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Glanzmann Thrombasthenia: Managing Gingival Bleeding Triggered by Tooth Eruption—A Rare Case Report

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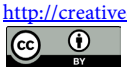

Abstract

Glanzmann thrombasthenia (GT) is a rare and often underdiagnosed congenital bleeding disorder caused by mutations in the genes encoding glycoproteins GPIIb or GPIIIa, resulting in platelet dysfunction. Inherited in an autosomal recessive manner, GT is characterized by the inability of platelets to aggregate. Clinically, it presents with mucocutaneous bleeding, such as easy and extensive bruising, severe epistaxis, menorrhagia, gingival bleeding, postpartum hemorrhage, and unexpected bleeding following procedures, despite a normal platelet count. We present a case involving a 6-year-old male patient who experienced spontaneous gingival bleeding for the past 4 weeks due to the eruption of his first permanent molars. The bleeding was particularly severe at night, disrupting the child's sleep. The patient had been diagnosed with GT at the age of 16 months. Dental management was pursued, and the use of tranexamic acid mouthwash, combined with meticulous oral hygiene, resulted in an excellent response.

Keywords

Glanzmann Thrombasthenia, Bleeding, Tranexamic Acid, Epistaxis, Platelet Aggregation

1. Introduction

Platelet is the most important component of the primary hemostatic process (response of platelets to endothelial damage and plug formation) and the secondary hemostasis is coagulation factor-associated [1].

Inherited platelet function disorders (IPFDs) are bleeding diathesis that is rare

and under-diagnosed, they are classified according to the causative molecular defects involved in the process of primary hemostasis of platelets, which include the following: 1) adhesion (e.g., Bernard-Soulier syndrome and Pseudo-von Willebrand disease), 2) activation (e.g., adenosine diphosphatase receptor defect and thromboxane A2 receptor defect), 3) signal transduction and granule secretion (e.g., grey platelet syndrome, Paris-Trousseau/Jacobsen syndrome, Chediak-Higashi syndrome, and Hermansky-Pudlak syndrome), 4) aggregation (e.g., Glanzmann thrombasthenia), and 5) procoagulant activity (e.g., Scott syndrome) [2].

Glanzmann thrombasthenia (GT) was first described by a Swiss paediatrician called Eduard Glanzmann in 1918 as a type of purpura with normal platelet count and size in patients with absent or decreased clot retraction and prolonged bleeding time [3].

GT is an autosomal recessive disorder of platelet aggregation caused by quantitative or qualitative defects in integrins αIIb and β3. These integrins are encoded by the ITGA2B and ITGB3 genes chromosome 17 and form platelet glycoprotein (GP) IIb/IIIa, which acts as the principal platelet receptor for fibrinogen [4].

GT is inherited in a recessive manner with increased incidence in areas of high consanguinity; with a ratio of 1 in 200,000 compared to 1 per million in non-consanguinity populations [5].

The diagnosis of GT typically takes place very early in life (before the age of 5 in most affected children) as a result of unexpected and spontaneous bleeding. Prothrombin time (PT), partial thromboplastin time (PTT), platelet count, morphology, and extended bleeding time are the only changing characteristics [6]. Purpura, epistaxis, gingival bleeding, and menorrhagia are important clinical characteristics [7].

One major issue for female GT patients is menorrhagia [8]. Pediatric dentists may see these young patients complaining of severe bleeding after tooth eruption, exfoliation, dental trauma, cavities, and other pathological diseases of the mouth such as cysts and dentoalveolar abscesses. Bleeding can also result from harmless things like sneezing, weeping, coughing, or having a common cold [9]. The diagnostic tests for GT include flow cytometry, platelet function analysis, and light transmission aggregometry. The afflicted gene can be identified by western blotting [10].

The general principle of managing patients with GT focuses on prophylactic before high-risk surgical procedures and routine check-ups to maintain healthy well-being and patients' and families' education about appropriate techniques to manage blood loss [5].

Particular attention is paid to the bleeding of the gingiva which can be caused by gingivitis, regular flossing, loss of the primary teeth and eruption of the permanent teeth. These conditions were treated with anti-fibrinolytic treatment (mouthwash) and fibrin glue to reduce blood loss [11] [12], in addition to a plastic splint that may be used as physical support for the thrombus [13].

