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DISCOVERY
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Diagnostic and treatment difficulties in a patient with anemia: Review with Glanzmann's Thrombasthenia

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ABSTRACT

Introduction: Glanzmann's thrombasthenia (GT) is a rare disease inherited in an autosomal recessive manner. Qualitative or quantitative defect of the adhesive protein that binds to the platelet receptor in the coagulation process causes this disease. In most cases, symptoms appear in early childhood. *The aim:* This study aims to present the diagnostic and therapeutic problem in a patient with GT. *Case report:* A 70-year-old patient hospitalized due to symptomatic anemia. Initially the patient was diagnosed with hemophilia, later the diagnosis was changed to Glanzmann thrombasthenia. The patient's last hospitalization was in 2024, during which gastroscopy and colonoscopy was performed. No pathological changes were detected. *Results:* Glanzmann thrombasthenia is characterized by an average platelet count and morphology, standard prothrombin time, and standard partial thromboplastin time, accompanied by prolonged bleeding time. The diagnosis is usually based on flow cytometry, which shows the absence of GPIIb or GPIIIa molecules on the platelet surface. *Conclusions:* Glanzmann thrombasthenia (GT) is a rare genetic disease that causes symptoms of bleeding diathesis. Quick diagnosis and appropriate treatment are crucial for managing this condition. Treatment options include transfusions of platelet concentrate, antifibrinolytic drugs, recombinant factor VIIa, and hematopoietic cell transplantation.

Keywords: Glanzmann's thrombasthenia, Bleeding, diagnosis, treatment, inherited thrombocytopathy

1. INTRODUCTION

The ability of platelets to adhere to the subendothelial layer of the vascular epithelium layer and aggregate enables the formation of a hemostatic cap. Under physiological conditions, platelets maintain the integrity of blood vessels (Choińska et al., 2016). Platelet function abnormalities divide into primary (congenital) and secondary (acquired). Primary defects are rare. Acquired platelet abnormalities are far more common and often occur in chronic diseases. There are several classifications of congenital thrombocytopathies. Based on the clinical course, it is possible to distinguish severe forms, which include Glanzmann's thrombasthenia. Glanzmann's thrombasthenia is a very rare thrombotic diathesis with a congenital disability in platelet function (Grassetto et al., 2017).

The synthesis of the Glycoprotein IIb/IIIa complex (GPIIb/IIIa) is impaired, which is a receptor for fibrinogen, fibronectin, Von Willebrand factor, and thrombospondin (Noris and Pecci, 2017; Nurden et al., 2015; Nurden, 2017). GT is a genetic autosomal recessive disease. Patients present with symptoms of haemorrhagic diathesis, even during childhood, e.g. from the gingiva, nose, gastrointestinal tract (Jiménez-Castillo et al., 2023). Prolonged post-traumatic and post-operative bleeding is characteristic (Botero et al., 2020; Ahammad et al., 2020). The treatment of Glanzmann's Thrombasthenia is symptomatic. In patients with severe platelet defects, platelet concentrate is transfused (Nurden, 2019; Poon et al., 2015; Poon et al., 2016; Poon et al., 2023; Balduini, 2022; Rodeghiero, 2022). In our work, we will present the case of a patient suffering from Glanzmann's Thrombasthenia.

2. METHODOLOGY

This case report was conducted by searching for current papers on PubMed and Google Scholar using the search phrases (Glanzmann's thrombasthenia) AND (inherited thrombocytopathy) AND (Bleeding) AND (treatment). After eliminating duplicates, we appraised all publications using the titles and abstracts. Following an exact revision of complete manuscripts, 18 articles met the inclusion criteria. The research took place in May 2024.

