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Case Report

Glanzmann's thrombasthenia: a rare case presented with recurrent nasal bleeding

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ABSTRACT

A rare congenital condition of platelet aggregation known as Glanzmann's thrombasthenia is caused by mutations in the Glycoprotein IIb or Glycoprotein IIIa gene, which leads to platelet malfunction. Glanzmann's thrombasthenia is difficult to diagnose on basis of routine physical examination and is usually mis diagnosed because platelet morphology is normal as well as the platelet counts are in normal range, but bleeding duration is noticeably longer. The most prevalent signs of Glanzmann's thrombasthenia include numerous types of bleeding, such as menorrhagia in females, recurrent nasal bleeding, mucocutaneous haemorrhage, continuous bleeding after injury or surgery, etc. Recurrent severe intractable causes of massive nasal epistaxis are relatively less common, particularly in cases where local causes do not explain the findings, then haematological causes should be suspected. Here we present a case of a 3 years old Indian boy who presented with recurrent massive epistaxis, fatigue, severe anaemia, and breathlessness who was diagnosed with Glanzmann's thrombasthenia upon undergoing various investigations such as genetic testing and platelet assays. The patient was immediately started with supportive treatment and progress was made by the patient. Counselling was done to the patient's family that it is a lifelong disorder and upon taking prescribed treatment bleeding episodes will be reduced. Overall Glanzmann's thrombasthenia is a lifelong disorder which is difficult to diagnose, and misdiagnosis is very common regarding this disease, hence the clinician should remain alert regarding this rare congenital disorder and appropriate lab investigations should be done and treatment must be started in due time.

Keywords: Epistaxis, Bleeding, Platelets

INTRODUCTION

Glanzmann's thrombasthenia is easy to miss or misdiagnose since the anomalies linked with the condition are not immediately visible during a routine physical examination. In patients with Glanzmann's thrombasthenia, the platelet morphology and platelet count are often within normal levels, but the bleeding duration is noticeably greater. Therefore, the diagnosis of Glanzmann's thrombasthenia is based on the detection of platelet aggregation abnormalities, and it is crucial to carry out more specialized procedures like genetic testing or gene detection to make a firm diagnosis.[1,2] Glanzmann's thrombasthenia does not currently have a known comprehensive cure; instead, symptomatic therapy is the mainstay of care. Only 9% of the deficits in platelet functionality are caused by this disease, which has a very low incidence.[3] A positive prognosis is carried by early detection and rapid treatment of Glanzmann's Thrombasthenia.[4]

CASE REPORT

A toddler presented with profuse bleeding from the nose which was reported to the hospital 6 hrs from the onset of the bleeding. At birth, no abnormalities were noted but when he started walking and playing and doing other physical activities the patient developed ecchymosis over his body which was neglected by his parents. When he was about a year old his parents noticed blood in his urine and stools. He was admitted to the general practitioner for the same. There he was treated with platelet infusion which improved his symptoms, after a couple of years the patient had bitten his lips which resulted in profuse bleeding from the lips for which he was admitted to the hospital, and was given a platelet transfusion that leads to the cessation of the bleeding, two (2) months ago he was admitted in our hospital for severe epistaxis, and he swallowed his blood which lead to haemoptysis upon arrival. He was presenting with profuse nasal bleeding and was investigated in detail for an etiologic point of view till basic tests like complete blood count, bleeding time, activated prothrombin time, were performed. Haemoglobin was found to be low the patient was severely anaemic, platelet count was normal. On the peripheral smear, no abnormal platelets like large granular platelets were seen. PT and ApTT were normal. The child responded to one packed cell volume transfusion and received two (2) single donor platelet for three (3) days, after consideration of the above reports aetiology for bleeding was not found and a provisional diagnosis was made that ruled out quantitive platelet disorders, Serum Von Willebrand factor activity was also normal. Upon consultation with the haematology department and examination done by them on the patient, they suggested a genetic testing in view for ruling platelet aggregation disorder. On genetic testing, the deficiency of Gp-II and GP-III was revealed then our final diagnosis of Glanzmann thrombasthenia was made.

Investigations

On 14/03/2022, the complete blood count examination revealed that the haemoglobin (Hb) was 10.7 g/dl (normal range:12 g/dl-14 g/dl), Prothrombin time were 20.3 sec (normal range:12-16 sec), the prothrombin time control was 12.9 sec, INR was 1.6 (normal range: 0.64-1.17), total leukocyte count, differential white blood cell count and platelet count was 2,01,000.

On 10/03/2022, the haemoglobin was 8.3 g/dl (normal range: 12 g/dl-14 g/dl), and prothrombin time was 16.2 (normal range: 12-16), prothrombin time control was 12.9, INR was 1.3 (normal range: 0.64-1.17). Total leukocyte count, differential white blood cell count and platelet count were normal. Upon these unusual profound findings, a flow cytometry was advised.