Controlling bleeding becomes a complicated procedure when teeth are extracted or when bleeding results from the loss of deciduous teeth. Tranexamic acid and other antifibrinolytic drugs have been widely utilized in oral surgery. By preventing the thrombus from degrading, it stops bleeding [14]. Platelet transfusions are the first line in major surgeries or severe bleeding that the anti-fibrinolytic failed to control [5].

GT is an uncommon bleeding disorder with little information available in the literature about treating oral bleeding in juvenile patients. This case report aims to raise awareness of this rare bleeding disease and discuss potential oral symptoms related to tooth eruption and the effectiveness of oral tranexamic acid in reducing oral bleeding episodes.

2. Case Presentation

A 6-year-old boy with a previously confirmed diagnosis of Glanzmann thrombasthenia type I was referred to a pediatric dentist due to excessive bleeding from his gums following the eruption of upper and lower right first permanent molars (#16, 46) overnight (**Figure 1**). The history of bleeding episodes began three weeks ago, with severe bleeding occurring at night. In the mornings, significant blood clots were observed on the bedsheets and pillows, which raised the attention of the family to the issue.

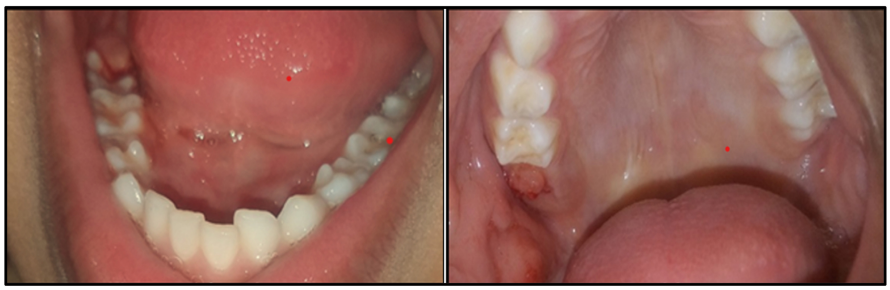

Figure 1. Intraoral photographs show spontaneous bleeding and gingival polyps opposite to the erupting first permanent molars (#16, 46).

The parents reported a previous milder episode of bleeding from the gums associated with the eruption of primary molars.

During the extraoral examination, purpuric spots were noted on the left cheek, along with bruising around the lips (**Figure 2**). The intraoral examination showed a noticeable operculum on the occlusal surface of the erupting upper right first permanent molar, and a gingival polyp originating distally from the lower right first permanent molar. Both operculum contributed to increased bleeding episodes during the day, particularly during meals (**Figure 1**).

The boy was diagnosed with Glanzmann thrombasthenia at 1 year and 4 months old after a severe nosebleed episode that required hospitalization and a platelet transfusion. In addition, he has a history of bruising easily and developing ecchymosis.

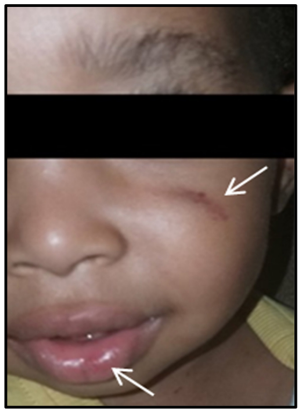

Figure 2. Extraoral photograph showing bruises and purpura on the left cheek and lower lip.

Consanguineous marriages were noted in the family, and his younger brother was subsequently diagnosed with Glanzmann thrombasthenia (GT). His first dental visit took place at the age of 2 due to gingival bleeding during the eruption of primary molars. The haematological report, at that time, indicated normal platelet count, clotting, and bleeding time. However, flow cytometry analysis of platelet surface glycoproteins revealed deficiencies in CD41 (GPIIb) at 1.02% and CD61 (GpIIIa) at 2.00%, confirming the diagnosis of GT. The bleeding was mild and did not require a dental intervention. However, mild falls and traumas resulted in a marked area of subcutaneous haemorrhage as illustrated in **Figure 3**.

