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Bernard-Soulier Syndrome in Pregnancy: A Case Report

Amanda Vilaverde Perez[1], Cilomar Martins de Oliveira Filho[1], Tássia Cividanes Pazinato[1], Mariana Sbaraini[1], Edimárlei Gonsales Valério[1,2], Sheila Nogueira do Amaral[3], Fernanda Grossi[2], Daniela Vanessa Vettori[1,2], Janete Vettorazzi[1,2*]

[1]Obstetrics and Gynecology, Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil
[2]Postgraduation Program in Health Sciences: Gynecology and Obstetrics, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil
[3]Hematology, Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil
Email: *jvettorazzi@hcpa.edu.br

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Abstract

Background: Bernard-Soulier Syndrome (BSS) is a rare autosomal recessively inherited bleeding disorder of platelet function. Pregnancy in BSS is associated with a high risk of serious bleeding for both mother and neonate, and current data show no consensual approach. **Aim:** To report the case of a pregnant woman with BSS, in order to provide more information about management of these cases. **Case Presentation**: This case report describes a successful pregnancy outcome in a woman with BSS who was closely monitored throughout pregnancy and postpartum period, and had a judiciously planned birth. **Conclusion:** Management of BSS during pregnancy is still unclear. However, it is important to strictly control platelet counts and plan the birth in advance.

Keywords

Bernard-Soulier, Hemostasis, Thrombocytopenia, Pregnancy, Obstetrics, Postpartum Hemorrhage

1. Introduction

Bernard-Soulier syndrome (BSS) was first described in 1948 in a young patient with hemorrhagic symptoms and prolonged bleeding time, thrombocytopenia and giant platelets [1].

The syndrome is inherited as an autosomal recessive condition and it is caused by defects within the membrane glycoprotein (GP) Ib-IX-V complex which lead to defective platelet adhesion and incapacity of platelets to bind to von Wille-

brand factor and thrombin [2].

Common clinical manifestations include recurrent episodes of epistaxis, gingival and cutaneous bleedings, and trauma-related bleedings. The severity of bleeding can vary depending on the underlying mutation. In women, menorrhagia is a highly prevalent symptom, which can present as very severe, and can be challenging to manage [3].

The international literature shows that pregnancy and BSS are not commonly related, and therefore should be closely monitored [3] [4]. Such cases bear an increased risk for primary postpartum hemorrhage, meaning worse prognosis for both the mother and the newborn. Other major complications such as blood transfusion, alloimmune thrombocytopenia in neonates, and even hysterectomy were described. In these situations, a multidisciplinary approach is often required [3] [5].

Because of the limited data in the literature, case reports and systematic reviews [3] [4] [5] are not consensual regarding the best way to deliver in this condition. In most cases, cesarean was the preferred form of birth by obstetricians. In addition, there is no prenatal routine set for such patients. A multidisciplinary follow-up and referral to specialized services are recommended. Thus, this report aims to discuss how BSS in pregnancy was managed at a tertiary hospital in Brazil.

2. Case Report

A 21-year-old caucasian primigesta from southern Brazil with BSS presented to her obstetric appointment at 33 weeks and 4 days of gestation. She was asymptomatic. The diagnosis of BSS was made at the age of 5 years old due to positive family history for the syndrome—her father was diagnosed after undergoing surgical procedure with bleeding complications. She also reported one paternal cousin bearing the syndrome. Ristocetin test showed no platelet aggregation; there was also thrombocytopenia—these features suggested her diagnosis. She denied having any bleeding history, except for a few episodes of gingival hemorrhages, with no need of medical intervention. She denied receiving platelets transfusion or any further treatment for this syndrome during her lifetime.

The patient had no other past medical history and had not undergone any previous surgeries. She denied history of tobacco, alcohol or other substances abuse. Her weight was 66 kg at the time.

Her gynecological exam showed a fundal height of 31 cm and fetal heart rate of 140 bpm with transient accelerations. Besides that, her physical exam was unremarkable. She had severe thrombocytopenia (30×10^3 platelets/μL), with presence of giant platelets in the peripheral blood smear. Group B Streptococcus swab test was positive. Other routine laboratory tests during pregnancy were unremarkable for any pathology.

