Glanzmann`s Thrombosthenia: A rare cause of Recurrent Epistaxis

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Abstract
Platelets play an important role in the process of homeostasis in endothelial injuries. Glanzmann`s thrombasthenia is very rare inherited functional disorder of platelets. It is characterized by failure of platelet aggregation due to the lack of cell membrane glycoproteins IIb/ IIIa. It presents with bleeding in young age. The bleeding episodes are usually mild and recurrent but sometimes bleeding may be severe enough to be life threatening. The platelets are the first major component of coagulation system at the site of injury and bleeding. In case of trauma platelets adhere to the exposed sub-endothelial tissue. Platelets release biochemical mediators (Adenosine biphosphate and serotonin) and more cells are recruited towards the injured area in a process called activation of platelets. We report a twelve years old boy with recurrent epistaxis where nasal packing was ineffective to control bleeding. His bleeding profile showed significantly prolonged bleeding time and platelet function studies confirmed the diagnosis. He was managed with platelet transfusions.

Key words: Glanzmann`s thrombasthenia, inherited platelet disorders, epistaxis, platelet function studies. Glycoprotein IIb/IIIa.

Introduction
Platelets play key role in primary homeostasis in endothelial injury. Platelet aggregation results in formation of white thrombus and prevents further bleeding. The aggregation of platelets is regulated by glycoproteins of cell membrane. There are two different sets of glycoprotein receptors. The first contact between platelets and Van Willebrand factor is established by glycoprotein Ib-V-IX. The congenital deficiency of these factor results in Von Willebrand disease and Barnard Soulier syndrome respectively. The interaction between already adhering and still circulating platelets is established through glycoprotein IIb/IIIa. The deficiency of this glycoprotein membrane receptor is responsible for Glanzmann`s thrombasthenia. Its incidence is less than 1 in one million populations. We are reporting this case first time from Pakistan.

Case Report
Twelve years old boy was presented with history of recurrent epistaxis. He had been suffering from frequent episodes of epistaxis since early childhood. There was no history of mucosal or overt bleeding from any other site. There was strong background of consanguinity in family. The
younger sister of his mother died at the age of eight years during an episode of severe nasal bleeding (Figure-1). There was no history of significant medical illness in his parents. He had three brothers and three sisters, all are normal with no history of bleeding.

His minor bleeding episodes are mostly self limiting. He had two episodes of severe epistaxis needing nasal packing and admission in the hospital. During these episodes nasal packing was ineffective to control bleeding and he was transfused with platelet aggregates for haemostasis. His circumcision was performed in hospital on the second day of his birth. No hospital record was available and parents did not remember any significant bleeding at that time.

On physical examination his radial pulse was 92/min, regular, B.P 110/70 mmHg. He was pale and rest of general physical examination was normal. There was active oozing of fresh blood from right nostril. There were no bruises, ecchymosis or purpuric spots on the skin. There was no lymphadenopathy; liver and spleen were not palpable. The examination of his cardiovascular, respiratory, musculoskeletal and central nervous systems was normal.

The provisional clinical diagnosis of bleeding diathesis was made and following investigations were carried out.

His Blood C/P revealed Hb.7.8 gm/dl, TLC 6.2 X 10^3/ dl with normal differential counts, Platelet count 194 X 10^3/ dl. The morphology of platelets appeared normal on peripheral smear. Screening for Hepatitis B and C infections was negative. His bleeding time was more than 15 minutes (Normal 2-7 minutes). Hess test was negative. Prothrombin and activated Prothrombin time of patient were normal. The assay of factor XIII showed no deficiency. Platelet function studies showed no response to platelet agonists. (Table-1)

<table>
<thead>
<tr>
<th>Table 1: Platelet Function Study</th>
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<tbody>
<tr>
<td>Platelet count</td>
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<tr>
<td>Bleeding time</td>
</tr>
<tr>
<td>1-Collagen</td>
</tr>
<tr>
<td>2-ADP</td>
</tr>
<tr>
<td>3-Epinephrine</td>
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<tr>
<td>4-Ristocetin</td>
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<tr>
<td>Hess test</td>
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*Opinion: Glanzmann,s thrombasthenia.*

**Discussion**

This rare disorder was suspected in this patient due to typical history of excessive bleeding and significantly prolonged bleeding time. The diagnosis was confirmed by platelet function studies. The normal platelet aggregation response to platelet agonists ADP, Epinephrine and collagen was absent while it was normal with ristocetin. Patients with Glanzmann’s thrombasthenia normally present in childhood or early adolescence with epistaxis, bleeding due to tooth extraction, menorrhagia, mucosal, gastrointestinal or skin bleeding. The differential diagnosis includes other inherited platelet disorders e.g. Bernard Soulier, Hermansky-Pudlak and Wiskott-Aldrich syndromes. The other condition which may present with similar bleeding is Von Willebrand disease.