On 08/03/2022, the liver function test had the following findings: serum glutamic oxaloacetic acid -20 IU/l (normal range: 0.0-45 IU/l), serum glutamate pyruvate transaminase- 15 IU/l (normal range: 0.0-45 IU/l), alkaline phosphate- 135 IU/l (normal value: 95-460 IU/l), total bilirubin 0.3 mg/dl (normal range: 0.2-1.2 mg/dl), direct bilirubin 0.2 mg/dl (normal range: 0.1-0.5 mg/dl), indirect bilirubin 0.10 mg/dl (normal range: 0.0-0.3 mg/dl), total proteins 5.9 gm% (normal value: 6-8.3 gm%), albumin proteins 3.2 gm% (normal range: 3.2-5 gm%), globulin 2.70 gm% (normal range:1.3-3.2 gm%), creatinine 0.7 gm/dl (adult male:0.6-1.4 gm/dl).

Serum Von Willebrand factor activity was normal. Ultrasonography of the abdomen was normal; no hepatosplenomegaly was noted.

Upon these unusual profound findings, flow cytometry was advised and the results are as follows which confirms Glanzmann's thrombasthenia

Differential diagnosis

Platelet count is normal, so we are suspecting qualitative defect in platelets like thrombocytopenia, considering this a qualitative disorder like Von Willebrand disease (which may be also quantitative depending on the type) was suspected which was ruled out because the serum von Willebrand factor activity was normal. Bernard-Soulier syndrome which has prolonged bleeding time was also considered and was later ruled out, thrombocytopenia has a variable presentation, it was also considered, but then later was ruled out because the peripheral smear examination showed normal platelet morphology and count which further ruled out Bernard-Soulier syndrome.

Treatment

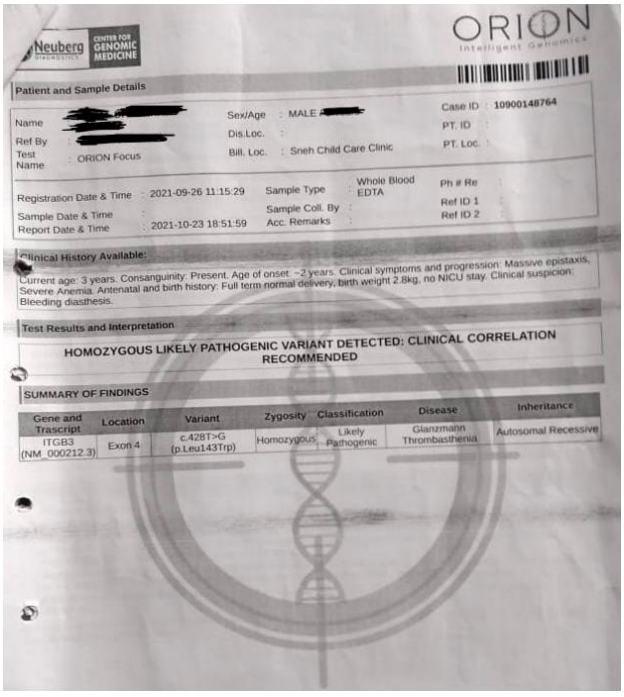
Some patients have been cured of Glanzmann's thrombasthenia by undergoing bone marrow transplant, factor VII is also available for the treatment but in India these treatment modalities are too expensive and not acceptable for our patient. Only supportive treatment is available in peripheral locations of India. As there is severe anaemia because of the bleeding patient received three (3), packed cell volume (PCV) and daily two (2) single donor platelet admission for 5 days was given after which continuous epistaxis came under control. Particularly for a continuous nasal bleeding the patient has received following treatment: (1) Inj PAUSE I/V / 2 hourly for 5 days, (2) Inj TRANEXAMIC/ 2 hourly for 5 days then later he was given an oral tablet of TRANEXAMIC acid and Syrup TASIRON was also given. After this treatment the patient was operated by ENT surgeon where nasal packing was done to control the bleeding which was later removed under general anaesthesia and treatment with NASOMIST nose drops was advised (3) BUTROPHASE nasal drops were added for mild oozing, (4) GEL FOAM of topical THROMBIN was received by the patient. The patient has received 2 RDP'S every day for 5 days, the nasal pack was removed on 5th day after bleeding was stopped.

As of now the child is on the maintenance therapy which is as follows: (i) TAB PAUSE- oral and local application, (ii) BUTROPHASE NASAL DROPS to stop oozing of blood and (iii) Iron tablets for anaemia.

The treatment advised upon discharge is as follows: (i) BUTRECLOT Nasal Drops: 2 drops in each nostril, (ii) syrup VITCOFOL 5 ml twice a day, (iii) syrup BEVON 5 ml twice a day and (iv) Vitamin D3 Sachet (60000IU) once a week for 6 weeks.

Outcome and follow-up

Relatives were counselled at the time of discharge and the following advice were given. The patient should avoid trauma/ physical punishment/ contact sports and preventive therapy was emphasised and use of TRANEXAMIC acid paste/solution during minor bleeding.


