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RESEARCH ARTICLE

A CASE REPORT OF BERNARD SOULIER SYNDROME AND ITS MANAGEMENT IN MINOR ORAL SURGICAL PROCEDURES

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ABSTRACT

Bernard-Soulier Syndrome (BSS) is a disorder which manifests prolonged bleeding time, thrombocytopenia, and giant platelets. The prevalence of this disease has been reported to be less than 1 in 1,000,000. Bleeding disorders patients can be among the most difficult surgical patients to manage and deal with. Intra-operative and post-operative hemorrhage can be a life-threatening complication in even the most routine surgical procedures. There are no standards methods to deal with management of intra operative bleeding associated with BSS, since this disorder is very rare. Management of intraoperative hemorrhage with pre-operative or during operation HLA-matched platelets, and topical hemostatic agents (gel foam, thrombin), systemic aminocaproic acid, transfused rVIIa, and DDAVP (desmopressin), resulted in good hemostasis and a long-lasting healing response. For these rare disease, we present case report in which a combination of systemic and topical methods may be contributing in achieving good hemostasis during intra-operative hemorrhage.

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INTRODUCTION

The Bernard-Soulier syndrome (BSS) is a disorder which mainly manifests prolonged bleeding tendency, macrothmbocytopenia and low platelet counts and is inherited as an autosomal recessive trait. The defect is restricted to the megakaryocyte/platelet cell lines. In 1948, French hematologists, Jean Bernard and Jean-Pierre Soulier [Bernard, 1983], reported a male patient who was young and had a severe bleeding disorder with a prolonged bleeding time, a low platelet count macrothrombocytopenia. They called the disorder "Dystrophiethrombocytaire-hémorragiparecongénitale" (Hemorrhagiparousthrombocytic dystrophy) after considering their defects (Bernard, 1948). He finally died at a very young age of 28 after suffering an intracranial hemorrhage in a barroom brawl due to his disorder (Bernard, 1983). There are many cases reported with an identical disorder to this syndrome, usually inherited as an autosomal recessive trait and also associated with consanguinity (de la Salle, 1995; Lopez, 1998). It is not easy to distinguish Congenital macrothrombocytopenia (CMTP) on the basis of clinical features and therefore require exclusive laboratory tests. In order todifferentiate BSS from other CMTP, aggregometry is essential to determine the functional analysis ofplatelets (Nurden, 2005).

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A firm diagnosis needs conjunction of, macro thrombocytopenia, prolonged bleeding times, defective ristocetin-induced agglutination and deficiency of platelet GPIb-V-IX (CD42a-d) done by flow cytometry. Here we present a patient with BSS who underwent multiple teeth extractions and the therapy applied to achieve hemostasis.

Case report: A 78-year-old male was referred to the oral and maxillofacial surgery clinic of the Saraswati Dental College and Hospital, Lucknow for multiple teeth evaluation. His chief complaint was decayed tooth with mobility in lower front tooth region of jaw for several years and wanted the replacement of the same. Patient was already diagnosed with this bleeding disorder with low platelets count and defective Ristocetin-induced agglutination test followed by no family medical history of the same disorder. Patient had underwent extraction 20 years back without any complication. Physical examination revealed that patient does not had any other systemic problem. Ecchymosis or petechiae were not present on skin and oral mucosa. No systemic or localized infection was present at the site. Oral examination revealed multiple root stumps I.R.T 13 14 18 23 24 27 35 36 37 47 associated with generalized gingival recession. Mobility was present i.r.t 31 32 41 42 and tooth 45 was grossly decayed.

It was unclear as to whether the patient required transfusion of platelets after surgical procedure.

