transported to the operating room following premedication with intravenous midazolam (2 mg). Routine American Society of Anesthesiologists monitors were placed followed by anesthetic induction with propofol (200 mg), lidocaine (100 mg) and sufentanil (20 µg). Endotracheal intubation was facilitated by the administration of rocuronium (65 mg). Following anesthetic induction, two large bore peripheral intravenous cannulas and an arterial cannula were placed. To facilitate neurophysiological monitoring per our usual protocol, maintenance anesthesia included desflurane titrated to maintain the bispectral index at 50 - 60 and a sufentanil infusion adjusted from 0.1 - 0.3 µg/kg/h to maintain the mean arterial pressure at 55 - 65 mm Hg [5]. Maintenance anesthesia was supplemented by continuous infusions of lidocaine and esmolol. Prior to the start of the surgical procedure, a second unit of pheresed platelets was infused along with a single dose of recombinant factor VIIa (1 mg). The dosing of rFVIIa was repeated every 2 - 3 h intraoperatively. Tranexamic acid was administered intraoperatively (loading dose of 50 mg/kg followed by a continuous infusion of 5 mg/kg/h during the procedure). The ROTEM® was followed during the perioperative course and remained at baseline except for a persistent mild elevation of the CFT. Intraoperatively, surgical hemostasis was adequate as judged by the surgical team. No allogeneic packed red blood cells were administered. Intraoperative cell salvage was used with the return of 350 mL of salvaged and washed blood. The surgical procedure was accomplished in 4 h 25 min with an estimated blood loss of 900 mL. At the completion of the procedure, the patient’s trachea was extubated and she was transferred to the post-anesthesia care unit and then to the pediatric ICU for 24 h. Her postoperative hemoglobin remained stable at 9 - 10 g/dL. On postoperative day 1, she received one unit of pheresed platelets for a platelet count of 56,000/mm³. Postoperatively, á-amino caproic acid (Amicar) was administered intravenously and then by mouth for a total of 10 days. No other allogeneic blood products were administered during the postoperative course and although her platelet count decreased to a nadir of 39,000/mm³, there was no clinically concerning bleeding and her ROTEM® values remained stable. Her postoperative course was unremarkable and she was discharged to the inpatient ward on postoperative day 1 and home on postoperative day 5.

Discussion

BSS is a rare inherited disorder affecting platelet function with decreased aggregation, decreased numbers and decreased function. As such, excessive bleeding may occur spontaneously, following trauma or during surgical procedures. Although the glycoprotein defect results in the ineffective interaction of vWF with the vascular endothelium, the disorder cannot be corrected by the administration of vWF and other strategies are needed. Our case was unique in two respects including our patient’s refractory state to the administration of allogeneic platelets with minimal increase in the platelet count. Despite this, work-up did not reveal platelet antibodies or other issues that might be amenable to corticosteroid therapy or plasmapheresis.

While the mainstay remains the administration of allogeneic platelets, adjunctive strategies have included the administration of antifibrinolytic agents (ε-amino caproic acid or tranexamic acid), recombinant factor VIIa and 1-deamino-8-d-arginine vasopressin (DDAVP). To date, there are a limited number of reports in the literature regarding the perioperative care of pediatric patients with BSS (Table 1) [2, 6-15]. While the mainstay of therapy includes platelet transfusions, adjunctive therapies have included desmopressin, anti-fibrinolytic agents (tranexamic acid or ε-aminocaproic acid) or recombinant factor VIIa. Given our patient’s inadequate response to platelet transfusions, we chose to use adjunctive agents to augment platelet and coagulation function including tranexamic acid and recombinant VIIa.

Tranexamic acid is a synthetic, lysine-derived antifibrinolytic agent used to slow the breakdown of thrombin and fibrin, thereby limiting blood loss in various surgical procedures and in trauma patients [16]. By reversibly blocking the five lysine binding sites on plasminogen, tranexamic acid prevents the conversion of plasminogen to plasmin and the degradation of fibrin. Tranexamic acid has been shown to effectively limit blood loss during orthopedic procedures on the spine even in patients with normal preoperative coagulation function [17, 18]. In addition to its effects on the fibrinolytic process, tranexamic acid also improves platelet function through poorly understood and controversial mechanisms [19]. Clinical studies have demonstrated that tranexamic acid attenuates platelet aggregation defects created by antiplatelet treatment or by uremia [20, 21]. These effects may explain its anecdotal success in patients with BSS and other platelet defects.

In addition, we chose to use recombinant factor VIIa (rFVIIa), a synthetic hemostatic agent originally used to treat bleeding in hemophilia A patients who had developed inhibitors to factor VIII [22, 23]. Given its integral effect of coagula-
Adjunctive in preventing or the treatment of bleeding in patients with qualitative and quantitative platelet disorders [27].}

In addition to these proposed cellular mechanisms, rFVIIa has been shown to be a valuable adjunct in preventing or the treatment of bleeding in patients with qualitative and quantitative platelet disorders [27].

Given that the routine laboratory parameters of coagulation function (PT and PTT) do not demonstrate the clinical interaction of the various components of the coagulation cascade or adequately demonstrate platelet function, we used the ROTEM® to evaluate and follow in vivo coagulation function in our patient. Despite the presence of persistent thrombocytopenia following platelet transfusions, coagulation function was clinically adequate to allow for completion of the surgical procedure. The ROTEM® is a modification of the thromboelastogram that identifies clot formation and strength by using an electromechnical transduction system that measures the amount of rotational force transmitted by the developing clot [28, 29]. The system involves the suspension of ball from a rod in a rotational device. The rotation of the ball is impeded as the clot develops, thereby characterizing the patient’s hemostatic ability. Clot development in vivo is dependent on the interaction of platelets with coagulation factors which can be evaluated by the pattern seen on the ROTEM®. The propagation of clot and the pattern can also be followed to evaluate for clot lysis (fibrinolysis), hence evaluating the efficacy of agents. We utilized the coagulation profile provided by ROTEM® to assess our patient’s qualitative response to platelet transfusions, response to adjunctive agents (tranexamic acid and rFVIIa), the risk for perioperative bleeding and transfusion needs in the perioperative period.

In summary, we present the perioperative care of an adult patient with Bernard-Soulier Syndrome for cesarean section and circumcisions. The patient developed insensitivity to random platelet transfusions during childbirth; therefore, HLA-matched platelets were administered during surgery. Platelet function was monitored with TEG and ROTEM® to evaluate and follow coagulation function. The patient was treated with topical thrombin, ε-amino caproic acid, and oral tranexamic acid. Platelet transfusions and perioperative intravenous tranexamic acid were administered to prevent further bleeding. Coagulation function was monitored with TEG postoperatively.
ROTEm®. With such care, even invasive surgical procedures can be accomplished with minimal sequelae related to the primary bleeding disorder.

References