3. CASE DESCRIPTION

A 70-year-old patient with Glanzman's thrombasthenia diagnosed about 15 years ago, previously diagnosed with hemophilia, repeatedly hospitalized at the Gabriel Narutowicz City Hospital in Krakow, Department of Internal Medicine and Endocrinology, for transfusions of blood products, the last time in April 2024, currently readmitted for symptomatic anemia with diffuse ecchymoses on legs (Figure 1). The patient negates symptoms of bleeding. On admission, average condition, conscious, in logical contact, weakened, with exertional dyspnea, lasting for two days. There are no features of bleeding on physical examination. Patient with concomitant chronic diseases; life-threatening anemia, hypertension, cholelithiasis without cholecystitis, diaphragmatic hernia, status after removal of a polyp from the hepatic fold of the colon, history of gastric ulcer disease, esophageal hiatal hernia, abnormal glucose tolerance, spinal disc herniation, convergent strabismus, blindness of the left eye, bleeding nodules.

In laboratory tests, life-threatening anemia with Hb=5.7 g/dl, WBC=13.31 thousand/uL, RBC=2.03 million/uL., HCT=18.7%, Creatinine=76 umol/L, Glucose=7.37 mmol/L, Urea=6.0 mmol/L, CRP=2.5 ml/L, Sodium=137 mmol/L, Potassium=4.2 mmol/L, INR=1.20. On gastroscopy, gullet unchanged. Stomach: Polyps in the pre-pyloric part with a diameter of 4-7mm. Pylorus unobstructed. The jejunum and the extra-duodenal part of the duodenum unchanged. Reverse gastroscopy-single soft small polyps below the pylorus. There were no features of upper gastrointestinal bleeding. Histopathological Description: 1. Location: Pre-pyloric part of the stomach (antrum). 2. Changes: Single erosions. During colonoscopy: Examination of the entire large intestine up to the cecum visualized the Bauhin valve and the base of the appendix. Inferior bowel preparation for the examination, with BBPS classification of 1+1+1= 3/9, sectionally retained food debris.

On the fold opposite the Bauhin valve in the cecum, a polyp about 2 mm in diameter was removed with forceps (1s, Kudo II). A cauliflower-shaped polyp about 15-17 mm in diameter on a thin pedicle was removed with a coagulation snare at a distance of about 22-24 cm from the sphincter (1p, Kudo IV). Other than that, no changes were found in the extent of the fragmentary mucosa. Electrocardiogram: Sinus tachycardia 140/min. Intermediate axis. No fresh ischemic changes. The ward transfused nine units of packed red blood cells and four packs of interim platelet units, achieving clinical improvement and increasing blood morphotic parameters. Treatment administered: 9 units PRBC, four packs IPU, Paracetamol, Prestarium, Amlozek, Emanera, Cyclonamide. Laboratory tests at

discharge: WBC= 4.80 thousand/uL, RBC= 3.53 million/uL, HGB= 9.9 g/dL, HCT= 30.5%, Na= 139 mmol/L, Potassium= 4.6 mmol/L (Table 1). Discharged home in general good condition.

Figure 1 Diffuse ecchymoses in a 70-year-old patient with Glanzmann's thrombasthenia.

Table 1 Table showing morphology changes during hospitalization.

Date	2024.06.26	2024.06.25	2024.06.23	2024.06.21	2024.06.19	
Amount of Blood products transfused	-	+2 units of blood platelets	+4 units of blood platelets +4 units of red blood cells	+2 units of blood platelets +2 units of red blood cells	-	-
	-	-	-	-	-	Units
Changes in morphology after transfusions	-	-	-	-	-	-
WBC	4.80	4.20	5.94	7.21	13.31	109/L
RBC	3.53	3.49	3.03	2.81	2.03	1012/L
HGB	9.9	9.7	8.3	7.7	5.7	g/dL
HCT	30.5	29.9	26.6	24.2	18.7	%
PLT	136	83	121	159	190	109/L

*Source photo, taken from a private gallery, made by the authors in the Emergency Room of the Hospital