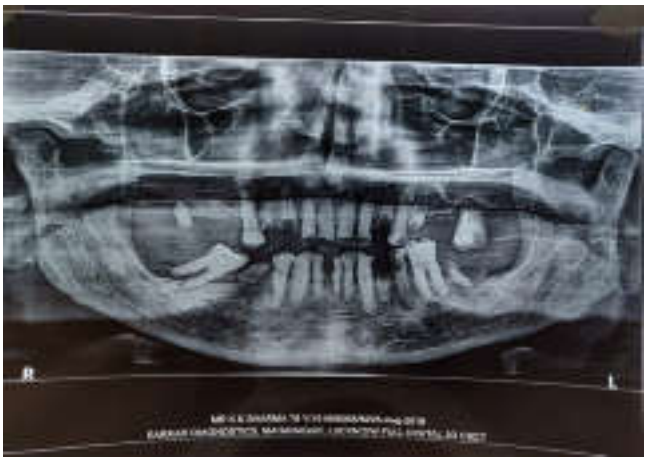

Figure 1. revealed OPG of the above patient

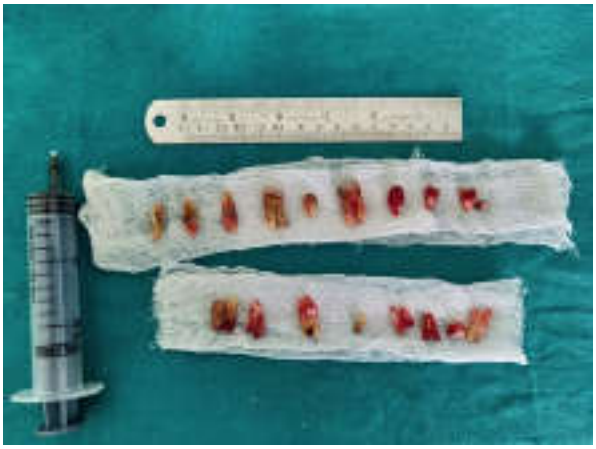

Figure 2. Extracted teeth of the patient

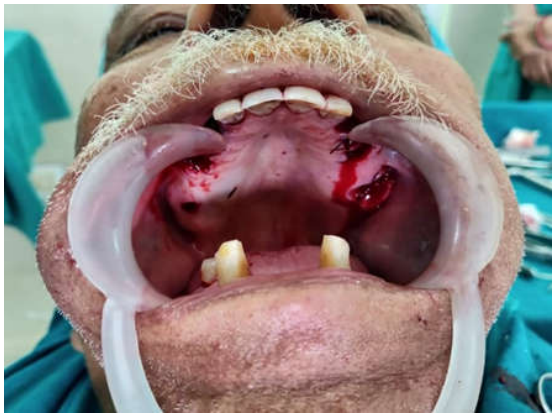

Figure 3. Hemostasis achieved in upper jaw

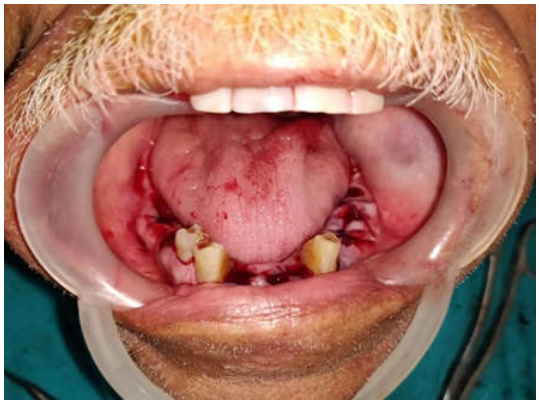

Figure 4. Hemostasis achieved in lower jaw

The patient was otherwise healthy and had never had a major bleeding episode. As the patient required extraction of multiple teeth, a decision was made to remove remaining teeth prophylactically followed by prosthetic rehabilitation. A physician consultation was obtained, and HLA-matched platelets should be administered perioperatively was suggested. Further suggestions included pursuing the Tranexamic acid 500mg daily till the operative sites get healed. Preoperative blood investigations showed a normal Prothrombin concentration (PC), prothrombin time (PT), international normalized ratio (INR) and a platelet count of 20,000. Before the procedure, the patient received a two unit of HLA- matched platelets (~50ml) and a platelet count of 80,000 was achieved followed by 500mg tranexamic acid intravenously. The teeth were extracted, with care taken to protect the soft tissue from excessive trauma as shown in Figure 2. The extraction sites were packed with gel foam in maxillary region and closed with non-resorbable sutures. Excellent hemostasis was achieved at the end of the case as shown in Figure 3. and Figure 4. and the patient received one unit of platelet concentrate post-operatively. At 1-week follow up, there was evidence of secondary healing and sutures were removed after 10 days followed by satisfactorily healing.

DISCUSSION

Bernard-Soulier syndrome is a platelet disorder characterized by giant platelets, prolonged bleeding time, and thrombocytopenia. It is a rare disorder which is inherited as an autosomal recessive trait. Approximately less than 1/1,000,000 is the prevalence of this syndrome which can be sometimes higher due to wrong diagnosis and underreporting (François, 2006). Both male and female ratio affected by this syndrome is 1:1. Majority of cases reveal that bleeding symptoms manifest quickly post birth or during early young age. Clinical manifestations include gingival bleeding, epistaxis, purpura, menorrhagia and rarely gastrointestinal bleeding hematuria can occur (Angie, 2007). Severe bleeding episodes are associated with extraction and various other minor and major surgical procedures and even during menstrual period. Bleeding episodes can also occur during parturition in pregnant women. The incidence of bleeding episodes may vary from individual to individual suffering from this disorder. Rarely serious hematomas can be observed. Prolonged PT or PTT times on blood investigation are due deficiencies of these plasma factors.