She was then admitted to inpatient care for closer monitoring of both platelet count and coagulation factors. Several multidisciplinary discussions including

the patient and her family were conducted. It was decided that an elective cesarean section with previous platelet transfusion would be performed, since there was family history in which other surgical cases were managed similarly, with platelet transfusion preceding the respective procedure. Written consent for c-section delivery was obtained from the patient. The hematology assistant team was contacted for clinical expertise and hemostatic assessment arrangements in case of crisis situation. Platelets, red blood cells, and factor VII were ensured for the patient if necessary. Tranexamic acid was prescribed for use one day prior to the procedure and three days following it at the dosage of 10 mg/kg, thrice a day. During hospitalization, the patient received four doses of intramuscular Dexamethasone. After evaluations by the hematology and anesthesiology teams, interruption by cesarean with general anesthesia was indicated (contraindication to neuraxial block due to thrombocytopenia).

With gestational age of 37 weeks and 4 days, she underwent a cesarean section with midline incision under the supervision of the most experienced obstetrician of her medical assistant team. The procedure was performed under general anesthesia as per advise. On the day of cesarean section, the platelet counts were $35 \times 10^3/\mu L$. There was special attention regarding haemostatic care during the operation. This was necessary to prevent any excessive or unnecessary bleeding, once major intraoperative and postoperative hemorrhage was the primary concern. She remained hemodynamically stable throughout the procedure with minimal blood loss (the estimated amount of blood loss was 700 ml). A healthy female baby was born, cephalic, weighting 2820 grams. Apgar scores were both 9 for 1st and 5th minute.

Soon after the procedure, the platelets count was $56 \times 10^3/\mu L$ and the coagulation tests were normal. In total, the patient received the following platelet concentrates: 6 U on the day before the procedure, 9 U 1 h before the procedure and 6 U on the first and second postoperative days. The patient didn't experience any major bleedings in the postpartum. Surgical wound healing occurs as expected, without any complications. Tranexamic acid was maintained for 24 hours post-procedure. She was then discharged at 4 days postpartum with a platelet count of 70×10^3 platelets/μL and hemoglobin of 11.5 mg/dL. Table 1 shows the platelet count and values of coagulation factors during pregnancy and puerperium.

On ultrasound examination, the fetus had no evidence of bleeding. Cordocentesis with platelet count was not performed.

The first platelet count of the newborn was 53×10^3 platelets/μL and the hemoglobin was 19.1 g/dL. She did not present episodes of bleeding in the neonatal period and was discharged with her mother. The diagnostic suspicion was of BSS in the autosomal dominant form (OMIM 153670), based on family history and thrombocytopenia. She is currently following as outpatient with the hematology team.

3. Discussion

BSS is an inherited autosomal recessive syndrome often diagnosed after spontaneous

Table 1. Platelet counts and coagulation factors during pregnancy and puerperium.

Gestational age	Platelet counts	Coagulation tests (INR, aPTT)
33w + 4d—prenatal consult and hospitalization	6000 (manual evaluation)	Values within normal limits
34w + 5d—hospitalization	30,000 (manual evaluation)	Values within normal limits
35w + 4d—hospitalization	5000 (manual evaluation)	Values within normal limits
36w + 4d—hospitalization	15,000 (manual evaluation)	Values within normal limits
37w + 4d—after receiving 6 IU of platelets the previous day and before cesarean section	36,000 (manual evaluation)	Values within normal limits
37w + 4d—during cesarean section and after receiving 9 IU of platelets one hour before the procedure	58,000 (manual evaluation)	Values within normal limits
37w + 4d—after the procedure and after receiving 6 IU of platelets postoperatively	54,000 (manual evaluation)	Values within normal limits
First day of puerperium	48,000 (manual evaluation)	Values within normal limits
Second day of puerperium	50,000 (manual evaluation)	Values within normal limits
Third day of puerperium	70,000 (manual evaluation)	Values within normal limits
Fourth month of puerperium	25,000 (manual evaluation)	Values within normal limits

INR: international normalized ratio; aPTT: activated partial thromboplastin time; w: weeks; d: days.

bleeding episodes. An autosomal dominant form has also been described [1]. It is marked by moderate thrombocytopenia and inability of the platelets to interact with the von Willebrand factor (VWF), which acts as a bridge between the subendothelial matrix and platelets. There is no platelet induction induced by ristocetin, caused by a qualitative or quantitative defect in the membrane glycoprotein Ib-IX-V complex, a primary platelet adhesion receptor. This complex mediates the adhesion of platelets to the blood vessels walls at injury sites and increases the ability of thrombin to act in low contractions to activate platelets [1]. More than 30 mutations that cause BSS have already been identified, and the intensity of manifestations depends on the mutation found. The most common symptoms are epistaxis, gingival bleeding and/or trauma related cutaneous bleeding. Laboratorial changes can appear, such as prolonged bleeding time (greater than 20 minutes); change in platelet count (thrombocytopenia) and morphology (platelets greater than 3.5 mm), and absence of platelet aggregation in the presence of ristocetin. Clotting factors are normal.

