The perioperative management of Bernard-Soulier syndrome: a case report and review of the role of perioperative factor VIIa

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Abstract

This article presents the perioperative anaesthetic management of a patient with Bernard-Soulier syndrome (BSS). A literature search was conducted to examine the perioperative haemostatic management of BSS, with particular focus on the developing role of recombinant factor VIIa. The early use of factor VIIa at doses of 90 to 100 µg/kg as a first-line therapy, alongside platelet transfusion, may result in a reduction in the perioperative use of blood products.

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Introduction

Bernard-Soulier syndrome (BSS) is a rare platelet disorder with an incidence estimate of less than 1:1 000 000.[1] First described in 1948, it commonly presents as an autosomal recessive disorder, although there have been cases described that follow an autosomal-dominant pattern. Patients have a defect of the glycoprotein Ib-IX-V complex, expressed on the surface of unactivated platelets, which results in severe bleeding tendencies following tissue damage.

The first step in haemostasis following vessel injury is the formation of a platelet plug. Vessel damage results in the exposure of subendothelial connective tissue to which circulating von Willebrand factor (vWF) binds. vWF then acts as a bridge between the damaged vessel wall and the circulating platelet. Sheer forces expose the A1 active zone on vWF, which reversibly binds with the glycoprotein Ib-IX-V complex, the missing component in BSS.[2] The binding of the Ib complex results in a reduction of the rolling velocity of platelets as they flow past the damaged vessel wall. A more permanent bond is then formed between glycoprotein IIb-IIIa and vWF1, with subsequent platelet aggregation and activation.

Characteristic features such as large platelets, prolonged bleeding time, abnormal consumption of prothrombin and thrombocytopenia may be variable in nature. The definitive diagnosis of BSS is made by identifying isolated defective ristocetin-induced agglutination when placed in an aggregometer. The diagnosis may be confirmed biochemically or by genotyping.[1]

Case report

A 48-year-old woman presented for elective repair of an irreducible supraumbilical hernia, which had been repaired five years previously. She had been diagnosed with BSS at the age of three, for which she had undergone elective splenectomy. She was hypertensive, on hydrochlorothiazide and enalapril, and had previously received extracorporeal shockwave lithotripsy for left-sided renal calculi.

Her coagulation and haematological investigations were as follows: Hb 10 g/dl, haematocrit 31.3%, platelet count 85 to 100 x 10^9/L with giant platelets identified, INR 0.88, PT 10 seconds (control 11.2), APTT 27.9 seconds (control 28.5), fibrinogen 9.3 g/L. The smear identified anisocytosis, Howel Jolly bodies, burr cells, schistocytes, basophilic stippling and poikiolocytosis.

The patient was anaesthetised with 150 mg propofol and 200 µg fentanyl, and maintained with sevoflurane 2.3% in 40% oxygen. Tracheal intubation was facilitated with rocuronium 40 mg.

Venous access was established by means of two 16 G cannulas. During the two-hour surgical repair, four units of packed red blood cells, ten units of platelets and four freeze-dried plasmas were transfused, guided by intraoperative thromboelastographs (TEGs) and hourly blood gasses. In addition, the patient received tranexamic acid (25 mg/kg) and desmopressin (0.3 µg/kg). Following repair with a mesh, two drains were left in situ, which drained a total of 900 ml over a period of four days. During this time, the patient was transfused four units of packed red blood cells, and twelve units of platelets. The drains were removed on day 4 and the patient was discharged on day 6.

Discussion

As the primary defect in BSS is due to an abnormal glycoprotein on a platelet, attempts to improve clotting by adding normal plasma will be ineffective, making the supply of functional platelets the cornerstone of effective patient management. With the development of recombinant factor VIIa, this pre-eminence has been challenged. Factor VIIa causes an increase in thrombin and fibrin generation while facilitating platelet aggregation.[3] It should be noted that the other agonists, such as adenosine diphosphate and collagen, will still trigger platelet activation and aggregation. Its efficacy has been of such a nature that it has been proposed as first-line therapy in some units.[4] In addition, the avoidance of recurrent platelet transfusion reduces the risk of the development of antiplatelet allo-antibodies.

