

# Case Report

## Adolescent menorrhagia due to platelet function disorder

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### Abstract

The prevalence of menorrhagia in adolescent populations with bleeding disorders varies between 14% to 48%. The common conditions associated with menorrhagia include von Willebrand disease (VWD), platelet function disorders and coagulation factor deficiencies. The majority of studies, which have been conducted in the West, report VWD, as the most common inherited bleeding disorder leading to menorrhagia, whereas studies from South-East Asia have found platelet function disorder as the leading inherited bleeding disorder in women with menorrhagia. The other common conditions which can lead to increased blood loss in this age group are anovulatory bleeding and hormonal disorders. We report here three cases of adolescent menorrhagia due to platelet function disorders, along with review of literature.

### Introduction

The role of inherited bleeding disorders in adolescent menorrhagia has been well recognized.<sup>1</sup> Among the inherited bleeding disorders, Platelet function defects are also an important cause of menorrhagia. Studies from West have also found an increased incidence of platelet dysfunction in Black women, compared to Caucasians.<sup>2</sup> Though, there are no local studies on the above subject, Saxena et al from India, evaluated 337 women with menorrhagia and found the incidence of platelet function disorder to be around 83%.<sup>3</sup> Among the platelet dysfunction, the commonest disorder is decreased aggregation response to ristocetin, in the presence of normal VWF:RCo and VWF(von willebrand factor). This has been reported in a number of studies.<sup>4</sup> Pakistan has a strong tradition of consanguineous marriages, so it is assumed that the incidence of platelet disorder will be higher.

Platelet disorders can be broadly classified into following categories:

- 1) Platelet Adhesion
- 2) Platelet Secretion
- 3) Platelet Activation
- 4) Platelet Aggregation

The initial laboratory test should include platelet count, peripheral blood smear, Prothrombin time and activated partial thromboplastin time.

Disorders of platelet adhesion include Von Willebrand disease, Bernard-Soulier Syndrome (BSS) and Collagen receptor defects.

Disorders of platelet secretion include Platelet Storage Pool Deficiencies and include Gray Platelet syndrome, delta storage pool deficiency and alpha-delta storage pool deficiency.<sup>5</sup>

We describe here three cases of adolescent menorrhagia due to platelet function disorder.

### Case 1:

A 13-year-old, girl had her menarche three months before her first visit to a doctor.

Her first two menstrual cycles were uneventful. On her third menstrual cycle, she bled heavily and required massive transfusion of blood and blood products. Eight units of packed red cells and 4 units of platelets were transfused for correction of anaemia and thrombocytopenia. There was a history of recurrent epistaxis, since the age of 4 years. Recurrent nose bleed 2-3 times, each month occurred, however, the teenager never required medical attention. There were no history of bruises, joint or muscle bleeding. Parents were first cousins. She had two other sisters, who had not yet started menstruation.

On examination, she was conscious, well oriented and weighed 74 pounds. Her heart rate was 120 beats per minute, blood pressure of 90/60 mm hg. Her systemic examination did not reveal any lymphadenopathy or hepatosplenomegaly. Laboratory investigations included the following: haemoglobin 6.0 gm/dl, total leukocyte count 6.900/mm and platelet count 17,000. Her peripheral blood smear showed large platelets. Her prothrombin time was 11 seconds, against a control of 13 seconds, whereas partial thromboplastin time and factor VIII levels were normal. Her von Willebrand antigen (VWF: Ag), VWF- ristocetin co-factor (VWF: RCo) were within normal limits. Platelet function tests showed a decreased response to adenosine diphosphate (ADP), collagen, ristocetin and epinephrine - induced aggregation. She was diagnosed as a case of combined platelet storage pool defect with Bernard-Soulier syndrome. She was started on oral contraceptive pills to prevent the excessive menstrual blood loss during her menstrual cycle, along with tranexamic acid during the first 4-5 days of her cycle in a dose of 250 mg every eight hours and oral iron therapy. She was also advised against the use of NSAID (non steroidal anti inflammatory) drugs in the future.

**Case 2:**

A 14-year-old girl, who had her menarche at the age of 13 years, was admitted in emergency with complaints of heavy and prolonged bleeding for two weeks. She was a known case of Glanzmann's thrombasthenia, and was receiving norethisterone (norethindrone), a progestin. She gave a past history of heavy and prolonged bleeding during her menstrual cycle. There was a history of recurrent epistaxis, since the age of 6-7 years, along with a history of bruises. There was no history of joint bleeding. She had not undergone any major surgery. Her parents were first cousins. She also had one more sibling affected with the disease. On examination, she was pale; her blood pressure was 90/60 mm hg. Her abdominal examination did not reveal any visceromegaly. Her laboratory investigation showed haemoglobin of 4 gm/ dl, a platelet count of 139,000 and bleeding time was prolonged to 8 minutes. Her prothrombin time was 11 seconds (control 13 seconds), and partial thromboplastin time was 34 seconds (control 30 seconds). Her previous laboratory reports had shown defective aggregation with epinephrine, ADP and collagen, and normal aggregation with ristocetin, findings which were consistent with Glanzmann's thromosthenia. Although she had reported massive bleeding with her first menstrual cycle, she was not given effective hormonal therapy. Her anaemia was corrected with a transfusion of packed red blood cells. Parenteral tranexamic acid was started to control bleeding in dose of 500 mg every eight hours. She was started on oral contraceptive pills. She was also advised against the use of NSAIDs. The blood loss during her menstrual cycle decreased in subsequent cycles. At present, she is being maintained on oral contraceptive pills.