Literature shows a prevalence of 1 pregnancy case of BSS in 1 million, but limited data is available. These women are at risk for postpartum haemorrhage and may need an emergency hysterectomy. The newborn has an increased risk of severe bleeding, such as intracranial bleeding (caused by autoimmune thrombocytopenia). The course of the disease varies in each pregnant woman and also in the same patient during different pregnancies. The most common occurrence is intrapartum and postpartum bleeding, rarely occurring in the antepartum pe-

riod. As postpartum haemorrhage is common, follow-up should be done for 6 weeks in the puerperium. Therefore, it is still not clear whether cesarean section is preferable over vaginal birth in women with such bleeding disorders. A systematic review by Peitsidis *et al.* [3] presents a guideline that should be applied to pregnant patients with BSS. This includes warning the patient about the risks of pregnancy before conception, having prenatal care at a tertiary center, using of coagulation factors or tranexamic acid and platelet transfusion—depending on the mode of delivery—, and a close observation in the postpartum period concerning for postpartum hemorrhage [3].

This same review states that the mode of delivery is controversial, even though cesarean section was preferred for most cases. In one of the few reports of a patient who underwent vaginal delivery, Peng *et al.* described a 35 year-old woman at her fourth pregnancy, with most of them requiring blood transfusion in the postpartum (and one ending with in utero fetal death) [6].

Since the best practice for safe labour in these cases remains controversial, the mode of delivery appears to be a decision that the obstetrician has to make majorly considering the patient's personal and familial history, as well as consulting a multidisciplinary team of haematologists and anesthetists in a tertiary care center. Regional analgesia and anesthesia are contraindicated because of the risk of spinal or epidural hematoma. For cesarean section, general anesthesia is recommended [3]. The use of dibocaine as an anesthetic agent should be avoided due to the risk of platelet depletion. The aggressive use of uterotonics in the third period of labor is recommended to minimize the risk of postpartum haemorrhage.

Planning ahead for critical situations taking into consideration obstetric and bleeding risk factors is also of paramount importance. Both prophylaxis and treatment for major bleeding should be extensively covered before delivery. Newborns should also be considered for this decision, regarding their bleeding risk assessment [6].

As the risk of bleeding is increased in these cases, bleeding prophylaxis may be done with tranexamic acid, desmopressin (DDAVP), recombinant factor VIIa (rFVIIa), and platelet transfusion. If possible, it is preferable to avoid platelet transfusion due to the risk of alloantibody formation. Alloantibodies may be formed from platelet transfusion or from fetal platelet antigens [9].

The fetus is usually heterozygous for the disease, and its platelets may contain antigens that do not exist in platelets from the mother. These antigens reach the maternal circulation, leading to the development of antibodies which can overcome the placental barrier and cause neonatal autoimmune thrombocytopenia. However, infusion of HLA-compatible platelets along with tranexamic acid is the first line in caesarean section or if bleeding occurs during vaginal delivery. Gamaglobulin, plasmapheresis and corticoid have been used to improve the response to platelet transfusion and to try to prevent neonatal autoimmune thrombocytopenia.

In our case, antenatal counselling was extensive and the patient's familial history took a major role in defining the mode of delivery. Multidisciplinary ap-

proach was thoroughly sought throughout the whole decision process. Prophylaxis with platelets transfusion, tranexamic acid, and haemostatic care during surgery seems to have been effective, since no complications were observed for both the mother and the newborn.

The management must be tailored for each individual and for different events for the same patient [7]. Use of platelet concentrates can be employed to stop active bleeding or to prevent it during a surgical intervention with a high haemorrhagic risk. However, that transfusions expose the patients to the risk of developing alloimmunizations (anti-HLA, anti-human platelet antigen or against glycoproteins that are absent), which can make subsequent platelet transfusions not effective [6] [8].

Report of further cases and individual experience in managing these pregnancies will be helpful to obtain better knowledge. The little published literature on this subject points to the need to collect more data worldwide.

4. Conclusion

BSS is a rare bleeding disorder that may complicate pregnancy. Pregnancy course of women affected by the syndrome is widely variable and, to some extent, unpredictable. Strict vigilance of the mother's hematocrit and platelet count is advised, in order to readily diagnose and treat any ongoing bleeding in the peripartum period. Management of pregnancy in these cases is still controversial, and it requires a multidisciplinary team and individualized medical decisions.

Consent

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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