

Case Report

Glanzmann's Thrombasthenia: Role of Angioembolization and factor VII in recurrent bleeding from ulcerated duodenum

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Abstract

Introduction: Glanzmann's thrombasthenia (GT) is a rare, genetically inherited, functional disorder of platelets. The pathology is deficient or dysfunctional platelet glycoprotein IIb/IIIa (GP IIb/IIIa) complex resulting in bleeding diathesis. *Case Report:* Here in, we report the effectivity of angioembolization with factor VII in a patient with Glanzmann's thrombasthenia (GT), who presented with recurrent bleeding from duodenal ulcer. *Conclusion:* Angioembolization with added infusion of factor VII, can be considered an equally effective alternate to platelet transfusion in patients of GT, who present with recurrent bleeding

Keywords

Glanzmann's thrombasthenia (GT), functional disorder of platelets, angioembolization, bleeding diathesis

Introduction

Glanzmann's thrombasthenia (GT), a rare functional disorder of platelets, inherited in autosomal recessive pattern with only few acquired cases reported (Varkey, 2014). It is highly prevalent in those ethnic populations where consanguineous marriages are common (George, 1990). The pathology lies in the platelet glycoprotein IIb/IIIa (GP IIb/IIIa) complex, in which case it is either deficient or dysfunctional. This glycoprotein aids in platelets aggregation, whose abnormality results in defective aggregation, hence bleeding diathesis ensues (Nurden, 2013). The disorder is characterized by prolonged bleeding time with normal platelet count, and morphology as well as normal coagulation profile (Gopalakrishnan, 2014). Clinically it manifests in childhood as spontaneous bruising, epistaxis, bleeding gums, heavy menstrual bleeding (HMB) and less frequently gastrointestinal bleeding, haematuria, haemarthrosis, muscle haematoma and nervous system haemorrhages. Bleeding complications are also seen frequently in post-partum mothers and post-operative patients (Duman, 2012 & Giordano, 2013). Mild bleeding is controlled by applying local pressure. For managing severe bleed, platelet transfusion is the standard therapy (Giordano, 2013). However multiple transfusions may not be of any benefit, because of the auto antibodies produced against GPIIb/ IIIa and/or human leucocyte antigens (HLA). Moreover, the risk of infection and allergic reactions and availability of transfusion products are also important question marks in the management of recurrent bleeding patients with standard option (Giordano, 2013). This necessitates the need of an alternative, equally

effective treatment, for managing such patients with recurrent bleeding, with or without refractoriness to platelet transfusion. In this case, we report the effectivity of angioembolization with factor VII in a patient with Glanzmann's thrombasthenia (GT), who presented with recurrent bleeding.

Case Report

A 22 years old male, known case of Glanzman's Thrombasthenia (GT), was admitted at the Agha Khan University hospital with chief complains of abdominal pain, melena and general weakness. On admission, Hb was 3g/dl, so he was shifted to special care unit. Packed red cells and platelets were transfused and started on I/V omeprazole, factor VII and somatostatin infusion. Endoscopy was done which showed altered blood at antrum and active blood at distal (2nd) part of duodenum oozing from an ulcer. Sclerotherapy was done with epinephrine followed by APC and 4 hemoclips were applied, partial hemostasis was achieved and referred for angioembolization. Selective catheterization of gastroduodenal artery was done and diluted non-ionic water soluble contrast was injected and multiple views were obtained but no discrete bleeding points were identified. Gastroduodenal artery was empirically embolised. Three coils were placed in the gastroduodenal artery proximally. One of the coils displaced into a branch of right hepatic artery due to highly flow in gastroduodenal artery. Distally gastroduodenal artery was embolised with (355-500 microns) PVA particles. No evidence of residual flow or active extravasation noted and no arteriovenous malformation was seen. Vascular access sheath was

removed and haemostasis secured with angioseal. Ultrasound was also performed for any intra-abdominal fluid collection or hematoma but minimal streak of peri-hepatic free fluid was identified.

Post-angioembolization, he developed active upper G.I bleeding and was again transfused. CT scan with multiple axial, reformatted, sagittal and coronal sections were acquired from abdomen and pelvis, with and without administration of IV contrast, using usual departmental protocol, which determined evidence of intraluminal contrast extravasation with pooling of hyperdense contrast on the delayed images in the second part of duodenum. Findings are consistent with active gastrointestinal bleed. Multiple low attenuation wedge shaped areas were seen in the spleen representing splenic infarcts and air specks and fat stranding were identified in soft tissues of right upper thigh representing postsurgical changes and multiple metallic densities identified in the right upper quadrant and right iliac fossa, these likely represent surgical clips and wires.

Re-angioembolization was done. There was tight stenosis / occlusion of the origin of celiac artery. The superior mesenteric artery was selectively catheterised. There was filling of gastroduodenal artery and hepatic artery through collateral vessels. Non-ionic water soluble contrast was injected and multiple views were obtained. Active extravasation was identified in the region of duodenum from gastroduodenal artery at the site of previous coiling. Gastroduodenal artery was selectively catheterized with micro catheter and successfully embolised with two metallic coils.