To determine whether the addition of factor VIIa to the perioperative management of BSS should be considered, a literature search was performed on PubMed on 23 July 2010 with the keywords "Bernard-Soulier" and "Bernard-Soulier recombinant factor VIIa". All case reports describing the surgical management of patients with BSS were extracted (Table I).

These case reports suggest that recombinant factor VIIa may have a role as first-line therapy in the management of patients with BSS. Consistent with the recommendation that factor VIIa be used early on in the treatment course and at a dose

Table 1: The perioperative management of Bernard-Soulier syndrome

Author	Surgery	Factor VIIa	Ancillary therapy	Transfusion
Bilal[11] (2010)	Off-pump cardiac bypass	None (available in theatre)	Platelets (6 adult doses) Tranexamic acid (2 g bolus, infusion at 16 mg/kg/h)	None
Cesar[12] (2009)	Splenectomy	None	Platelets (8 units)	None
Tefre[13] (2009)	Open-knee surgery Arthroscopy Strabismus repair	104 µg/kg Preoperatively Postoperatively (two- to six-hourly)	Tranexamic acid (25 mg/kg)	None
	Orchidopexy Molar extraction	96 µg/kg Postoperatively (two- to four-hourly)	Tranexamic acid (25 mg/kg)	None
Hartman[14] (2007)	Molar extraction	None	Platelets (7 units) Aminocaproic acid	None
Hacihanefioglu[15] (2007)	Dental extraction	90 µg/kg Preoperatively Two hours postoperatively	None	None
Kostopanagiotou[7] (2004)	Emergency laparotomy for bleeding	None	Platelets (15 units) Desmopressin 30 µg Hydrocortisone 100 mg	RBC (4 units) FFP (3 units)
Yuksel[16] (2004)	Gastrointestinal bleed (exploratory laparotomy)	Dose not reported	Platelets	RBC
Almeida (2003)	Dental extraction	100 µg/kg x 4 (90-minute intervals) First dose 30 to 45 minutes preoperatively	Tranexamic acid (15 mg/kg eight-hourly) 12 hours preoperatively	
Rodseth (2010)	Abdominal hernia repair	None	Platelets (10 units) Tranexamic acid (25 mg/kg) Preoperatively	RBC (4 units) FDP (4 units)

RBC – packed red blood cells; FFP – fresh frozen plasma; FDP – freeze-dried plasma

higher than 60 µg/kg,[5] all of the reported cases made successful use of a dose between 92 and 100 µg/kg. In all the cases where factor VIIa was used for elective surgery, no additional blood transfusions were required. Concern has been raised that factor VIIa is insufficient as a single therapy for severe bleeding episodes.[5] It should be noted that factor VIIa may result in an increased risk of thromboembolic events[6] and that a review of case reports may not identify this complication.

When platelet transfusion is planned, human leukocyte antigen matching should take place if possible.

The use of tranexamic acid (25–50 mg/kg) seems to be reasonable and is often used. The response to desmopressin is variable but may have some benefit.[1] Therapy should be guided by both clinical response and the use of a TEG.[7] Other than the avoidance of regional techniques, there is little evidence to suggest that a specific anaesthetic technique is superior to any other.[8]

The literature on BSS in pregnancy has been excellently covered in a meta-analysis by Peitsidis et al.[9] In this group, 12 patients underwent Caesarean sections with a wide variation in ancillary therapy, platelet transfusion (eight patients), desmopressin (three patients), tranexamic acid (three patients) and corticosteroids (three patients). There are no reports on the use of factor VIIa in this group, although its use has been advocated.[10]

In conclusion, it can be seen that factor VIIa has been successfully used as a first-line therapy alongside platelet transfusion in the perioperative management of BSS and that it may result in a reduction in the perioperative use of blood products.

Conflict of interest

I declare that I have no conflict of interest regarding this article.

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