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Case Report

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Hemorrhagiparous Thrombocytic Dystrophy (Bernard-Soulier Syndrome): A Case Report of a Rare Bleeding Syndrome

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Abstract

Bleeding syndromes, such as Bernard-Soulier Syndrome (BSS), are extremely rare with an incidence of 1 in 1,000,000 persons. Very few cases (approximately a hundred) have been reported in the literature. However, it is very important to quickly recognize this condition as soon as possible before life-threatening complications occur. Here, we present a case of a 25-yr-old with chronic thrombocytopenia who was found to have BSS on peripheral blood smear prior to a routine dental procedure. Rare disorders, such as BSS, need to be on the differential diagnosis for physicians because missing this condition could have led to catastrophic side effects, such as uncontrolled bleeding for our patient. She was transferred to a tertiary care center for her procedure to be managed for potential bleeding complications.

Introduction

Bernard-Soulier syndrome (BSS) is a rare bleeding disorder caused by a defect in platelet glycoprotein-GpIb-IX-V complex, which is the receptor for von Willebrand factor (VWF) [1]. This leads to a dysfunction of primary hemostasis. When considering inherited bleeding disorders, BSS is not often considered as part of the differential diagnosis due to its extreme rarity. The estimated frequency of homozygous cases is as low as one per million based on case reports. Inheritance of BSS is autosomal recessive. BSS is a dual quantitative and qualitative bleeding disorder characterized by abnormally large platelets, mild thrombocytopenia and platelet dysfunction. Patients usually present early in life with bleeding symptoms, such as epistaxis, ecchymosis, and gingival bleeding; rarely can it present with gastrointestinal bleeding and menorrhagia. Platelet counts may range from as low as 30,000/μL to as high as 200,000/μL and fluctuate considerably in individual patients over the years [2]. Diagnosis of BSS requires high clinical suspicion in suitable clinical settings, usually with a positive family history. Diagnosis can be confirmed with tests for platelet aggregation and flow cytometry [2]. We present a case of a 25-year-old female with chronic thrombocytopenia who was found to have BSS on peripheral blood smear prior to a routine dental procedure that could have had unfortunate complications without proper preparation.

Case Report

A 25-year-old female presented to the hospital for an elective wisdom teeth extraction after developing dental pain over several months. The patient has a past medical history of asthma, anxiety, depression, gastroesophageal reflux disease (GERD), and chronic thrombocytopenia, averaging 80,000/uL throughout her life. She was presumably diagnosed with Sebastian syndrome when she was 12 years old after a period of extensive bruising and petechiae and was subsequently found to have a platelet count of approximately 50,000/uL. Of note, her past surgical history revealed that she had a tonsillectomy at age 5 with excessive postoperative bleeding. On review of system (ROS), the patient reported ongoing easy bruising after mild trauma and excessive bleeding after finger cuts. She also reports heavy bleeding for several days of her monthly menstrual cycle.

Her family history revealed that her father and sister both had chronic thrombocytopenia and were diagnosed with Bernard-Soulier Syndrome after genetic testing. Due to the unlikelihood of two genetic bleeding disorders being present in first degree relatives, the patient was then also diagnosed with Bernard-Soulier Syndrome. Her home medications included omeprazole, sertraline, montelukast, and albuterol.

On a physical exam, there were some scattered ecchymosis over her arms and legs. Laboratory data showed her hemoglobin is 11.7 g/dL, white blood cell count 5900 cells per cubic millimeter of blood, and platelets 81,000/uL with a mean platelet volume that was increased at 12.8 fL. Upon further investigation of her peripheral blood smear, she was found to have very large platelets with a decreased platelet count consistent with BSS.

Due to concern for possible complications of her chronic thrombocytopenia, such as increased risk of bleeding, the patient was electively admitted to the hospital for routine wisdom tooth extraction. After admission and preoperative evaluation by internal medicine and hematology, it was decided with her hematologist that she would be transferred to a tertiary care hospital to have her dental procedure with oral maxillofacial surgery where blood product support could be provided.

The patient was transferred to the tertiary care facility and taken to the operating room the following day. She was pretreated with tranexamic acid 1,300 mg and 1 unit of platelets prior to the dental procedure. It was recommended that she continue tranexamic acid at 1,300 mg every 8 hours for 5 days after the procedure. She was seen in follow-up by oral maxillofacial surgery on postoperative day 3 and was found to have an unremarkable postoperative course. Since the patient did not have medical insurance at the time of initial hematology consultation, she was diagnosed with BSS based on a family history of confirmed diagnoses, findings noted on blood smear, and presenting clinical symptoms. Since then she has obtained medical insurance and is currently undergoing official genetic testing for the rare bleeding condition.