**Case 3:**

A 12-year-old girl, a known case of Bernard - Soulier Syndrome(BSS), diagnosed at the age of 2 years, was brought into the emergency room, with history of massive bleeding per vaginum, for the last 7 days. On examination, she was markedly pale, tachycardiac and her blood pressure was 90/60 mm hg. On examination, there was no hepatosplenomegaly. Her pelvic ultrasound was also normal. On laboratory examination, she had haemoglobin of 2 gm/dl, total white blood cell count was 7000, and a platelet count of  $46 \times 10^9/l$ . Her coagulation profile was normal. She received 10 units of red cell concentrates, 8 units of platelets. Tranexamic acid was administered at dose of 500mg intravenously to stop bleeding. Despite these measures, she continued to change sanitary pads at 2-3 hour intervals. She was given recombinant factor VIIa (rFVIIa) to stop bleeding at a dose of  $60\mu\text{g/kg}$  intravenously. Her bleeding slowed down for 24 hours, and then restarted after a break of 24 hours. A second dose of rFVIIa was given to stop bleeding. She received further blood and blood products, to raise her haemoglobin. She was started on oral contraceptive pills in the same cycle. She was advised to continue with them. Her subsequent period was lighter and did not require hospital admission.

### **Discussion**

Menorrhagia is a common clinical problem and affects the quality of life in majority of women affected. The most common cause of menorrhagia at adolescence is hormonal. An immature hypothalamic-pituitary axis, resulting in anovulatory bleeding is responsible for the majority of cases of adolescent menorrhagia.. Although the prevalence of inherited bleeding disorders in the general population in West is estimated to be between 1-2%,<sup>6</sup> they have been found to be responsible for up to 20% of cases of menorrhagia. Patients with inherited bleeding disorders can also present at puberty, with excessive menstrual bleeding requiring immediate medical attention. We have described a series of girls, in whom platelet function disorders have been identified as a cause of excessive menstrual blood loss.

Bernard-Soulier Syndrome (BSS) is an autosomal recessive disorder, characterized by a quantitative or qualitative defect in membrane glycoproteins, resulting in defective adhesion of platelets to subendothelial von Willebrand factor. This defect results in a severe haemorrhagic disorder due to thrombocytopenia, decreased platelet adhesion and increased thrombin consumption, as well as increased consumption of platelets. Adolescent menorrhagia is a recognized complication. Severe episodes of bleeding are commonly seen during surgery, dental extraction and childbirth. Presence of a prolonged bleeding time, and thrombocytopenia along with large platelets on peripheral smear should raise the suspicion for this disorder. Platelet aggregometry shows a normal response to all agonists, except ristocetin. Bleeding episodes in people with BSS require use of intranasal desmopressin (DDAVP), rFVIIa, and the use of platelet transfusions. Unfortunately, use of platelet transfusions is associated with risks of isoimmunization. There are numerous case reports in literature where use of rFVIIa, which does not cause the development of antibodies against platelets, has been found to be successful in controlling bleeding episodes. Intractable bleeding at puberty in BSS girls have been treated with endometrial ablation.<sup>7</sup>

Glanzmann's thrombasthenia (GT) is a rare autosomal recessive disorder, mainly seen in Jews, Iraqi's, Jordanians, and from individuals in communities where consanguineous marriages are common. The disease is characterized as a moderate to severe haemorrhagic disorder, with mainly mucocutaneous bleeding, and female

preponderance, hence menorrhagia is an important aspect of the disease. A hospital based study from Pakistan, quoted a prevalence of 2.2% in patients referred for laboratory evaluation of bleeding disorder.<sup>8</sup> GT involves a defect in the platelet glycoprotein IIb/IIIa. Platelets are normal in number, but due to the defect, they fail to adhere at the site of blood vessel injury. In the second case, it involved a failure to form a haemostatic plug in the endometrial lining of the uterus resulting in excessive bleeding. Options available for treatment in girls include hormonal therapy, DDAVP, tranexamic acid, and in severe cases, use of rFVIIa to prevent massive bleeding and transfusion of blood products and platelets. Recommendations for control of bleeding during the menstrual cycle include use of high doses of norethisterone to control acute bleeding followed by maintenance with oral contraceptive pills. Supportive measures include replacement therapy with platelets, rFVIIa and tranxemic acid.

### **Conclusion**

Awareness about these diseases is necessary for gynaecologists, to avoid unnecessary surgical treatment in these patients. Use of progestins to control acute episodes of bleeding, followed by maintenance with combined oral contraceptive pills in cyclical manner has been found to be effective.

Menorrhagia at all stages of life severely affects the quality of life. Common treatment modalities available in this age group include antifibrinolytic agents, DDAVP, replacement therapy with factor VIII concentrates (in diagnosed cases of VWD), hormonal therapy, blood and blood products and the use of rFVIIa, to control acute episodes of blood loss.

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