GLANZMANN'S THROMBASTHENIA-SPECTRUM OF CLINICAL PRESENTATION ON SAUDI PATIENTS IN THE EASTERN PROVINCE

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مقدمة : قصور لويحات الدم الوظيفي المعروف باسم جلانزمانز من أمراض النزف المتوارثة النادرة الحدوث . من علاماته السريرية النزعة إلى النزف في الأغشية تحت الجلد والأغشية المخاطية .

هدف البحث : هدفت الدراسة إلى البحث عن نوعية الأعتلال السريري للمرضى السعوديين في المنطقة الشرقية .

طريقة البحث : تم البحث في ملفات المرضى الذين يعانون من مرض قصور لويحات الدم الوظيفي المعروف باسم جلانزمانز الذين راجعوا مستشفى الملك فهد الجامعي بالخبر على مدى أحدى عشر عامًا .

نتائج البحث : لقد لاحظنا تشابه أعراض المرض مع ما ذكر في المدونات الطبية ماعدا التواتر الزائد نوعًا ما لحالات النزف المفصلي وهو يشبه المرض المعروف بالهيموفيليا.

الاستنتاجات والتوصيات : هذا التشابه في النزف المفصلي بين المرضين ربما يؤدي إلى علاج حالات جلانزمانز كالهيموفيليا ولذا يجب التأكد من التشخيص قبل علاج حالات النزف المفصلي .

الكلمات المرجعية : قصور لويحات الدم ، النزف الدموي المفصلي ، العلامات السريرية.

Introduction: *Glanzmann's thrombasthenia is a rare inherited hemorrhagic disorder characterized by abnormal platelet function. It usually presents with subcutaneous bleeding and bleeding from the mucous membranes.*
Objectives: *The aim of the study is to find out the clinical presentation of Glanzmann's thrombosthenia in Saudi patients, Eastern Province.*
Methods: *In this report we have reviewed the clinical presentation of sixteen Saudi patients suffering from this disorder presented at King Fahd Hospital of the University in Al-Khobar over a period of eleven years.*
Results: *We have noticed similarity in the frequency of the various symptoms with those reported in the literature except for the apparently more frequent hemarthrosis in our patients which mimics hemophilia.*

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Conclusion: *The spectrum of clinical presentations with Glanzmann's thrombosthenia appears to be wide and the occurrence of the various symptoms varies. Moreover, some of the presenting features tend to mimic those of hemophilia, a situation which, in some cases, has resulted in unnecessary treatment with Factor VIII-containing blood components.*

Key Words: *Glanzmann's thrombosthenia, clinical presentation, hemarthrosis.*

INTRODUCTION

Glanzmann's thrombasthenia (GT) is a rare hemorrhagic disorder characterized by abnormal platelet function. It is inherited as an autosomal recessive trait[1] and has been observed in both sexes equally. The disorder has certain epidemiologic predilection, being more common in Jordan, India and Saudi Arabia and among the Iraqi-Jews and Arabs living in Israel,[2-5] as compared to other parts of the world. The possible cause of this uneven geographic distribution is the frequent occurrence of intermarriage in these regions, allowing the expression of autosomal recessive traits.

In this report we present the clinical findings in Saudi patients with Glanzmann's thrombosthenia seen at King Fahd Hospital of the University in Al-Khobar over the period between January 1983 and December 1993.

MATERIAL AND METHODS

The charts of twenty-three patients with the diagnosis of Glanzmann's thrombasthenia were reviewed. Six patients were excluded because of inadequate clinical data and one more was excluded because of being a non-Saudi. The remaining sixteen Saudi patients constitute the subject of this paper. Clinical data, including family history and clinical examination, were recorded for each patient. The laboratory investigations included: peripheral blood counts; platelet count, using "Coulter Counter STKS, Hialeah, Florida, USA"; bleeding time, using Ivy's method; prothrombin time; activated partial thromboplastin time; thrombin time; clot retraction; and platelet aggregation using adenosine diphosphate (ADP), collagen, adrenaline, arachidonic acid and ristocetin. X-ray examination of the involved joints was performed whenever hemarthrosis was suspected. The diagnosis of GT was based on normal platelet count, prothrombin time, partial thromboplastin time, thrombin times, prolonged bleeding time, defective clot retraction, and lack of platelet aggregation response to ADP, collagen, adrenaline, and arachidonic acid. Facilities for the analysis of platelet glycoproteins were not available. Review of the patients' charts was carried out to identify the sex, age at presentation, severity and sites of bleeding, family history, including parents' consanguinity, and laboratory findings, including coagulation profiles.

RESULTS

All sixteen patients presented at an age of less than 15 years, the age range was from birth to 14 years. Male-to-female ratio was 1.3:1. Positive history of first degree consanguinity was observed in 93% (15/16) of the patients. Of these patients 75% (12/16) had a family history of bleeding tendency.

Clinically they showed a wide range of bleeding tendencies. The consistent symptoms were epistaxis, gingival bleeding, and subcutaneous bruises. Gastrointestinal

bleeding in the form of hematemesis and melena was frequent, while muscle involvement, hematuria and hemoptysis were less frequent. Table 1 summarizes the incidence of the various symptoms in the study group.

