JACC: CASE REPORTS VOL. 2, NO. 4, 2020

CASE REPORT

INTERMEDIATE

CLINICAL CASE

Multivessel Percutaneous Coronary Intervention in a Patient With Bernard-Soulier Syndrome

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ABSTRACT

Bernard-Soulier syndrome, a congenital bleeding disorder, can rarely present with atherosclerosis and thrombosis. Acute coronary syndrome in such patients present a unique challenge as no standard set of guidelines exist for successful treatment. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2020;2:621–5) © 2020 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

The success of percutaneous coronary intervention (PCI) in the modern era is attributed to the introduction of newer generation drug-eluting stent platforms that resist restenosis and the emergence of potent antiplatelet drugs that steer the process safely during the initial period after stenting, threatened by stent thrombosis. Rarely, cases test the set standards of care and require a multidisciplinary approach for successful management.

LEARNING OBJECTIVES

- Bleeding disorders do not provide blanket coverage from atherosclerotic processes or their sequelae.
- Due to the rare nature of such cases, individualized decisions regarding stents, anticoagulation regimen, and dual-antiplatelet therapy should take into account risks and benefits of the intervention. Therefore, the role of multidisciplinary care in managing complex patients with hematological disorders is essential.

CASE

A 65-year-old male patient was referred to the authors' intervention cardiology clinics from the cardiothoracic surgery team for evaluation for PCI for symptoms of crescendo angina for the previous 2 months. The patient was referred to the present authors after the surgeons declined to perform coronary artery bypass grafting for multivessel coronary artery disease due to a platelet function disorder. On examination, the patient was hemodynamically stable and did not report any recent episodes of bleeding, including gastrointestinal or genitourinary bleeding.

MEDICAL HISTORY. The patient was known to have hypertension; type 2 diabetes mellitus, for which he was taking insulin therapy; a platelet function

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, or patient consent where appropriate. For more information, visit the *JACC: Case Reports* author instructions page.

Manuscript received November 13, 2019; revised manuscript received December 11, 2019, accepted December 17, 2019.

ISSN 2666-0849 https://doi.org/10.1016/j.jaccas.2019.12.025

ABBREVIATIONS AND ACRONYMS

BSS = Bernard-Soulier syndrome

CAD = coronary artery disease

DAPT = dual-antiplatelet therapy

DES = drug-eluting stent

PCI = percutaneous coronary intervention

disorder; Bernard-Soulier disease that was diagnosed at the 32 years of age when he developed bleeding after a dental procedure.

DIFFERENTIAL DIAGNOSIS. The most common differential for chest heaviness on exertion in an elderly man with diabetes and hypertension is coronary artery disease. Other plausible causes of chest pain in this case could include valvular pathologies such as aortic stenosis or vascular pathologies such as aortic aneurysms and chronic aortic dissection. Noncardiovascular differentials would include anemia or endocrine disorders such as hyperthyroidism causing demand ischemia.

INVESTIGATIONS. Blood analysis revealed prolonged bleeding time and low platelet counts with large clumped platelets (**Figure 1**). The diagnosis of Bernard-Soulier syndrome (BSS) was confirmed with ristocetin-induced aggregation studies that showed hypocoagulability (**Table 1**). The patient had been worked up for chest heaviness at an outside center, and a coronary angiogram showed obstructive disease in the left anterior descending, left circumflex, and right coronary arteries (**Figure 2**). Echocardiography showed normal left ventricular function with normal valves and aortic root.

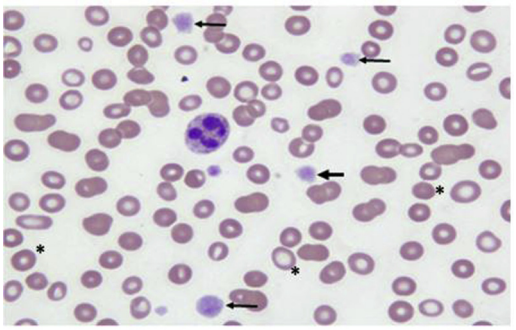
MANAGEMENT. Contemplating multivessel PCI and keeping in view his platelet function disorder, the authors referred the patient to a hematologist to plan the procedure. The main challenge faced by the operators was overwhelming bleeding with BSS and the drugs used during and after PCI.

After reviewing the patient's case and checking basic laboratory reports, the hematologist advised transfusing a single unit of apheresis platelets 1 h before the procedure and arranging for factor VII concentrates, which were to be transfused if overt bleeding was noted. It was also advised by the hematology team to use an access site where bleeding could be easily secured.

Judicious use of anticoagulation and antiplatelet loading with 75 mg each of aspirin and clopidogrel was advised after the procedure.

