Case Report

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Glanzmann's thrombasthenia with spontaneous upper gastrointestinal bleeding: a case report

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Abstract

Glanzmann's thrombasthenia (GT) is a rare bleeding disorder inherited in an autosomal recessive manner. The pathogenesis of GT mainly involves structural abnormalities and dysfunction of platelet membrane glycoprotein IIb/IIIa (integrin αIIbβ3). The most common symptoms of GT are various types of bleeding, including recurrent nasal bleeding, mucocutaneous bleeding, unremitting bleeding after injury or operation, and menorrhea in women. Such hemorrhage may be fatal in some patients. GT with spontaneous upper gastrointestinal bleeding is relatively rare. In the present report, we describe a middle-aged man who was hospitalized with spontaneous upper gastrointestinal bleeding. His main symptom was recurrent chronic and intermittent melena. Gastroscopy revealed oozing of blood in the gastric antrum wall. However, no obvious lesions such as erosion or ulceration were found. Upon further inspection, we found that the patient's platelet aggregation was poor, and flow cytometry assay revealed low expression of platelet membrane integrin αIIbβ3. The patient was eventually diagnosed with GT and exhibited clinical improvement after active treatment.

Keywords

Glanzmann's thrombasthenia, upper gastrointestinal bleeding, gastrointestinal manifestations, diagnosis, treatment, platelet aggregation, platelet membrane integrin αIIbβ3

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Introduction

Glanzmann's thrombasthenia (GT) was first reported by Glanzmann in 1918. GT is a severe congenital platelet disorder in which platelets are lacking glycoprotein IIb/IIIa (integrin αIIbβ3), inducing a serious defect in platelet aggregation.[1] GT is rare worldwide but more common in families of consanguineous marriage. No significant difference in the incidence of GT has been found between male and female patients.[2] The main clinical manifestation of GT is moderate to severe mucocutaneous hemorrhage; visceral hemorrhage is rare.[3] A general physical examination does not readily reveal abnormalities associated with GT; hence, missed diagnosis or misdiagnosis of GT readily occurs. Laboratory tests are essential for a diagnosis of GT. The platelet morphology and platelet count are usually within the normal ranges in patients with GT, but the bleeding time is markedly longer. Therefore, detection of platelet aggregation defects is the basis of the diagnosis of GT, and it is important to perform more specific methods such as flow cytometry or gene detection to achieve a definitive diagnosis.[4] A complete cure of GT has not been established; instead, symptomatic treatment is mainly performed.[5] We herein report a challenging case of GT and explore the clinical features, diagnostic points, treatment practices, and prognosis of this disease.

Case report

A 43-year-old man was hospitalized for chest tightness. He had developed recurrent chronic and intermittent melena 3 months before hospitalization, but these symptoms were not regarded as important. However, his symptoms subsequently worsened, developing into more frequent melena with new symptoms such as dizziness, nausea, and epigastric pain. The epigastric pain usually occurred with the bleeding, and it generally eased after the melena stopped. The patient had no history of taking any special drugs or having any infection before the onset of melena or chest tightness. We carefully reviewed his medical history and performed a complete medical examination. When he was young, he had often experienced large amounts of spontaneous bleeding from the nose and gingiva at a high frequency several times a year. Moreover, he had been previously diagnosed with severe anemia for which he received blood transfusions. His parents were in good health, and their marriage was non-consanguineous. Physical examination of the patient on admission revealed pale skin and epigastric tenderness. The main laboratory tests results were as follows: hemoglobin, 44 g/L; red blood cell count, 3.27×10^{12}/L; platelet count, 147×10^{9}/L; fibrinogen, 2.026 g/L; prothrombin time, 12.2 seconds; and activated partial thromboplastin time, 12.2 seconds.