Post embolisation showed no evidence of extravasation of contrast. No arteriovenous malformation was seen. Vascular access sheath left in situ and secured to skin by silk suture. Patient was transfused with blood products multiple times. His symptoms soon improved and Hb was static. He was observed and remained stable, thus was discharged and asked to follow-up.

Figures 1 (a)

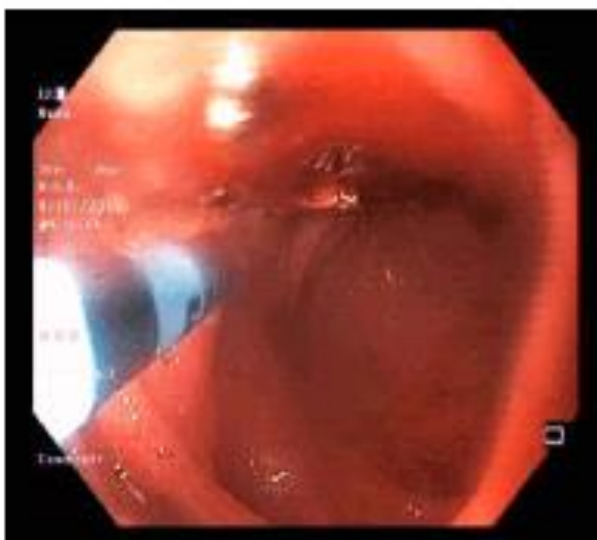


Figures 1 (b)



Bleeding point in duodenum

Figures 2



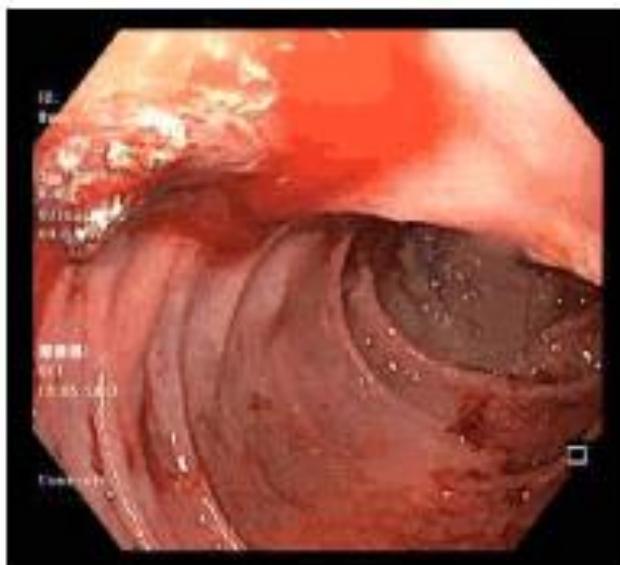
APC

Figures 3



Bleeding point in duodenum with hemoclip

Figures 2



Bleeding point in duodenum

Discussion

Glanzmann thrombasthenia is an inherited bleeding disorder characterized by the failure of platelets to aggregate in response to almost all stimuli (Ruggeri, 1982). It is a moderate to severe hemorrhagic disorder with mainly mucocutaneous bleeding. The

molecular basis is linked to quantitative and/or qualitative abnormalities of $\alpha\text{IIb}\beta\text{3}$ integrin, the receptor that mediates the incorporation of platelets into an aggregate or thrombus at sites of vessel injury (Nurden, 2006). The cardinal features of GT are defects in platelet aggregation and clot retraction,

prolonged bleeding times, and cutaneous and gastrointestinal bleeding (hodiala-Dilke, 1999). GI bleeding in patients with Glanzmann's disease has only rarely been reported and usually is not a main clinical problem in this disorder of platelet function. Common clinical manifestations include purpuric type bleeding, epistaxis, menorrhagia and gingival bleeding. Spontaneous bleeding is uncommon but posttraumatic and postoperative hemorrhage may be particularly serious. There is no specific treatment (Van Buuren, 2002).

Platelet transfusion is the standard treatment for severe bleeding and for surgical support (Poon, 1999). Most patients (>2/3) require blood and/or platelet transfusions at least once in their life (Di Minno, 2009). However, repeated platelet transfusions in such patients may result in alloimmunization to human leukocyte antigens (HLA) and/or platelet membrane GPIIb/IIIa, rendering future transfusions ineffective (Poon, 1999). rFVIIa seems a potential alternative to platelet transfusion in GT patients, particularly in those with antiplatelet antibodies and/or platelet refractoriness (Poon, 2004). Furthermore, platelet transfusions have risk for adverse reactions including virus transmission, and may not be readily available to patients living in remote areas (Poon, 1999). There are increasing reports documenting efficacy of high dose rFVIIa in GT patients with adverse events uncommon. The efficacy is supported by evidence that high concentration FVIIa binds to activated platelet surface and improves thrombin generation to enhance deposition (adhesion) and aggregation of platelets lacking GPIIb/IIIa. While there are increasing clinical experiences, evidence-based clinical data are not available (Poon, 2007). An international survey suggests that rFVIIa at about 90 µg/kg every 2 hours for 3 or more doses could be used for GT patients with severe bleeding, but confirmation by larger studies is needed (Poon, 2007). However, bleeding phenotype is dramatically variable, some patients having only minimal bruising, others frequent, severe, potentially fatal haemorrhages. Presently, no specific guidelines or algorithms for clinical management of GT are available (Di Minno, 2009).

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