

Multiple Gastrointestinal Arterio-venous Malformations: A Rare Presentation of Glanzmann Thrombasthenia

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Abstract

Glanzmann's thrombasthenia (GT) is a rare bleeding disorder characterized by abnormal platelet aggregation due to either an absent or dysfunctional glycoprotein IIb-IIIa receptor. These patients are at risk of mucocutaneous bleeding and excessive hemorrhagic blood loss during surgical procedures. However, it is rare and unusual to have massive upper gastrointestinal bleeding in patients diagnosed with GT. We report a case of a young female diagnosed with GT who presented to the emergency department in a state of hypovolemic shock due to hematemesis and melena, leading to an acute blood loss anaemia. The patient underwent an upper gastrointestinal (GI) scoping after initial hemodynamic stabilization. Endoscopic procedure confirmed the presence of multiple AV malformations at different levels, managed with endoscopic argon laser photocoagulation.

Keywords: *Glanzmann's Thrombasthenia; Arterio-Venous Malformation; Upper Gastrointestinal Bleeding*

Introduction

Glanzmann's thrombasthenia (GT) is a rare autosomal recessive bleeding disorder characterized by abnormal platelet aggregation. It is due to an abnormality in the glycoprotein IIb-IIIa receptor, which can no longer act as a ligand-receptor for fibrinogen and Von Willebrand factor, thus disabling platelet activation. Mucocutaneous bleeding is a common presenting symptom in these patients. To the best of the authors' knowledge, this is the first case of spontaneous internal bleeding due to gastrointestinal (GI) arteriovenous (AV) malformation in a patient with a past medical history of GT.

Case Presentation

The patient is a 15-year-old female with a known diagnosis of GT, presented to the emergency department with a 7-day history of hematemesis, melena, hematochezia, pallor, easy fatigability on exertion, and shortness of breath. She was diagnosed with GT one year back after the demise of her brother from the same bleeding disorder who was undiagnosed until death. All siblings screened for bleeding diathesis, and thus, a diagnosis of GT made based on prolonged bleeding time and lack of platelet aggregation with adenosine diphosphate, epinephrine, and collagen. On physical exam, the patient was in a state of hypovolemic shock with a blood pressure of 90/50 mm of Hg, heart rate of 112 beats per minute, the temperature of 98 degrees Fahrenheit, and pulse oxygen saturation of 96%. She had palmar and conjunctival pallor, koilonychia, cyanosis and bruises on the hands, forearms, and face. She also had a flow murmur on auscultation of the precordium best heard over the aortic area. The rest of the systemic examination was unremarkable. Laboratory workup showed hypochromic microcytic anemia with a hemoglobin of 2 g/dL (Ref: 12 - 15 g/dL), a mean corpuscular volume of 60 fL (Ref: 80-100 fL), a

reticulocyte count of 5% (Ref: 0.5 - 1.5%), a white blood cell count of $12 \times 10^9/L$ (Ref: $4 - 10 \times 10^9/L$), and a platelet count of $174 \times 10^9/L$ (Ref: $150 - 400 \times 10^9/L$). A stool guaiac test was positive. Prothrombin time was 20 seconds (Ref: 11-14 sec) and activated thromboplastin time was 46 seconds (Ref: 20 - 40 sec). A proctoscopy performed confirmed no other obvious source of bleeding. A colonoscopy not performed due to the patient's hemodynamic instability. The patient received massive blood products transfusion with four units of packed red blood cells (PRBC) and four units of fresh frozen plasma (FFP). Despite the aggressive replacement of blood products, there was continuous blood loss accompanied by a persistent drop in haemoglobin, which led to an additional transfusion of a few more units of PRBC and FFP. Once hemodynamic and clinical stabilization achieved, an urgent esophagogastroduodenoscopy performed to look for possible sources of bleeding. Scoping showed multiple arteriovenous malformations (AVM) with one AVM identified at the distal oesophagus and a few at the gastroesophageal junction, where two were actively bleeding. A few AVMs were also identified in the second part of the duodenum and injected with 4 ml of adrenaline with heat probing. This procedure stopped the GI bleed for the time being. An hour later, the patient started to bleed again despite the initially performed corrective measures during the esophagogastroduodenoscopy. She underwent an emergent second esophagogastroduodenoscopy which demonstrated corrective changes performed during the first scoping with no bleeding from the corrective sources except for the AVMs that in the second part of the duodenum were bleeding despite previous corrective measures. Argon laser-plasma coagulation performed for those AVMs and also prophylactic laser coagulation performed for the non-bleeding AVMs at the distal oesophagus and gastroesophageal junction (Figure 1-3). The patient did not bleed after the second scope and thus was discharged home with a one month outpatient follow up visit in which she clinically improved with a haemoglobin of 13 g/dL. A third upper GI endoscopy showed no further active bleeding from the AVMs. She received information regarding the alarm signs and symptoms with continuous regular outpatient follow up and advised to have regular follow up visits.