On the day of the procedure, the patient was transfused with 1 mega unit of platelets. Access for the procedure was obtained through the right radial artery by using a 6-F sheath (Terumo, Tokyo, Japan). After access was obtained, 100 IU of intravenous unfractionated heparin per kilogram (total of 7,000 IU) was administered, targeting an activated clotting time of 300 s. Stenting was performed in the left circumflex artery by using a 3.0- × 15-mm drug-eluting stent (Promus Premier, Boston Scientific, Marlborough, Massachusetts) followed by stenting in the left anterior descending artery with 2.5- × 24-mm and 3.0- × 28-mm drug-eluting stents (Onyx, Boston Scientific). Finally, stenting in the right coronary artery was performed using a 2.5- × 38-mm and a 3.0- × 24-mm drug-eluting stent (**Figure 3**, Videos 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10). During the procedure, the activated clotting time was checked every 15 min and was kept at approximately 300 s by using intravenous heparin. After the PCI, the patient was given 75 mg each of aspirin and clopidogrel. The patient remained hemodynamically stable after the procedure and did not develop any bleeding complications. A transradial band (Terumo) was applied, inflated with 12 cc of air and deflated following a protocol of 3-cc deflations every 30 min. The transradial band was safely removed, and the patient remained hemodynamically stable overnight in the cardiac care unit. No transfusions were given after the procedure.

FIGURE 1 Peripheral Blood Smear Showing Giant Platelets Suggestive of Bernard-Soulier Syndrome



Significant numbers of erythrocytes that are smaller than normal (microcytes) can also be observed **(asterisks)**. **Arrows** show giant platelets.

DISCUSSION

BSS is a rare congenital bleeding disorder first described in 1948 by Bernard and Soulier (1). It occurs because of a mutation in the GPIbα subunit of the platelet membrane Ib/V/IX complex (2) and results in a lifelong diagnosis of mucocutaneous bleeding, epistaxis, and other symptoms, resulting from delayed platelet aggregation. BSS is identified with a prolonged bleeding time and low platelet counts with large clumped platelets seen on peripheral film. The distinctive abnormality seen in BSS is hypocoagulability on ristocetin-induced aggregation studies (3).

Like other bleeding disorders, the management of BSS lacks detailed guidelines in certain contexts,

TABLE 1 Blood Count and Platelet Aggregation Studies

Test	Value	Range
Hemoglobin	10.5 g/dl	12.3–13.6 g/dl
Hematocrit	34.2%	38%–50%
MCV	69.9 fl	78–96 fl
Platelet	38 × 10^9/l	150–300 × 10^9/l
Bleeding time	6.5 min	1–6 min
Collagen, 2 μg/ml	51%	46%–112%
ADP	69%	50%–110%
Ristocetin, 1.25 mg/ml	13%	53%–103%

Blood count shows hypochromic, microcytic anemia along with thrombocytopenia. Platelet aggregation studies show low platelet counts with normal responses on aggregation to collagen and ADP but defective response to ristocetin, characteristic of Bernard-Soulier syndrome.

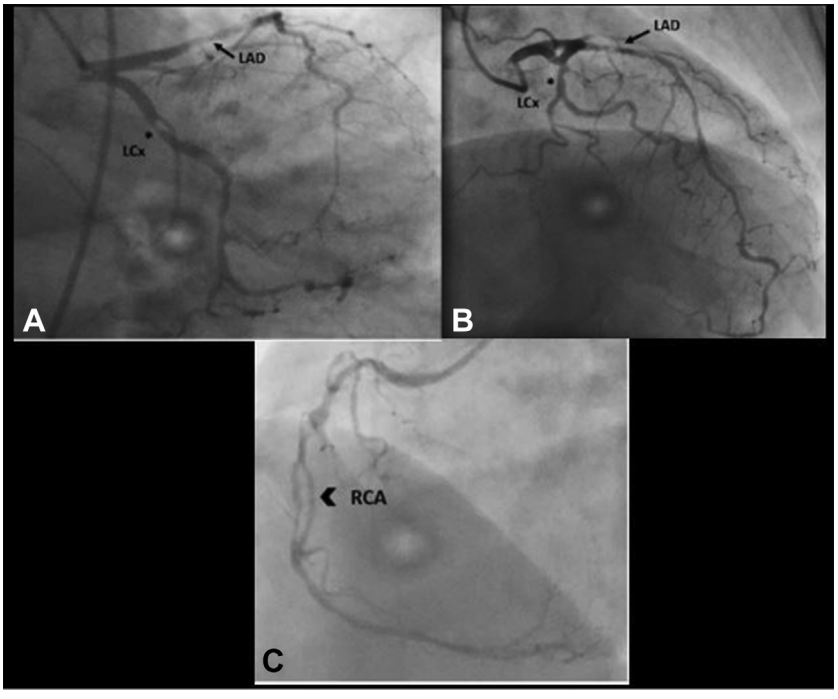
especially with regard to coronary artery catheterization and PCI. The management of BSS requires balancing the prevention of bleeding complications and the duration of dual-antiplatelet therapy (DAPT).

In order to achieve adequate hemostasis during and after the procedure, in the present case, the experience of BSS patients undergoing surgical procedures with prophylactic pre-procedural platelet transfusions was extrapolated (4), and the procedure was performed using a pre-catheterization transfusion of 1 megaunit of platelets to this patient. In the present case, the authors opted for a drug-eluting stent (DES) for tackling the coronary artery disease (CAD). This decision was dictated primarily by the presence of complex multivessel CAD and the lower risk of restenosis with DES. The risk of bleeding due to the requirement of a minimum 6 months of DAPT (5) was weighed relative to the benefit of reduced restenosis with the hematologist. Keeping in view the absence of recent bleeding episodes and the extensive CAD, it was decided to use newer DES.

