Case Report

Excessive Gingival Bleeding in Two Patients With Glanzmann Thrombasthenia

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Background: Glanzmann thrombasthenia (GT) is an exceedingly rare but well-defined inherited disorder of platelet function caused by a defect in the glycoprotein IIb/IIIa complex. The association of GT with consanguinity has been noted, especially in geographic regions in which intermarriage is common. In most patients, GT is diagnosed during early infancy or before the age of 5 years. Common manifestations of this disorder are gingival hemorrhage, purpura, epistaxis, petechiae, and menorrhagia. Chronic, prolonged, untreated, or unsuccessfully treated bleeding may be life threatening.

Methods: We report two female patients with GT who were referred by our hematology clinic to our periodontology department for the treatment of excessive gingival bleeding. The first patient was treated with a platelet transfusion and underwent periodontal therapy (scaling and root planing and dental polishing). The second patient, whose GT was undiagnosed at the time of her referral to our department, applied to our emergency service because of uncontrolled gingival bleeding that developed after scaling and root planing was performed by her dentist. Both patients had been called for regular dental visits.

Results: All treated sites healed without complications. The first patient was monitored for 2 years, during which she practiced proper oral hygiene and experienced no periodontal complications. The other patient did not participate in follow-up.

Conclusions: Gingival bleeding is usually the first sign of most hematologic disorders, and dentists must be alert for the signs of unusual gingival bleeding. In such cases, collaboration with a hematologist is essential. Under the proper circumstances, periodontal treatment can be performed with an acceptable outcome. With proper oral hygiene, we believe that there will be no complications and no gingival bleeding. J Periodontol 2007;78:1154-1158.

KEY WORDS
Gingival bleeding; Glanzmann thrombasthenia; oral hygiene.

Glanzmann disease, later termed Glanzmann thrombasthenia (GT), is an autosomal recessive bleeding syndrome that affects megakaryocyte lineage. GT, which is characterized by the absence of platelet aggregation in response to multiple physiologic stimuli, is caused by quantitative and/or qualitative abnormalities of platelet αIIbβ3 and/or glycoprotein IIa and IIb.1 In healthy individuals, platelets attach to fibrinogen by the action of glycoprotein IIb and glycoprotein IIa and IIb, which serve as platelet fibrinogen receptors on the platelet surface and are responsible for platelet–fibrinogen interaction.2 The defect of this glycoprotein in patients with GT leads to defective hemostasis and prolonged bleeding. The genes for both glycoproteins are on chromosome 17, locus 17q21.32. Thrombasthenic patients do not show aggregation in response to physiologic agonists such as adenosine diphosphate (ADP), epinephrine, collagen, thrombin, and other all aggregating agents; they have markedly reduced levels of platelet fibrinogen, and they exhibit reduced or absent clot retraction.3

In most patients, GT is diagnosed during early infancy or before the age of 5 years. This disorder is exceedingly rare. The incidence of GT is not dependent on race or ethnicity; however, there are several ethnic groups in which most cases of GT have been identified: a small number of patients from three French Gypsy families of the Manouche tribe,2 42 patients from South India,3 and 39 Iraqi Jewish patients from Israel.4 In a medical center in Iran, 382 patients were diagnosed as having GT between 1969 and 2001.5 GT is found frequently in geographic regions in which consanguineous marriages are common.3 It occurs no more often in men than in women, but men with GT often present with gingival bleeding, and women tend to present with menorrhagia.

Although GT is a severe hemorrhagic disease, the prognosis of most patients is generally good if careful supportive care is provided. Hemorrhagic symptoms vary from bruising to fatal bleeding caused by trauma or disease. Those symptoms occur only in people

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who are homozygous for mutations causing GT. Individuals with heterozygous conditions (i.e., carriers) are usually asymptomatic, even though they have only one-half the normal concentration of platelet αIIbβ3.6

The clinical symptoms of GT are clearly defined. Purpura, epistaxis, petechiae, gingival hemorrhage, and menorrhagia are constant features, and gastrointestinal bleeding and hematuria are less common.1 In people with GT, the results of blood tests reveal a platelet count within the reference range, but the results of other tests show a longer-than-normal bleeding time, poor clot retraction, and (possibly) a low red blood cell count and iron deficiency.

We report the cases of two female Turkish patients (11 and 26 years of age, respectively) with GT. Although we had monitored one of those patients for 2 years after her initial diagnosis, the other was newly diagnosed when she became our patient.

CASE 1
In 2005, an 11-year-old Turkish girl (weight, 28.2 kg; height, 1.36 m) was referred by the pediatric hematology clinic (where 6 months earlier she had been diagnosed as having GT) to the periodontology clinic at Baskent University for the treatment of spontaneous gingival bleeding. Her parents were first cousins, and no other family member had a hematologic disorder that was not confirmed with hematologic tests.