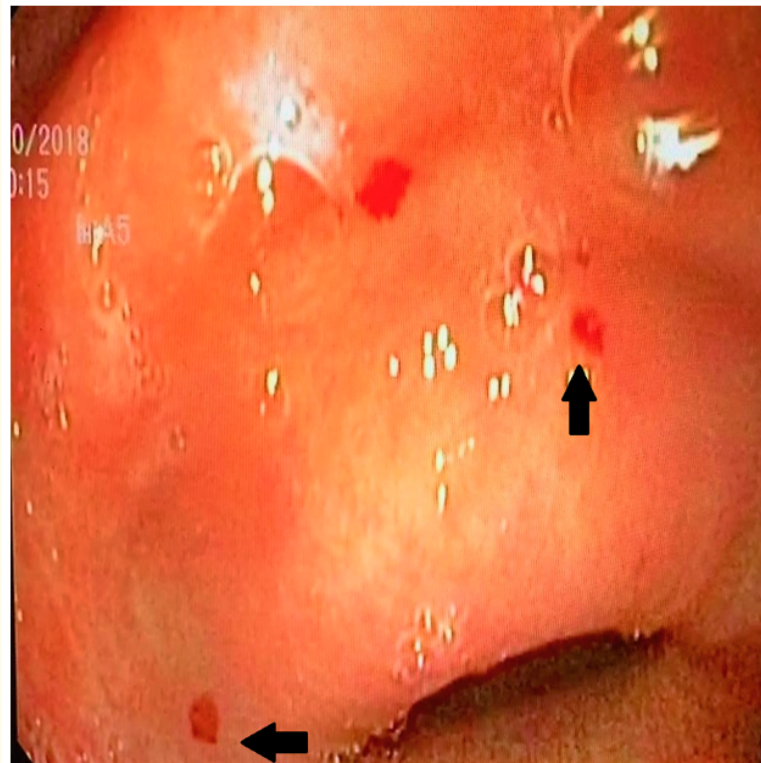


Figure 1: Multiple Arteriovenous malformations in the distal oesophagus.



Figure 2: Endoscopic intervention for Arteriovenous malformations.

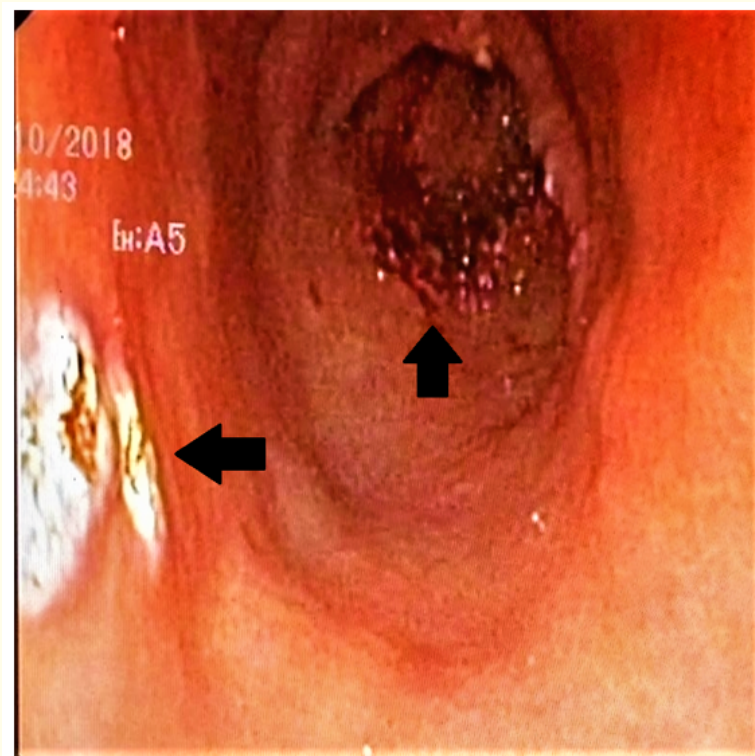


Figure 3: Arteriovenous malformations after Argon laser-plasma coagulation.