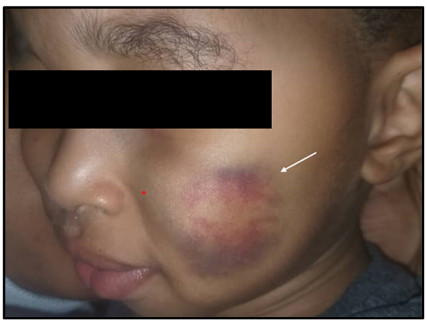

Figure 3. Well-defined area of subcutaneous hemorrhage as a result of a minor fall.

Following a consultation with the child's pediatrician to confirm the overall medical condition and general health, the patient and parents were educated about the importance of optimal oral hygiene and fostering a trauma-free environment.

The patient received instructions to use a 5% tranexamic acid mouthwash using a 500 mg tablet dissolved in 10 mL of water, to be used 3 - 5 times daily for 2 - 3 minutes each time. Emphasis was placed on maintaining good oral hygiene, using a soft-bristled toothbrush with fluoridated toothpaste.

The patient reported a significant improvement at the five-day follow-up appointment, with a faster reduction in the amount of bleeding and improved sleep quality. The patient was given a strict oral hygiene protocol and followed up after three months, bleeding was controlled and no bleeding episodes were reported by parents.

3. Discussion

Glanzmann thrombasthenia is a rare inherited platelet disorder caused by a mutation affecting glycoprotein (GP) IIb-IIIa, which is found on the surface of platelets [15]. This glycoprotein plays a crucial role in binding fibrinogen, essential for platelet aggregation. Consequently, individuals with this condition experience impaired platelet aggregation and may exhibit reduced or absent clot retraction. Notably, their platelet count and morphology typically remain normal [13]. Hence, GT patients need multifaceted approaches and comprehensive strategies to prevent and/or manage bleeding episodes. These include regular dental care, pharmacological intervention, blood product transfusion and emerging therapy like gene therapy [13].

Flow cytometry and platelet aggregation are the most crucial diagnostic tests for this illness. Due to their need for fibrinogen binding to the platelet for aggregation, adenosine diphosphate (ADP), thrombin, adrenaline, collagen, and arachidonic acid do not trigger platelets to aggregate in GT [16].

George *et al*. [17] have divided GT into three categories depending on the amount of the GP IIb-IIIa complex that can be found using flow cytometry. Those with GT types I (as in the present case) and II (inactive GP IIb-IIIa) may exhibit minor clinical signs, however, those with type III (inactive GP IIb-IIa) may still experience severe recurring hemorrhagic episodes. As such, utilizing the test or classification to ascertain the precise severity of the condition is challenging [17].

Purpura, epistaxis, gingival hemorrhage, and menorrhagia are among the bleeding abnormalities that are well-defined and reported in the literature in patients with GT. Patients who receive regular dental care were not found to be susceptible to gingival bleeding, which is typically linked to poor oral hygiene [17]. It is claimed that significant acute blood loss is not usually linked to it. In our case, and line with the literature, recurrent epistaxis was the lead cause of hemorrhage. However, gingival bleeding was generally linked to an erupting tooth rather than poor oral hygiene. The permanent teeth had more severe bleeding episodes as compared to the primary counterpart. This finding was consistent with the ones reported in many studies [17] [18]. Hematuria, hemarthroses, and gastrointestinal bleeding have also been documented in the literature [17], nevertheless, none of these outcomes were positive for our patient.

Certain bleeding illnesses, such as Von Willebrand disease, coagulation factor deficits, and uncommon hereditary platelet function disorders linked to impairments in particular areas of platelet function, can manifest as epistaxis. Alt-

hough there are differences in the severity of platelet function problems, some of the more severe ones include Bernard-Soulier syndrome and Glanzmann thrombasthenia (GT). However, even illnesses that are normally milder can sometimes cause significant bleeding symptoms. The presenting symptoms that lead to a bleeding disorder diagnosis include frequent epistaxis and other mucocutaneous forms of bleeding, which are more frequently linked to Von Willebrand disease and platelet function abnormalities than to coagulation factor deficits [19]. Bernard-Soulier syndrome is ruled out by normal platelet size and ristocetin-induced aggregation [13].