Neuberg CENTER FOR GENOMIC MEDICINE

ORION intelligent Genomics

Patient and Sample Details

Name [redacted] Sex/Age : MALE [redacted] Case ID : 10900148764

Ref By : [redacted] Dis.Loc. : PT. ID :

Test Name : ORION Focus Bill. Loc. : Sneh Child Care Clinic PT. Loc. :

Registration Date & Time : 2021-09-26 11:15:29 Sample Type : Whole Blood EDTA Ph # Re :

Sample Date & Time : Sample Coll. By : Ref ID 1 :

Report Date & Time : 2021-10-23 18:51:59 Acc. Remarks : Ref ID 2 :

Clinical History Available:

Current age: 3 years. Consanguinity: Present. Age of onset: ~2 years. Clinical symptoms and progression: Massive epistaxis, Severe Anemia. Antenatal and birth history: Full term normal delivery, birth weight 2.8kg, no NICU stay. Clinical suspicion: Bleeding diasthesis.

Test Results and Interpretation

HOMOZYGOUS LIKELY PATHOGENIC VARIANT DETECTED: CLINICAL CORRELATION RECOMMENDED

SUMMARY OF FINDINGS

Gene and Trascript	Location	Variant	Zygosity	Classification	Disease	Inheritance
ITGB3 (NM_000212.3)	Exon 4	c.428T>G (p.Leu143Trp)	Homozygous	Likely Pathogenic	Glanzmann Thrombasthenia	Autosomal Recessive

Figure 1: Genetic testing confirming diagnosis of Glanzmann's thrombasthenia.

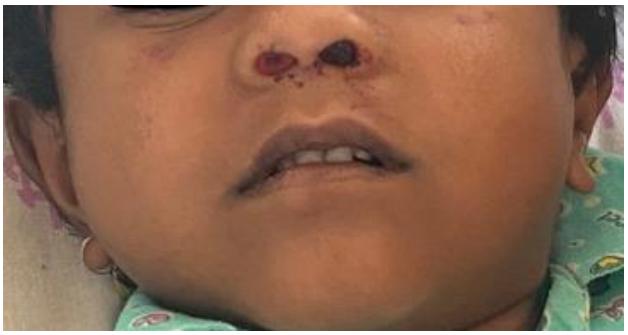


Figure 2: A minor young patient with nasal bleeding and oozing which was treated with a nasal pack.

DISCUSSION

Glanzmann's thrombasthenia is thought to affect 1 in 1,000,000 people in the general population. The incidence is approximately 1:2,000,000 or more in some locations, such as those with significant consanguinity. Since some people may only exhibit minor symptoms and never be diagnosed with Glanzmann's thrombasthenia, the real prevalence might be higher than previously thought.[5] According to studies, women are impacted slightly more frequently than men. Children and young adults are most frequently affected by Glanzmann's thrombasthenia, however it can affect people of any age. A uncommon form of autosomal recessive haemorrhage known as Glanzmann's thrombasthenia is characterised by a protracted bleeding period, improper platelet aggregation, and poor clot retraction. The symptoms of Glanzmann's thrombasthenia include bleeding, menorrhagia, gingival haemorrhage, and epistaxis. Bruising frequently follows mild injuries.[6] Common laboratory examinations of Patients with Glanzmann's thrombasthenia exhibit aberrant platelet aggregation in response to physiological stimuli, delayed bleeding time, and diminished or absent clot retraction. Detailed inquiries about the patient's medical and family history may be useful for the diagnosis of Glanzmann's thrombasthenia which was done in this case the patient is 1st issue of non consangious marriage. The patient is of Asian Ethnicity. In particular, Glanzmann's thrombasthenia should be considered in patients with repeated bleeding since their infancy or childhood; as epistaxis is a common source of serious bleeding in children with Glanzmann's thrombasthenia. Additionally, ecchymosis of the skin can often be found in patients with Glanzmann's thrombasthenia through careful physical examination. Laboratory inspection has high clinical significance for confirmation of the diagnosis of Glanzmann's thrombasthenia. The test results of patients with Glanzmann's thrombasthenia have the following characteristics: a prolonged bleeding time, normal platelet count, defective blood clot retraction, and decreased platelet aggregation.[5]

Learning points

To be able to diagnose cases of bleeding disorders. Any child with a bleeding disorder has to be taken seriously and should be evaluated in detail to reach the aetiology so that appropriate intervention can be applied. To be able to differentiate between quantitative and qualitative platelet function disorders based on clinical features and patient's history.

CONCLUSION

Glanzmann's thrombasthenia is a rare congenital disorder of platelet aggregation. So a high index of suspicion is necessary, while evaluating patients with spontaneous oral bleeding or persistent epistaxis where routine coagulation profile comes normal. Early diagnosis and

prompt treatment carry good prognosis. Any child with a bleeding disorder should be taken seriously and should be evaluated with laboratory investigations in detail to reach the aetiology so that appropriate intervention can be applied.

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