Discussion

GT is a rare autosomal recessive bleeding disorder first described by Glanzmann in 1918 as “hereditary hemorrhagic thrombasthenia” [1], affecting the megakaryocytes [S1] lineage and is characterized by the impairment of platelet function. It is a hemorrhagic disorder with mucocutaneous bleeding as a predominant manifestation. The molecular basis of its pathology is linked to quantitative or qualitative abnormalities of IIb 3 integrin, the receptor that mediates the incorporation of platelets into an aggregate and thrombus formation at the site of vessel injury. In the early era, the diagnostic criteria for this disease was a prolonged bleeding time and an isolated rather than the clumped appearance of platelets on a peripheral blood smear. In 1956, Braunsteiner and Pakesch reviewed the disorders of platelet dysfunction and described thrombasthenia as an inherited disease characterized by platelets of average size that failed to spread onto a surface and did not support clot retraction [2]. Those patients with absent platelet aggregation and absent clot retraction subsequently termed as having type I disease. Those with absent aggregation but residual clot retraction labelled as having type II disease. The variant disease was first established in 1987 [3].

The clinical presentation of GT ranges from mild bruising to severe fatal internal haemorrhages. However, hemorrhagic symptoms occur only in patients who are homozygous for mutations causing GT. The heterozygous condition is mostly asymptomatic, even though these subjects only have half the average concentration of platelet IIb 3 [3]. Mucocutaneous bleeding occurs more commonly, including purpura, epistaxis, gingival haemorrhage and menorrhagia. Another less common but serious complication is gastrointestinal bleeding [4,5]. This patient had signs and symptoms of an upper GI bleed, the causes of which can be classified depending on the anatomic and pathophysiological factors such as peptic ulcer disease (55 percent), esophagogastric varices (14 percent), arterial, venous, and other vascular malformations (7 percent), mallory-weiss tears (5 percent), erosions (4 percent), tumors (4 percent), and other causes (11 percent) [6]. The gastrointestinal vascular diseases further include angiodysplasia, arteriovenous malformation (AVM), cavernous hemangioma, hereditary hemorrhagic telangiectasia (Rendu-Osler-Weber disease), gastric antral vascular ectasia, and Dieulafoy’s lesion [6,7].

AVMs are rare clinical lesions consisting of abnormal shunts between the arterial and venous vascular systems and may present variably. Gastric AVMs may clinically be asymptomatic or may present as massive upper gastrointestinal bleeding or chronic iron deficiency anaemia [9]. The diagnosis is usually troublesome because routine barium contrast studies and endoscopy often fail to demonstrate the lesions. However, over the past 30 years, the increasing use of angiography in the assessment of gastrointestinal bleeding has made the diagnosis much easier [8].

For acute and massive gastrointestinal haemorrhage, immediate embolization can stop the bleeding and rectify hemodynamic instability. Endoscopic techniques used during the procedure include epinephrine injection, bipolar electrocoagulation, monopolar electrocoagulation, injection sclerotherapy, heater probe, laser photocoagulation, hemo-clipping, and banding [7]. Rarely, surgical removal of the lesion may be needed and only recommended if other treatment options have not been successful. Endoscopic therapy is said to be successful in achieving permanent hemostasis in 85% of cases. Of the remaining 15% where rebleeding occurs, 10% can successfully be treated by repeat endoscopic therapy, while 5% may ultimately require surgical intervention [10].

Conclusion

This case presentation emphasizes the rare and unusual association between multiple gastrointestinal AVMs and GT. This association must be considered in patients presenting similarly in order not to delay the timely diagnosis and treatment.

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