During physical examination, a few ecchymoses were noted on her legs and arms. Oral examination revealed gingival bleeding and blood clots along the gingival margin of her teeth (Fig. 1). There was a heavy accumulation of dental plaque, the gingival tissues were swollen, and the oral mucosa and gingiva were pale.

Therapy involved both preventive measures and the treatment of bleeding. Dental hygiene was important in minimizing the gingival hemorrhage. Treatment consisted of oral hygiene and removing blood clots from the oral cavity. To prevent possible bleeding during that periodontal treatment, the patient was referred to a pediatric hematologist for consultation before any procedure was performed. Hematologic data were as follows: hemoglobin, 11.5 g/dl; bleeding time, >10 minutes; activated partial thromboplastin time (APTT), 34.10 seconds; abnormal platelet aggregation (with ADP, collagen, epinephrine); prothrombin time, 14.9 seconds. She then received 1 unit of platelet transfusion. Twenty-four hours later, scaling and root planing were performed, and the twice-daily use of a 0.2% chlorhexidine digluconate oral rinse was recommended. To prevent mechanical trauma to the oral cavity, her diet was temporarily changed to include only soft, juicy foods. The patient underwent a clinical follow-up examination 10 days after her periodontal treatment, and no gingival bleeding was detected. She has been visiting a periodontist regularly for 2 years since that time (Fig. 2), but she does not receive platelets before each visit. In this patient, spontaneous gingival bleeding had sometimes occurred in the posterior buccal areas because of poor oral hygiene. During every visit to our clinic, she was encouraged to practice regular dental brushing and to return for scheduled follow-up examinations.

CASE 2
A 26-year-old Turkish woman (weight, 52 kg; height, 1.56 m) was referred by the hematology department at Baskent University to the periodontology clinic for the treatment of excessive gingival bleeding. She stated that she had been diagnosed as having thalassemia at another medical center and that since birth she had received a blood transfusion whenever a bleeding problem occurred. There were no data or laboratory test results of her previous therapies other than
self-reported information. After having undergone medical and physical examinations and laboratory testing in the hematology department, she was diagnosed as having GT. Hematologic data were follows: hemoglobin, 11.1 g/dl; bleeding time, >9 minutes; APTT, 38.90 seconds, abnormal platelet aggregation (with ADP, collagen, epinephrine); prothrombin time, 13.7 seconds. She had menorrhagia and joint, arm, and abdominal pain and had undergone splenectomy 4 years earlier.

This patient’s parents were first cousins. There were no available data or results of laboratory examinations for her three sisters, four brothers, or parents. Her 7-year-old brother and 4-year-old sister had died, and her mother had undergone the termination of three pregnancies. The patient had been hospitalized for detailed examinations for the diagnosis of her disease, which was identified as GT, when she was referred to the periodontology clinic. Her medical history revealed that scaling and root planing had been performed by a dentist in a private office 1 day before her hospitalization. That dentist could not control her gingival bleeding and referred her to the Baskent University Hospital Emergency Service. She received three units of platelet transfusion and was referred to the periodontology clinic. During her visit, plaque and blood clots and fresh blood around her teeth were gently removed (Fig. 3). There was no calculus around her teeth. At the conclusion of her initial periodontal examination, she was encouraged to practice good oral hygiene with a soft-bristle toothbrush. The soft-food diet was suggested for the short term, and a 0.2% chlorhexidine digluconate oral rinse was prescribed. Another visit was scheduled before she was discharged from the hospital; however, she did not visit the periodontology clinic again.

DISCUSSION
GT is an extremely rare disorder. Its clinical manifestations, which are similar to those of many other platelet function disorders, include abnormalities in bleeding time, clot retraction, and a platelet count and morphology that are within normal limits. Spontaneous gingival bleeding is one of the most common symptoms of GT. Gingival bleeding is rarely associated with major acute blood loss, but it is a common cause of iron deficiency.6 Minor bleeding can be controlled with local measures. Folic acid and oral iron may be needed to prevent anemia and iron deficiency in patients who experience continuous hemorrhaging. Antifibrinolytic agents, such as tranexamic acid, may help to control bleeding. Appropriate periodontal treatment and dental care, which are safe for patients with GT, improve the patient’s life quality by preventing eating difficulties, oral diseases, and esthetic concerns and facilitate the management of the disease by the hematologist.