Platelets play an important role in the process of hemostasis. The normal platelet count is 150,000-450,000 /µL. Platelet are released from the megakaryocyte and regulated by hormone
thrombopoietin (TPO). Platelets are disc shaped cells without nucleus or DNA with an average life span of 7-10 days. They are physiologically active but have very limited capacity to synthesize new proteins. One third Platelets are stored in spleen and two third circulate in blood and remain inactive before removed by spleen from circulation. The platelet glycoprotein II b/IIIa is the most abundant receptor on the cell membrane⁴. It has about 50,000 fibrinogen binding sites. It can rapidly form fibrin mesh while platelets are activated.

There is efficient natural balance between procoagulant and anticoagulant factors to maintain haemostatic system of human body. The main procoagulant factors are activated platelets and fibrin clot formation. The anti coagulation is provided by natural inhibitors of coagulation and fibrinolysis. In healthy individuals the balanced haemostasis is regulated in favour of blood flow. However, this system is primed to clot blood immediately in case of bleeding. The platelets are the first major component of coagulation system at the site of injury and bleeding. In case of trauma platelets adhere to the exposed sub-endothelial tissue. Platelets release biochemical mediators (Adenosine biphosphate and serotonin) and more cells are recruited towards the injured area in a process called activation of platelets⁵. This process is further amplified by certain factors present in the extra cellular matrix of vessel wall e.g. collagen and von Willebrand factor. It is also enhanced by epinephrine and thrombin humoral mediators present in the plasma. The naturally present anti coagulant endothelial cell factors are inhibited at this stage. The activated platelets during release reaction secrete various biochemical mediators to promote more platelet aggregation. This leads to the formation of occlusive platelet plug at the site of injury and bleeding. It is stabilized and firmly anchored to the vessel wall by developing fibrin mesh.

There are two types of platelet disorders. In quantitative platelet disorders total number of platelets is either decreased or increased. In rare inherited qualitative disorders total number of platelets is abnormal in the presence of normal counts.⁶ Glanzmann’s thrombasthenia is very rare inherited qualitative disorder of platelets due to lack of glycoprotein IIIb/IIa.⁷ The first description of this disorder was given by a Swiss pediatrician Dr. Eduard Glanzmann in 1918.⁸ It is inherited as autosomal recessive disorder and genes for these proteins are located on chromosome 17⁹. The absence of these proteins leads to failure of platelet aggregation and significant prolongation of bleeding time. These receptor proteins are activated by platelet agonists like ADP, extra cellular matrix protein collagen, plasma protein thrombin or by epinephrine. The understanding of these receptors has led to the development of anti IIIb/IIa inhibitors, a class of very potent anti platelet agents.

This rare disorder has been reported in families with high consanguinity in certain areas of Israel, Jordan and Iran. In our patient there was history of close family marriages since several generations in a close community. The younger sister of his mother died in young age while history was highly suggestive of Glanzmann’s thrombasthenia in her.

The treatment of bleeding or preoperative prevention in these patients often requires platelet transfusions. It is preferred to use prestorage leuko depleted platelets to avoid alloimmunization. Patients with mild symptoms respond to desmopressin. It is useful for mucosal bleeding and can be used in conjunction with tranexamic acid. Oral contraception is used for menorrhagia. These patients should not receive anti-coagulants or anti
platelet drugs like Aspirin, warfarin, clopidogrel, prisogrel, ticlodipine, dipyridamole, or anti thrombolytic agents. This condition has good prognosis but needs appropriate management and prolong follow up.

**Conclusion**

In young patients with recurrent epistaxis there is possibility of rare underlying causes. Glanzman,s thrombosthenia is among one of those rare causes of nasal bleeds. Young physicians need to be aware of its possibility in these circumstances.

**References**

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