Discussion

Bernard-Soulier Syndrome (BSS), also known as Hemorrhagiparous Thrombocytic Dystrophy, is a rare autosomal recessive disease affecting less than 1 in 1,000,000 people [3]. The disease is characterized by deficiency in the platelet membrane proteins GPIb, GPIX and GPV which leads to prolonged bleeding and thrombocytopenia. Within the GPIb complex, it is composed of GPIba and GPIb subunits in which GPIb binds to GPIX and GPV. The amino terminal type a domain of GPIa then binds to vWF which mediates platelet adhesion and forms the first step in primary hemostasis [4]. This inhibits the complex to mediate adhesion at the blood vessel wall at sites of injury by binding to vWF as well as inhibiting the ability of thrombin at low concentrations to activate platelets [3].

The disease is often suspected early in life and is characterized by symptoms, including purpura, epistaxis, gingival bleeding and menorrhagia [4]. Our patient presented with this constellation of symptoms, with easy bruising, heavy menstrual bleeding with menses lasting an average of 7 day, and excessive bleeding after finger cuts. Prolonged and severe bleeding after surgery can be seen. To avoid this complication, our patient was going to have her wisdom teeth extraction at a tertiary care center. The first patient was described by Bernard and Soulier who suffered from bleeding problems, including cerebro-spinal hemorrhage, orbital and periorbital hematomas and died at 28 after an intracranial hemorrhage after a bar fight [3].

For the diagnosis of BSS, the blood smear will be characterized by the hallmark finding of "giant" platelets, with a diameter of up to 10 ug. A confirmatory test used is the defective response of platelets to ristocetin. This is a distinct characteristic which differentiates Bernard Soulier Syndrome from other inherited platelet disorders including von-Willebrand Disease. The defective response with a prolonged bleeding time and decreased or absent GP1b levels of flow cytometry leads to the diagnosis of BSS. In our case, the patient's sister was recently diagnosed with BSS via genetic testing. She is currently pending genetic testing. However, given clinical findings, histologic findings and family history, the patient was diagnosed with BSS.

Treatment starts with prevention of bleeding, including avoiding trauma and avoiding antiplatelet medications. Procedures, such as dental procedures, should be performed in a center where the patient can be monitored for prolonged bleeding so that the patient would be able to receive blood and platelet products if necessary. Bleeding time can be shortened with Desmopressin and rFVIIa in some patients [4]. Furthermore, a common complication with frequent transfusions is the development of iso antibodies in which patients may require HLA-matched platelets.

Currently there is limited information regarding preoperative and postoperative care of patients with BSS [5]. There is no consensus on the treatment guidelines for patients undergoing surgery. The current approach involves the use of allogeneic platelets and anti-fibrinolytics such as recombinant factor VIIa and 1-deamino-8-d-arginine vasopressin/desmopressin and tranexamic acid (TXA) [5]. In this case, TXA and platelets were given to the patient. Our case highlights the need for broad differential diagnosis and a strong clinical suspicion to diagnose BSS. Initially our patient was misdiagnosed with Sebastian syndrome, which would have altered her management with potentially catastrophic complications, such as severe bleeding. Going forward, there needs to be a consensus on treatment and an emphasis on patient education.

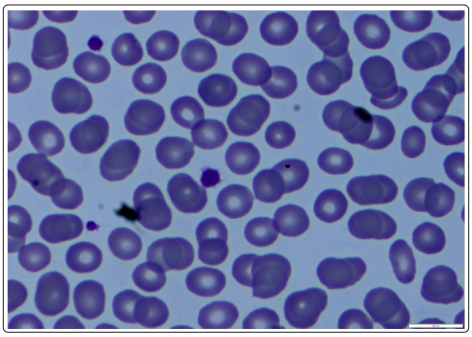

Figure 1: Peripheral blood smear with very large platelets and decrease in number of platelets

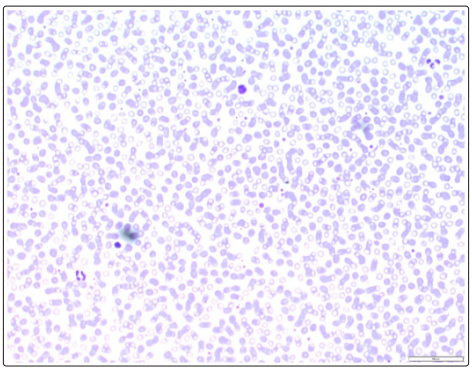

Figure 2: Peripheral blood smear with very large platelets and decrease in number of platelets

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