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**CASE REPORT**

**Quebec Platelet Disorder**

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**ABSTRACT**

A case of Quebec platelet disorder is hereby reported. A 33 years old woman presented with history of epistaxis and gum bleeding since childhood and menorrhagia and bleeding per vaginum after puberty, also had history of excessive blood loss after birth of child. Her coagulation profile was normal but platelet function testing by platelet aggregation assay showed abnormal aggregation of platelet with epinephrine. This type of response is seen in “Quebec platelet disorder” which is a rare autosomal dominant disorder of platelet function characterized by increased bleeding after any injury or trauma.

**Key words:** Quebec platelet disorder. Platelet function test. Bleeding time. Abnormal aggregation. Epinephrine.

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**INTRODUCTION**

Hemorrhagic and thrombotic disorders are largely mediated by congenital or acquired abnormalities of blood coagulation, platelet number, or platelet function. Abnormal bleeding can result from excessive expression of plasminogen activators or from deficiencies of fibrinolysis inhibitors. Most inherited bleeding disorders result from genetic defects that reduce hemostatic protein expression, secretion, or function. Inherited conditions that cause bleeding by increasing gene expression are uncommon and include Quebec platelet disorder (QPD), an autosomal dominant disorder with high and possibly complete penetrance. QPD is associated with a unique gain-of-function abnormality in fibrinolysis due to increased platelet stores of urokinase plasminogen activator (uPA) without systemic fibrinolysis or increased uPA in plasma, urine, or CD34_ hematopoietic progenitors. QPD increases risks for a number of bleeding symptoms, including delayed-onset bleeding after hemostatic challenges that respond only to fibrinolytic inhibitor therapy. Diagnostic tests for QPD include assays for increased platelet uPA and alpha granule protein degradation from intraplatelet plasmin generation, platelet function test is assessed with the help of platelet aggregation assay by exposing platelets to various stimulants like ADP, arachidonic acid, collagen, epinephrine, thrombin, and ristocetin. In QBD, platelets show very abnormal aggregation with epinephrine because there is defect in alpha granules proteolysis of proteins and a deficiency of alpha granule multimerin, a protein that binds factor V within granule and leads to a decreased content of factor V and several other proteins like fibrinogen, vWF etc.

This case report describes a rare clinical condition in a young female.

**CASE REPORT**

A 33 years old woman presented with generalized weakness, weight loss, pallor and history of epistaxis and gum bleeding since childhood and menorrhagia after puberty. She also had increased blood loss after birth of her all three children who were born by normal delivery. Patient had undergone multiple blood transfusions in her past history for low hemoglobin. She had 5 sisters and 6 brothers. There was positive family history for bleeding episodes among her siblings (two sisters), but their workup for bleeding disorders was not done. There was no history of any bleeding disorders among parents, her parents are not available so pedigree tracing is not possible but assumingly her mother was as the affected parent for pedigree tracing (Figure 1).

On examination she was thin, lean and pale. The rest of physical examination was normal except for having easy bruising after needle prick. Chest examination showed dull percussion note over the left lower lung base.

On investigations, chest X-ray was done which showed left sided mild pleural effusion. Workup for pleural effusion...
raised strong suspicion of tuberculosis as effusion was exudative lymphocytic, which was augmented with positive tuberculin skin test (Mantoux test). She was started on anti-tuberculosis treatment.

Further workup was done due to her symptoms of bleeding. Her complete blood count showed hemoglobin of 5.2 g/dl with mean corpuscular volume of 56 FL. The white cell and reticulocyte count were normal. Peripheral smear showed microcytic hypochromic anemia. Her platelet count was normal. Coagulation profile showed normal PT and APTT which bleeding time (BT) was more than 9 minutes. Platelet function testing was done by platelet aggregometry which showed normal response to other factors like collagen, ADP, thrombin, but an abnormal aggregation response to epinephrine. All other factor assays like factor VIII, vWF, factor XIII were normal. This type of platelet response is seen in Quebec platelet disorder. So she was diagnosed to have Quebec platelet disorder and was started on fibrinolysis inhibitors (tranexamic acid) after which her gum bleeding stopped but she needed blood transfusion for severe anemia.

**DISCUSSION**

Quebec Platelet Disorder (QPD) is an autosomal dominant bleeding disorder which is more prevalent in province of Quebec in Canada. The disorder is characterized by large amounts of the fibrinolytic enzyme urokinase-type plasminogen activator (u-PA) in platelets. Consequently, stored platelet plasminogen is converted to plasmin, which is thought to play a role in degrading a number of proteins stored in platelet α-granules. These proteins include platelet factor V, Von Willebrand factor, fibrinogen, thrombospondin-1, and osteonectin. There is also a quantitative deficiency in the platelet protein multimerin 1 (MMRN1). Furthermore, upon QPD platelet activation, u-PA can be released into forming clots and accelerate clot lysis, resulting in delayed-onset bleeding (12-24 hours after injury). Individuals with QPD are at risk for experiencing a number of bleeding symptoms, including joint bleeds, hematuria, and large bruising. This patient likewise also experienced bleeding episodes especially from gums, and menorrhagia. The genetic cause of QPD has not yet been determined. Whether the abnormal bleeding in this disorder results from the degradation of platelet hemostatic factors, premature lysis of thrombi due to u-PA release from platelets, or both, is unresolved. However, studies of transgenic mice with platelet-specific over-expression of u-PA suggest that premature clot lysis due to localized release of u-PA from platelets is the predominant cause of bleeding.

In bleeding patients with the factor V Quebec platelet disorder, platelet transfusions are generally without effect; fibrinolytic inhibitors are reported to be effective. Tranexamic acid and aminocaproic acid are lysine analogues that bind to the kringle domains of plasminogen and disrupt interactions between plasminogen (and plasmin) and lysine residues within fibrin. Uptill now tranexamic acid has benefitted in resolving bleeding episodes in our patients. A meta-analysis of clinical trials indicated that lysine analogues significantly reduce perioperative blood loss in patients undergoing coronary artery bypass grafting with cardiopulmonary bypass, without increasing the incidence of myocardial infarction.

This lady, admitted with history of bleeding gums, epistaxis and menorrhagia and history of multiple blood transfusions, was diagnosed to have “Quebec platelet disorder” on the basis of history, examination and laboratory findings of increased bleeding time and on platelet function testing by platelet aggregation assay showing abnormal aggregation to epinephrine. She was managed with giving lysine analogues like Tranexamic acid which act as fibrinolytic inhibitors. She responded well to treatment and her bleeding symptoms resolved.

**REFERENCES**