Table 1: Incidence of various symptoms

Clinical Feature	No. of patients (%)
Epistaxis	14/16 (88)
Gingival bleeding	10/16 (62)
Subcutaneous bruises	12/16 (75)
Hematemesis	06/16 (38)
Melena	06/16 (38)
Menorrhagia	04/07 (57)
Hemarthrosis	03/16 (19)
Muscle involvement	01/16 (06)
Hematuria	03/16 (19)
Hemoptysis	01/16 (06)

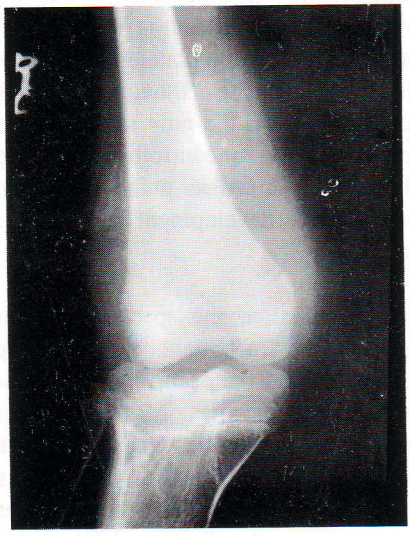

***Figure 1**: X-ray showing hemarthrosis in the knee joint*

In all cases the results of laboratory investigations showed normal platelet count, prothrombin time, partial thromboplastin time and thrombin time. Bleeding time was prolonged in all patients with an average of 19.8 minutes; clot retraction and aggregation with ADP, collagen, adrenaline, and arachidonic acid were defective in all patients. The diagnosis of hemarthrosis was done clinically, X-rays for the involved joints revealed effusion (Figure 1), and the knee aspirated in 2 patients. The analysis of platelet glycoproteins was not performed due to lack of respective facilities.

DISCUSSION

Glanzmann's thrombosthenia appears to be the second commonest inherited bleeding disorder among Saudis in the Eastern Province.[5] It commonly presents with bleeding tendency which begins during the neonatal period of the first weeks of life and early childhood.[5-7]

Geographical distribution of GT is uneven, the incidence being high in areas with frequent occurrence of intermarriage. The rate of consanguinity in the current study (93%) seems to be close to that reported before (100%) in patients with Glanzmann's thrombosthenia in Eastern Saudi Arabia[5] as compared to those reported in other studies i.e., in 67% of 84 patients and in 39% of 64 patients reported in Paris.[7]

Our study group has shown slight male predominance (56%) as compared to slight female predominance in previous reports which revealed 53% in 113 patients and 66% in 64 patients.[7] This is not significant as GT is an autosomal recessive disease.

Although purpura, epistaxis, gingival bleeding and menorrhagia are nearly constant features, epistaxis is the most common cause of severe bleeding in GT. It is typically more severe in children than in adults. It occurred in 88% of our patients. Easy bruising is the next most common manifestation in our study, occurring in 75% of the patients. These findings are similar to those reported by George et al

where epistaxis occurred in 73% and purpura in 86% of their patients.[7] Gingival bleeding was observed in a higher percentage of our patients (71%) as compared to 55% in the series of George et al.[7] However, poor dental hygiene might have contributed to the increased prevalence of gingival bleeding in our patients.

Menorrhagia was found to occur in only 57% of our female patients while it has been reported as the most common feature in the group of George et al, occurring in 98% of their female patients.[7] It has also been reported by others to be one of the most common and most serious bleeding tendencies necessitating repeated blood transfusions.[8,9]

The lower incidence of menorrhagia in our patients could be explained by their younger age at presentation, since all of them presented at age < 15 years and their age of menarche was not recorded. It is important to note that endoscopy was rarely performed on our patients to verify this bleeding tendency.

Hematuria was reported in three of our patients (19%) which appears to be higher than reported elsewhere,[7] while hemoptysis occurred in only one patient (6%).

Hemarthrosis, predominantly occurring in the knee, was relatively common in our group (19%) and it was provisionally attributed to hemophilia in the male patients by the referring physicians. It is more common than reported in the literature, where it was said to occur in 5/177 (3%) of the group studied by George et al and in 1/64 (1.6%) of the patients studied previously in Paris by the same authors,[7] in 1/50 (2%) of the patients reviewed by Caen,[10] and in none of the 20 patients of Agarwal and associate.[8]

No intracranial or visceral hematomas were observed in our patients. However, two of our patients have cerebral palsy and one of them has a sibling with a similar condition. As these patients were born at home, there was a possibility of intracranial hemorrhage occurring during labor.

The majority of our patients presented with anemia which was mostly microcytic and hypochromic in nature, therefore the majority required blood transfusion or red cell transfusion and iron supplement. Platelet transfusion was the hallmark of management protocol. Treatment with cryoprecipitate and/or fresh frozen plasma and needle aspiration of the knee hematoma, adopted in 2 patients with hemarthrosis (before a definitive diagnosis of Glanzmann's thrombosthenia was made), were ineffective. Bleeding in the joint was only controlled by platelet transfusion in these patients. Even though platelet transfusion might be the only available therapy in severe or uncontrolled bleeding, it should be avoided as much as possible to preclude the development of platelet antibodies.

In conclusion, the spectrum of clinical presentations in patients with GT appears to be wide and the occurrence of the different symptoms varies. Moreover, some of the presenting features tend to mimic those of hemophilia, a situation which, in some cases, has resulted in the unnecessary treatment with Factor VIII-containing blood components.

It is not clear whether such clinical presentation could be partly attributed to other factors such as age, environment, or physical activity. Therefore, it would be informative for more extensive studies and follow-up of patients to be performed.

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