The patient was initially diagnosed with upper gastrointestinal bleeding and underwent gastroscopy, which revealed oozing of blood in the wall of the gastric antrum (Figure 1(a)). He underwent endoscopic hemostasis therapy with no complications. A proton pump inhibitor and somatostatin were administered postoperatively. The patient also received blood transfusions, and his condition gradually stabilized. No obvious lesions such as erosions or ulcerations were found by gastroscopy (Figure 1 (b)–(d)). Because of the patient's bleeding history, we considered that he may have had various blood diseases. Platelet aggregation assays revealed no aggregation with 2 μmol/L adenosine diphosphate or 2 μmol/L adrenaline, while a slightly weaker response to ristocetin was noted (23% (60S), 29% (180S), and 31% (300S)). Finally, flow cytometry revealed that the integrin αIIbβ3 concentration was 14% of normal, while the levels of the other

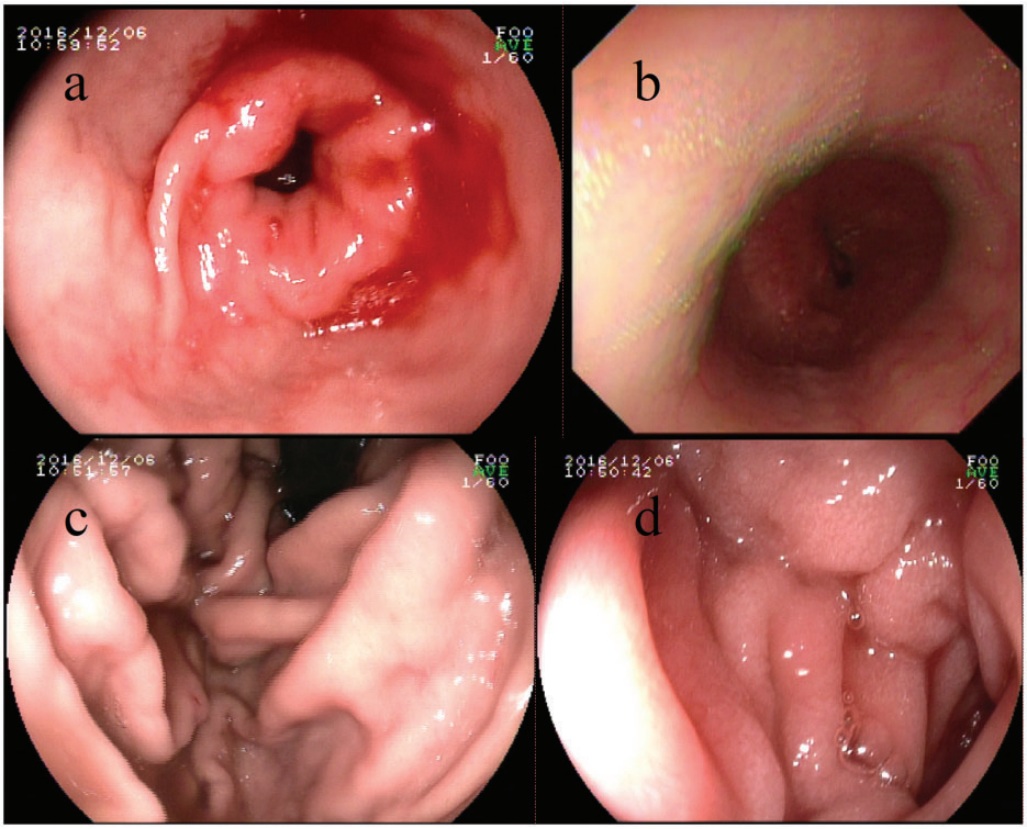

Figure 1. Endoscopic findings of the patient. (a) Oozing of blood was found in the gastric antrum wall. (b–d) No obvious lesions, such as erosions or ulcerations, were found by gastroscopy.

glycoproteins were approximately normal. The patient was diagnosed with GT (type II). Genetic studies revealed a compound heterozygotic mutation in the ITGA2B gene, and the mutation bases were c.2333A>C and c.1750C>T.

Upon confirmation of the diagnosis, the patient was treated with a platelet transfusion to prevent surgical bleeding. The melena stopped and he was gradually transitioned to a normal diet. Soon afterward, he fully recovered and was discharged from the hospital. The patient was seen for follow-up visits once every 6 months after discharge. He underwent several endoscopic examinations, which showed no recurrence of the upper gastrointestinal bleeding.