4. DISCUSSION

Glanzmann's thrombasthenia is a congenital disease first described by Dr. Eduard Glanzmann in 1918, when he reported a patient with prolonged bleeding time and a lack of platelet aggregation. The absence or improper functioning of glycoprotein IIB/IIIa, which plays a crucial role in binding to fibrinogen and participating in the formation of the platelet plug in the process of hemostasis, causes this disease. In the results of blood tests, the level of platelets is usually average or slightly reduced, but their improper functioning prevents the formation of a proper clot (Solh et al., 2015). Understanding the pathogenesis of Glanzmann's thrombasthenia expands our view of the function of platelets in maintaining hemostasis (Lane et al., 2005). This disease usually presents its first symptoms in childhood, when as a result of trauma, there is a significantly prolonged bleeding time, which raises concern and leads to further diagnostics.

When Glanzmann's thrombasthenia is suspected, other more common causes of prolonged bleeding time should first be ruled out. Laboratory tests report an average platelet count and morphology, standard prothrombin time, and normal partial thromboplastin activation time with prolonged bleeding time (Botero et al., 2020). This disease characterizes excessive tendency to bleed, which appears in early childhood. Most often, these are bleeding from the gums, nose, gastrointestinal tract, hematuria, and possible petechiae on the skin. Post-traumatic and postoperative bleeding time is prolonged, and women may experience significantly increased bleeding from the genital tract. In about 3% of patients, intra-articular bleeding occurs, causing damage and, as a consequence, a significant reduction in the quality of life (Pontara et al., 2014).

The diagnosis of the disease bases on the performance of significantly prolonged bleeding time with normal morphology and platelet count values, reduced or no clot retraction, no platelet aggregation under the influence of ADP, collagen, adrenaline, arachidonic acid, with normal aggregation under the influence of ristocetin in flow cytometry, no GPIIb and (or) GPIIIa molecules on the platelet surface (Botero et al., 2020). Currently, there is no effective cure for Glanzmann's thrombasthenia. Transfusions of platelet concentrate and antifibrinolytic drugs, are still the main health treatments methods. Due to the need for frequent transfusions of blood components, it is best to transfuse them following the recipient's HLA, reducing the risk of alloimmunization. In cases where this treatment is insufficient or alloimmunization has occurred, recombinant factor VIIa (Eptacog alfa) can be used. As a last resort, when other therapeutic options have been exhausted, hematopoietic cell transplantation can be performed (Solh et al., 2015).

5. CONCLUSIONS

Glanzmann's thrombasthenia is a rare disease, classified as a congenital thrombocytopathy. The main symptoms of this disease are similar to the symptoms of haemorrhagic diathesis, such as frequent bleeding from the gums and gastrointestinal tract, and petechiae on the skin. Prolonged bleeding after trauma and surgery affect the quality of life of Glanzmann's thrombasthenic patients. The main problem for people struggling with this disease is getting an early correct diagnosis. Although there is no effective cure for Glanzmann's thrombasthenia, symptomatic treatment is applicable. In the absence of such treatment, physicians use recombinant factor VIIa, while in severe Glanzmann's thrombasthenia, haematopoietic cells are transplanted.

Author's Contribution

Anna Józefiak: Conceptualization, methodology, investigation
Magdalena Szczepanik: Conceptualization, methodology, investigation
Cezary Bochyński: Methodology, Review and editing
Przemysław Hałasiński: Conceptualization, writing- rough preparation
Dominika Kropidłowska: Resources, writing- rough preparation
Maciej Horbaczewski: Conceptualization, writing- rough preparation
Kinga Piela: Formal analysis, supervision
Jolanta Mazurek: Review and editing, supervision
Gabriela Mazurek: Visualization, data curation
Maria Myślicka: Formal analysis, supervision
Patryk Góralski: Resources, writing- rough preparation
Klaudia Włodarczyk: Visualization, data curation
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Informed consent

Not applicable.

Ethical approval

Not applicable.

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Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

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