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Case Report
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GLANZMANN'S THROMBASTHENIA

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Abstract

A family with two kids; a boy, 9 years old & his sister, 5 years old from Al-Nashwa, Basrah, Iraq, is presented in this article with a bleeding tendency since childbirth manifested as easily bruising after minor trauma or even spontaneously which necessitate their hospital admission & relief after giving them fresh blood or platelets concentrate but not a fresh plasma. The boy had been discovered since he was three years old. There was a positive family history with a consanguineous marriage of parents (both are cousins). Both kids have the same clinical manifestation, normal complete blood count, normal platelets count & morphology. All coagulation screening tests were normal except a prolonged bleeding time (by Ivy's method). Both cases had been diagnosed as Glanzmann's thrombasthenia,. Unfortunately there is no platelets aggregation test available in the country to ascertain that.

Case description

The story started in 1999 when a 3 years old boy had been brought because of spontaneous muco-cutaneous bleeding or sometimes after even a mild trauma since child birth. There was no history of a swollen joint. He hadn't been circumcised because of fearing from a problematic bleeding that may occur. His parents were cousins. He had an older sister who died at 18 month of age because of a sudden episode of bleeding from nose, hematuria & bleeding from rectum without being aware of the reason at that time and the parents didn't realize actually the inherited problem they had until the delivery of their next baby. They mentioned that on repeated hospital admissions, their boy did not benefit from the transfusion of fresh frozen plasma which he had been given. On the contrary, his bleeding used to stop after the transfusion of fresh compatible blood.

On examination, the baby was quite healthy apart from multiple ecchymotic patches scattered all over the body. He had no sign of hemarthrosis whatsoever.

Laboratory investigations showed a mild normochormic anemia, normal white cell total & differential counts, with normal morphology, normal platelets count & morphology with no evidence of an existence of abnormal platelets. ESR was normal, his chest X-ray was normal, abdominal ultrasound study was normal too. His coagulation screen showed a prolonged bleeding time (more than 30 minute by standard Ivy's method), normal prothrombin time, partial thromboplastin time, thrombin time, & normal plasma fibrinogen level.

All biochemical tests available were normal. There was no evidence of any acquired platelets dysfunctional abnormality. Glanznann's thrombasthenia was the most probable diagnosis at that time but unfortunately there was no platelets aggregation test available to confirm.

The baby was kept under observation with a card notification of his problem. His condition was on & off with gaining benefit from transfusion of platelets concentrates when in need.

Five years later the family did have

a girl baby who soon had the same problem like her older brother. Again, she had been investigated and the same laboratory findings seen in her older brother were noticed These findings did strengthen the original diagnosis of Glanzmann's thrombasthenia in the family.

Both kids, since that time, were on repeated platelets transfusion with a much suffering to their parents, grand family & themselves.

Awing to the rarity of that problem, we thought it is worth to report these two cases.

Review of literature

Glanzmann's thrombasthenia(GT) is a rare inherited disorder of platelet function caused by a quantitative or a qualitative defect of the platelet membrane glycoprotein(GP) Iib/IIIa complex[1,2]. The condition is rare & has a worldwide distribution with most cases were reported from South India(42 cases), Iraqi Jewish in Israel(39 cases), Arab patients from Israel, Jordan & Saudi Arabia (46 cases for all)[1-8]. The disorder was first described by Edward Glanzmann[9], a Swiss pediatrician, who did initially describe thrombasthenia in 1918 when he noted purpuric bleeding in patients with normal platelet counts[10,11]. Clinical manifestations includes easy bruising, purpura, epistaxis, gingival bleeding, menorrhagia and, less frequently, gastrointestinal bleeding, or hematuria[12].

The disease is inherited as an autosomal recessive trait[13]. The platelets GP Iib/IIIa complex is required for platelets aggregation induced by all agonists (ADP, epinephrine, thrombin, collagen, thromboxane A2) in vivo. When this receptor is abnormal or absent, those physiological agonists fail to induce platelet aggregation[14], resulting in defective platelet plug formation and excessive bleeding and bruising. The GPIIb/IIIa receptor is also very important for uptake of fibrinogen from plasma into platelet alpha granules[15] and for clot retraction, thus patients with Glanznann's thrombasthenia have usually reduced levels of platelets fibrinogen and abnormal clot retraction test[16,17]. Different molecular and biological abnormalities have been identified in patients with Glanzmann's thrombasthenia. They are listed in an Internet database that is updated continuously (http:/med. mssm.edu/glanzmanndb). At the present time, 38 mutations in GPIIb and 25 mutations in GPIIIa have been recorded[18]. Many patients with identified mutations are compound heterozygotes, indicating that a sizable number of silent carriers are present in the population. The gene frequency of these mutations is different in various groups, being higher where consanguinity is common. Analysis of the most common mutation causing Glanzmann's thrombasthenia in the Iraqi-Jewish population revealed 6 of 700 individuals to be carriers[3].