The patient provided written informed consent for publication of this report. This was a retrospective case report; therefore, institutional review board approval was not required.

Discussion

GT is a rare autosomal recessive genetic disease with characteristics of platelet aggregation dysfunction resulting from a congenital defect of the platelet fibrinogen receptor integrin αIIbβ3.[6] The incidence of this disease is quite low, accounting for only 9% of platelet functional deficiencies. Increasing numbers of cases of GT have been reported in recent years.[7] Purpura, mucosal bleeding,

and menorrhea are the most common clinical features of GT. Most hemorrhagic signs are caused by trauma, surgery, or delivery; idiopathic bleeding is infrequent.[8] The severity of hemorrhagic symptoms is unpredictable. Some patients die of massive hemorrhage when they are young, and for others, symptoms are mild. Bleeding in patients with GT sometimes gradually improves with age.[9] Because the clinical features of GT involving digestive tract hemorrhage are similar to those of bleeding caused by common gastrointestinal diseases, GT tends to be misdiagnosed.[10] Previous studies have shown that upper gastrointestinal bleeding occurs intermittently and that the amount of bleeding can become massive and difficult to control, similar to our case. Furthermore, patients with GT who develop spontaneous gastrointestinal hemorrhage often also have gastrointestinal diseases such as gastroduodenal ulcers, alimentary tract polyps, or *Helicobacter pylori* infection.[1,4,6] In the present study, the patient had upper abdominal pain, but no organic diseases were found by gastroscopy; thus, the epigastric pain may have been associated with gastrointestinal spasm caused by bleeding.

Detailed inquiries about the patient's medical and family history may be useful for the diagnosis of GT. In particular, GT should be considered in patients with repeated bleeding since infancy or childhood. Additionally, old ecchymosis of the skin can often be found in patients with GT through careful physical examination. Laboratory inspection has high clinical significance for confirmation of the diagnosis of GT. The test results of patients with GT have the following characteristics: a prolonged bleeding time, normal platelet count, defective blood clot retraction, and decreased platelet aggregation.[11] In general, platelet aggregation induced by ristocetin is normal; however, it was decreased in our patient. This may have been related to the decrease in fibrinogen caused by massive gastrointestinal hemorrhage and the drug action of low-molecular-weight dextran, which was used to replenish the blood volume after admission. Flow cytometry can lead to a definite diagnosis and classification of this disease. Moreover, gene diagnosis is a new method that has been used to reveal the etiology of GT more accurately in recent years.[12] For patients who have GT with gastrointestinal bleeding, digestive endoscopy examinations are needed to exclude other causes of hemorrhage, such as peptic ulcers, gastrointestinal malignancies or polyps, vascular diseases, and inflammatory bowel disease.[13]

The major therapeutic methods of GT are symptomatic and supportive treatments.[14] Gastrointestinal bleeding is a potentially life-threatening condition in patients with GT. The bleeding in our patient was stopped by endoscopic therapy, drug hemostasis, and other active measures; thus, our treatments were successful. Moreover, avoiding the use of nonsteroidal anti-inflammatory drugs and eradicating *H. pylori* can prevent some gastrointestinal hemorrhagic episodes.[6] Platelet transfusion is an effective treatment measure for GT, especially when general hemostatic measures are ineffective. Patients also need platelet infusion to prevent excessive bleeding during trauma, surgery, or childbirth. However, the routine use of platelet transfusions is not recommended.[15] Such treatment is associated with the risk of hematogenous transmission of infection and can result in an increase in platelet antibodies, potentially causing platelet refractoriness.[16] During the last several years, research has shown that recombinant factor VIIa is able to relieve the hemorrhagic symptoms of GT. This way may, recombinant factor VIIa may provide an alternative therapeutic option for the treatment of GT.[17,18] Hematopoietic stem cell transplantation is the only possible cure

for GT at present, though a few successful cases have been reported.[19]

In summary, spontaneous upper gastrointestinal bleeding in patients with GT is a relatively rare but severe situation requiring emergency intervention. Early diagnosis and treatment is important and can lead to a better prognosis.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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