Both patients described in this report had been diagnosed as having GT when they were referred to our periodontology clinic. In each case, the patient’s parents were first cousins. Both patients had stopped brushing their teeth to prevent gingival bleeding, as do many others with that symptom, but poor oral hygiene resulted in the accumulation of dental plaque and inflammation of the gingival and periodontal tissues. Individuals with GT who experience significant blood loss after having undergone a dental procedure may require close observation in a critical care setting, but dental and periodontal visits are mandatory for those individuals. Under the proper circumstances and with adequate precautions (consulting with a hematologist, formulating a treatment plan, educating the patient and his or her relatives about the disease and the importance of prevention), dental treatment does not result in adverse sequelae.7,8 In individuals with GT, treatment modalities should be as conservative as possible, and each patient’s medical condition must be well defined before a dental procedure is performed.

In patients with GT, bleeding after a traumatic accident or a surgical or dental procedure may be profuse and could require vigorous

Figure 3.
Second patient: initial examination. Gingival bleeding was noted.
medical treatment. Gingival bleeding can be a source of chronic blood loss. Pretreatment with prophylactic platelet transfusions is necessary before surgical procedures, including oral surgery. The more patients are exposed to platelets, the higher the risk of developing antibodies against the platelets. The immune system generates antibodies that attach to the donor platelets and impair their function. Platelet transfusions are reserved for the treatment of life-threatening bleeding or for use in procedures in which bleeding is likely.

Menorrhagia occurs in nearly all female patients with GT, especially at the time of menarche. Because GT is a platelet disorder, female patients may experience heavy menstrual bleeding or have an iron deficiency. Postpartum purpura may develop immediately after parturition but is often not dramatic. In neonates and infants, petechiae of the face and subconjunctival hemorrhage associated with crying may be the first symptoms of GT. Epistaxis, which is a common symptom of GT and can be life threatening, usually abates in adulthood. The severity of hemorrhagic symptoms can vary significantly during the lifetime of the patient, and the severity of hemorrhagic events seems to decrease with increasing age. Gas-trointestinal bleeding, which occurs in 12% to 49% of patients, is usually intermittent, and identifying the site of bleeding is often difficult. During pregnancy, excessive bleeding requires treatment with platelet transfusion, as does immediate postpartum hemorrhage, which is very common. Postpartum hemorrhage is less likely to occur in patients who are delivered of their infant by cesarean section.

Our treatment protocol consisted of conservative but conventional therapy. Before they underwent treatment, the patients were encouraged to brush their teeth with a soft-bristle toothbrush and to change their dietary habits. They and their relatives were educated about GT and the importance of periodontal care. Platelet transfusion, scaling, root planing, and dental polishing were performed in the first patient, whose gingival bleeding was controlled. There is no cure for GT, but bone marrow transplantation may be performed when the hemorrhagic manifestations of the disorder are severe and refractory to treatment with platelet infusions. The management of GT consists primarily of avoiding the risk of trauma that may induce bleeding. Because recombinant activated factor VIIa is a costly treatment and has a short half-life (doses are often required every 2 to 3 hours), platelet transfusion is preferable. The efficacy of recombinant factor VIIa in children with GT has not been established.

In our patients, as in others, the main goal of therapy was to remove the underlying causes of gingival hemorrhage, which can include dental plaque, calculus, and/or granulation tissue from the gingival bleedin g site. To ensure good oral hygiene, the use of a 0.2% chlorhexidine digluconate oral rinse was recommended after treatment and was found to be effective during the postoperative period. If a local anesthetic is required during dental procedures, lidocaine 2% with 1:100,000 epinephrine can be administered without the risk of serious bleeding.

In a case report by Bisch et al.,7 a patient with GT received a loading dose of 5 g aminocaproic acid intravenously 3 hours before dental extractions. At the beginning of the extractions, a continuous infusion of 1 g of aminocaproic acid per hour and a pack of platelets were administered. The patient tolerated the extractions well, and wound healing was uneventful. In another report,11 three siblings with GT were studied. The first had mild gingivitis, the second had severe gingival inflammation and spontaneous gingival bleeding, and the third had severe gingivitis and a periodontal pocket in one aspect of a tooth. The first patient received a platelet transfusion, the second was treated with localized therapy (proper brushing, the use of a 0.12% chlorhexidine mouthrinse, and oral antiplaque agents), and the third was treated with an antifibrinolytic mouthwash (250 mg of tranexamic acid). The periodontal treatment was successful in all three patients, who reported no additional complaints of bleeding.

Although there is no cure for GT, the prognosis for people with that disorder is quite good, and their life-span is approximately that of the general population. If a child exhibits gingival bleeding that lasts for >15 minutes or has a nosebleed that will not stop when pressure is applied for 15 minutes, a health care provider should examine that child immediately. Systemic and periodontal health are important for people with a hematologic disorder (in whom reducing bleeding episodes is essential) and for their healthy counterparts. Dentists must be vigilant in detecting gingival bleeding, which is usually the first sign of many hematologic disorders, and collaboration with a hematologist is needed to ensure a good outcome of treatment for patients with GT.

REFERENCES


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