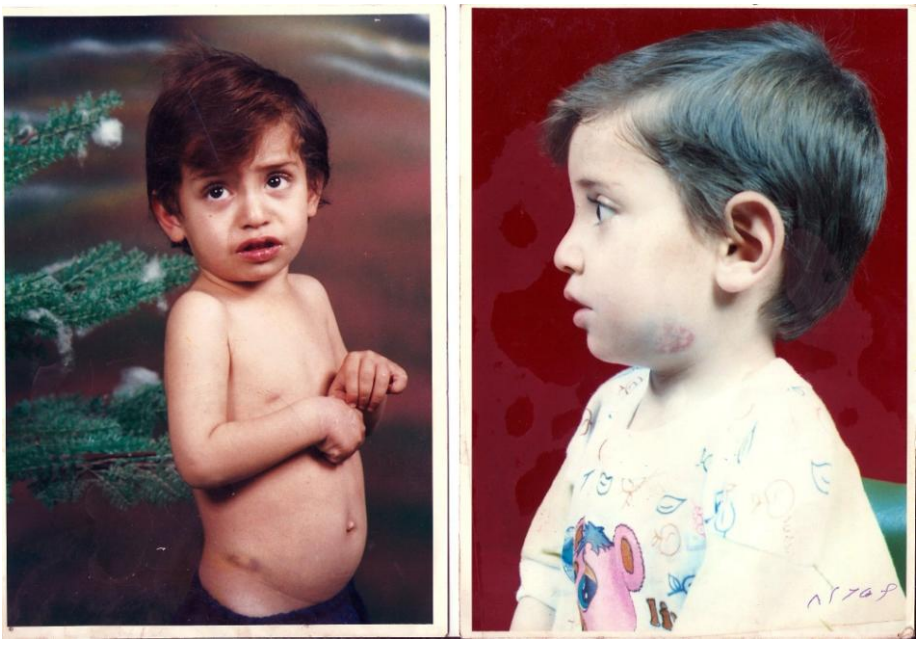
The most common clinical manifestations of Glanzmann's thrombasthenia are menorrhagia, easily bruising, purpura, epistaxis and gingival bleeding. Less common are gastrointestinal hemorrhage and hematuria. Hemarthrosis and intracranial hemorrhage are rare. Carriers of Glanzmann's thrombasthenia appear to be asymptomatic[1].

Laboratory features include normal platelet morphology, prolonged bleeding times, decreased or absent clot retraction, and abnormal platelet aggregation responses to physiologic stimuli. The abnormalities reflect the inability of the platelets to bind fibrinogen and/or other adhesive glycoproteins. Platelets undergo normal shape change in response to ADP and thrombin, demonstrating their ability to undergo metabolic and cytoskeletal changes in response to those agents. Similarly, high doses of thrombin and collagen produce normal release of dense body and alpha-granule contents[18]. The release reaction abnormalities observed with lower doses

of these agents reflect the lack of augmentation of the release reaction normally produced by platelet aggregation[18]. Platelets of patients with Glanzmann's thrombasthenia have a normal (or near-normal) initial slope of ristocetin-induced aggregation, reflecting the normal level of plasma Von Willebrand factor and the normal platelet GPIb/IX content. Platelets from patients with Glanzmann thrombasthenia fail to adhere to glass[18], the basis of their abnormality in the glass bead retention assay. Platelet coagulant activity is normal in some patients[13]. A defect in platelet micro-particle formation and support of thrombin generation has been identified in some, but not all, patients. In flow chamber studies, thrombasthenic platelets adhere normally to de-endothelialized blood vessels at low and intermediate shear rates but do not spread normally or form platelet thrombi. A defect in adhesion occurs at higher shear rates. A paradoxical increase in fibrin formation on these surfaces has been observed with thrombasthenic platelets. Platelet fibrinogen is reduced to about 10% of normal in patients with marked reductions in GPIIb/ IIIa but is variably reduced in patients with significant amounts of GPIIb/IIIa[13].

Platelet GP IIb/IIIa & a VB3 can be quantitated by any one of several techniques including monoclonal antibody binding(using flow cytometry or radiolabelled binding, immunoblotting and surface labelling followed by sodium dodecyl-sulphate polyacrylamide gel electrophoresis (SDS-PAGE). Based on theresults of such studies, patients with Glanzmann's thrombasthenia can be categorized by GP IIb/IIIa content into three types: type I: PG IIb/IIIa , 5%, type II: GP IIb/IIIa 5-20%, & type III GP IIb/IIIa 50 % or more[1,19].

Carriers of Glanzman's thrombastheia have essentially normal platelets function[4]. Their platelets, however, only contain about 60 % of the normal number of GP IIb/IIIa receptors[20]. Carrier detection is most accurately performed by DNA analysis when the defect is known, and advances in PCR technology allows this to be performed even with DNA obtained from cells in random urine samples[21,22].



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