Similar to how a normal platelet count rules out thrombocytopenia, a normal level of clotting factors rules out other clotting diseases such as hemophilia and Von Willebrand's disease [13].

Since one-third of patients with recurrent epistaxis are thought to have an underlying hemostatic problem, it is crucial to take this into account when examining children with severe or recurring epistaxis. Emergency physicians should be aware of any potential underlying hemostatic diseases since they are frequently the first to evaluate a patient with recurrent epistaxis [20].

At the time of the dental examination, no tests were conducted since our case was diagnosed when the patient was just a year old.

The management process includes supportive treatment, platelet transfusions, and hemostatic measures [17], whereas, the ultimate course of treatment is hematopoietic stem cell transplantation (HSBT) from the siblings. Nevertheless, given the elevated risk involved in this process, it is advised just in situations when there is significant bleeding or the onset of autoimmunization [21]. Since bleeding in GT is typically unpredictable [17], platelet transfusions prior to any invasive surgery are recommended, even in cases when minor bleeding is anticipated, and should continue until wound healing is complete. Historically, antifibrinolytic medications, hemostatic medicines, and physical barriers have been used to limit bleeding during extraction. Treatment for spontaneous bleeding often involves maintaining strict dental hygiene and providing oral prophylaxis [7] [22] [23], which was the protocol followed in the present case.

Non-steroidal anti-inflammatory medicines (NSAIDs) and aspirin are examples of medications that affect platelet function and are contraindicated [17]. As a result, Paracetamol [14] [24] and Tramadol [6] are thought to be the best analgesics for GT patients experiencing different levels of pain.

In oral surgeries and soft tissue management, the literature personalized the treatment of tranexamic acid and platelet transfusion [25]. For bleeding problems, desmopressin, tranexamic acid, and epsilon aminocaproic acid (EACA) are the indicated antifibrinolytic medicines [26] [27]. Although desmopressin has been tried as a treatment for GT, it was not employed in our case, since the literature did not provide sufficient clinical data [26]. The amino acid lysine is the source of tranexamic acid. It mainly works by obstructing the plasminogen molecules' lysine binding sites and locations on molecules of plasminogen. Con-

sequently, this hinders the production of plasmin, which obstructs fibrinolysis and stops the clot from disintegrating [28]. Transexamic acid was shown by Mannucci and Levi [29] to be 10 times more effective than EACA. Therefore, in the present case, tranexamic acid was utilized, and within five days, both the frequency and severity of the bleeding episodes significantly decreased. Therefore, it was recommended and consistently emphasized to both parents and child that he should practice good oral hygiene, which includes brushing twice a day with a soft toothbrush and fluoridated toothpaste while under parental supervision, attending diet counseling sessions, and scheduling regular dental examinations.

Pediatric dentists must be knowledgeable about bleeding disorders when diagnosing recurrent and continuous bleedings that arise on their own or are brought on by tooth eruption, minor injuries, etc. It is the pedodontist's responsibility to educate parents of children with GT proactively about preventing traumatic injuries, treating periodontal disease appropriately, and encouraging the maintenance of optimal oral hygiene in connection to the children's overall and local health.

4. Conclusion

Despite being one of the uncommon bleeding diseases, Glanzmann's thrombasthenia should be taken into consideration when assessing individuals who have spontaneous gingival bleeding in the context of a normal platelet count. A good prognosis is associated with early diagnosis and timely treatment. Communities ought to get advice on avoiding consanguineous marriage and the risks that go along with it. The patient should be educated on changing their lifestyle and preventing bleeding episodes. These preventative methods include avoiding trauma, using anti-platelet medications, and maintaining excellent dental hygiene.

Declaration of Patient Consent

The authors certify that the patient's parents have consented to the publication of their son's clinical case and photographs in the journal. Every precaution was taken to maintain the case's confidentiality, and all pertinent records were de-identified. The patient and parents are aware that although every attempt was made to conceal their identity and that their names and initials were not being published, anonymity cannot be guaranteed.

Conflicts of Interest

The authors declare no conflicts of interest.

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