Following injury to a vessel, the connective tissue between the endothelium and the inner elastic membrane in the intima of arteries is exposed and secretes a factor known as von Willebrand factor which is a blood glycoprotein involved in hemostasis. Von Willebrand factor is partially stored in Weibel-Palade bodies and during platelet adhesion it binds to the glycoprotein receptor Ib which is present on the surface membrane of the platelets. Damaged endothelium causes the properties of the platelet to changed itself when exposed to it. After injury platelets are recruited and accumulate around the breakage their sticky allows them to adhere to each other due to contractile proteins which is present within the platelet. These proteins contract and release certain granules, which make them sticky and ultimately lead to formation of platelet plug (Guyton, 1996). Abnormality in three genes is mainly responsible for platelet anomalies and clinical manifestation related to BSS. BSS defect mainly occurs due to multiunit structure of the affected GPIb-V-IX receptor.

The main function of the GPIb-V-IX receptor complex is to initiate the platelet adhesion at site of injured vessel to achieve primary hemostasis[9] Von Willebrand factor helps in platelet adhesion by binding to it.[10] These four distinct transmembrane proteins, GPIbα (MW 135 kDa), GPIbβ (MW 26 kDa), GPIX (MW 20 kDa) and GPV (MW 82 kDa) at the surface of megakaryocytes forms the functional receptor (Andrews, 1999). GPIbα, GPIbβ, and GPIX are closely linked proteins and are all necessary for well-organized biosynthesis of the receptor.[12] Even a single deficiency of a unit can ultimately reduces the surface expression of the whole receptor complex. GPV is loosely associated with the complex and therefore its absence had no effect on expression. GPIBA which is the largest unit and it also include the von Willebrand binding site and GPIBB and GP9 are responsible for the defect in BSS. The BSS mainly diagnosed by following criteria which include skin bleeding times in BSS are prolonged sometimes moderate around 6–10 min and severe more than 20 min. A diagnostic feature of BSS is low platelet count with abnormally giant platelets (main volume 12–18 μm3; diameter 5–10 μm). Initially examination of blood smear and blood cell count should be done. Platelet count ranges from 40,000 to 1,50,000/μl. Ristocetin- induced platelet agglutination defect is another diagnostic feature for BSS. Platelets in BSS will fail to agglutinate in presence of ristocetin. Since the defect in BSS is present on the surface of platelet, platelets in BSS will fail to agglutinate even if normal plasma is added in presence of ristocetin (López, 1998).

There is defect in binding of FXI due to less sufficient amount of GPIB because of which we observed defect in prothrombin consumption and may be useful for the diagnosis[15], and also there is decrease in thrombin generation.[16] Flow cytometry analysis, platelet glycoprotein analysis, genetic studies helps in confirmed diagnosis of BSS.BBS is mainly mistaken as idiopathic thrombocytopenic purpura (ITP), which is basically an immunological disorder, and followed by incorrect treatment with steroids and splenectomy (Noda, 1995; Noda, 1996; Cuthbert, 1988; Bunescu, 1994; Li, 1996). Treatment options include both universal and definite treatment for bleeding symptoms. Trauma due to any means should be avoided by patient and also precaution should be taken in patient who is receiving antiplatelet drugs, like clopidogrel, aspirin, heparin, etc. BSS patients are strictly advised to maintain good and healthy dental hygiene. Female patients with BSS should be warned against use of contraceptive during puberty. platelet transfusion may be required in treating bleeding symptoms during major and minor oral surgical procedures.

Transfusion of platelet is always associated some risk of developing antibodies against platelets. Transfusions are used when hemorrhage has not stopped with other measures. Platelets should be HLA -matched to avoid alloimmunization. Recombinant factor VIIa can be given in BSS patient where antibodies against platelets are formed due to multiple platelet transfusion. Peters and Heijboer,24 reported the stoppage of bleeding occur in their cases of BSS which are alloimmunized their BSS by transfusing rVIIa (77 ug/kg) which is given 4 hourly in 24 hours. In some patients DDAVP (desmopressin) can be used which may or may not helpful in achieving hemostasis in every BSS patient. It helps to release plasminogen, prostaglandins and factor VII which can be helpful in cessation of bleeding symtoms.25,26,27 Similar to DDAVP some of the agents like aminocaproic acid (Amicar) may be helpful in BSS patients (Bunescu, 1994; Li, 1996). Some recent advances in treatment of BSS include gene replacement therapy, umbilical-cord or bone-marrow stem cell transplantation which may be helpful in life threatening situations (Locatelli, 2003). Genetic counseling can be of importance in diagnosing the defect in gene of patient with BSS prenatally. Proper knowledge about the syndrome and its precaution as well as about the treatment will help the surgeons to effectively manage the BSS patient to avoid intraoperative and postoperative bleeding in minor oral surgical procedures.

Conclusion

Bernard-Soulier syndrome is familial platelet disorders which is rare and is characterized by large platelets. Genetic studies reveals that it is mainly due to abnormality of the GPIb-IX-V platelet GP receptor complex. The bleeding symptoms ranges from mild to severe Recent Advances like ristocetin-induced platelet agglutination, flow cytometry and genetic research provide distinguishing diagnosis of this disorder. Good knowledge about this syndrome, its diagnostic criteria and treatment approaches will help in managing this BSS patient effectively during surgical procedure.

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