The novelty of the present case lies in the fact that it is the first reported case of a BSS patient with multivessel CAD managed with PCI with DES and prolonged DAPT. There are few reported cases for BSS patients with CAD managed with PCI (2). The 1 documented case mentions the use of bare metal stents for PCI, likely selected for the shorter requirement of DAPT (5).

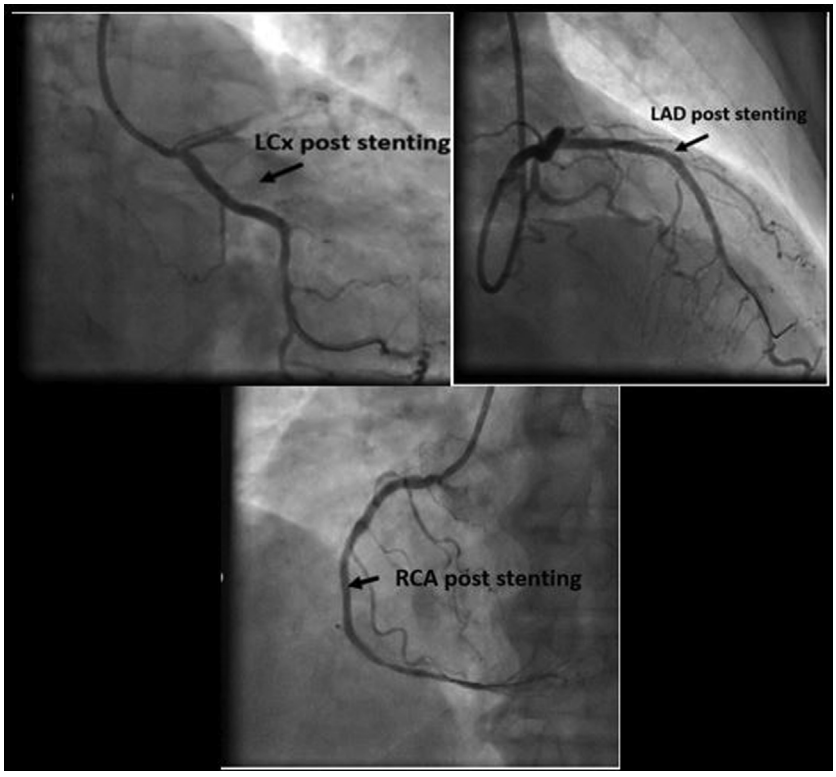
Although antiplatelet therapy is not recommended in BSS patients, there are limited reports of its use in a clinical setting. Girolami et al. (2) reported failed

FIGURE 2 Coronary Angiogram Showing a Long Stenotic Segment in the LAD



Coronary angiogram shows a long stenotic segment in the left anterior descending (LAD) artery **(A and B, arrows)**. A discrete focal stenosis is also seen in the left circumflex (LCx) artery **(A and B, asterisk)**. A long, diffusely stenotic lesion is seen in the right coronary artery (RCA) **(C, arrowhead)**.

FIGURE 3 Post-PCI Coronary Angiogram



Post-percutaneous coronary intervention (PCI) coronary angiogram after drug-eluting stent (DES) implantation in LAD, LCx, and RCA, showing minimal residual stenosis in the vessels after stenting. Abbreviations as in Figure 2.

attempts to maintain patients with BSS receiving DAPT, with bleeding observed in both cases, resulting in switching to single antiplatelet therapy. On a much extended follow-up of 1 year, the present patient remains asymptomatic, with no episodes of bleeding while taking DAPT. Thus, this case is unique because it highlights the fact that BSS patients with multivessel disease undergoing multivessel PCI can be managed successfully by using long-duration DAPT without bleeding complications (2).

FOLLOW-UP. This patient was discharged the next day on DAPT with stable hemoglobin and hematocrit and was followed in clinic. On clinic follow-up at 1 year after the procedure, the patient remained symptom free and did not report any bleeding events while taking DAPT at 1-year follow-up.

CONCLUSIONS

The present case highlights that, existing established guidelines for managing acute coronary syndrome do not cater to patients with unique platelet function disorders, such as BSS, with high chances of bleeding. In such cases, the collaboration among specialties can steer patients through demanding procedures such as PCI. In the current era of newer DES and refined therapies, the present case sets the precedence for managing BSS patients with preprocedural platelet transfusion followed by DES implantation and post-PCI DAPT. The current guidelines for the management of prophylaxis for BSS patients undergoing nonsurgical procedures warrant expansion, and the present case can shed some light on managing such cases in the future.

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KEY WORDS antiplatelets, Bernard-Soulier syndrome, bleeding disorder, percutaneous coronary intervention, stenting

APPENDIX For supplemental videos, please see the online version of this paper.