

Case Report

Factor XIII Deficiency in a Kuwaiti Child: Typical Presentation with Delayed Diagnosis

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ABSTRACT

Congenital factor XIII deficiency is a rare bleeding disorder, presenting usually during the neonatal period. We report here a case of a child with bleeding tendency due to congenital factor XIII deficiency. Though he had a typical presentation, the diagnosis was delayed due to

lack of a high index of suspicion. The patient was treated successfully with cryoprecipitate and is doing well on cryoprecipitate prophylaxis. This is indeed, the first case report of this disorder from Kuwait.

KEYWORDS: bleeding disorder, congenital Factor XIII deficiency, cryoprecipitate

INTRODUCTION

Factor XIII deficiency is a rare bleeding disorder occurring in approximately, one in two million persons^[1]. The main function of factor XIII is to convert the loose fibrin polymer into a firm, highly organized and cross-linked structure having increased tensile strength, firmly anchored to the site of the wound with an in-built resistance to fibrinolysis^[2]. The half life of factor XIII is long (11-14 days)^[2]. Clinical features include delayed bleeding in the form of umbilical cord bleeding, delayed cord separation, significant bleeding following circumcision and trauma, poor wound healing and an unusually high incidence (25-30%) of intracranial hemorrhage^[1,3]. The bleeding in this disorder characteristically occurs 12-36 hours post-trauma. Factor XIII deficiency is inherited as an autosomal recessive trait and is commonly due to absence of the Factor XIII-A subunit protein in the plasma^[4]. Antenatal exclusion diagnosis can be undertaken in subsequent pregnancy^[4]. We report a case of factor XIII deficiency in a male child who developed recurrent delayed bleeding and went undiagnosed upto the age of one year seven months. To the best of our knowledge, he is the first case of factor XIII deficiency reported from Kuwait.

CASE REPORT

This one year and seven months old Kuwaiti boy was admitted to our hospital with persistent bleeding from a cut wound on the tongue and bruise over the right groin following a fall in the swimming pool five days ago. In the surgical department, stitches were taken on the tongue to

stop the bleeding and he was sent home. He had recurrence of bleeding at home and hence he was brought to the pediatric department and was admitted.

He was born in a private hospital at 36-week gestation by caesarean section being small for date with a birth weight of 1.76 kg. The parents are second degree cousins and of Iranian ancestry. He is the first child in the family. There was no family history of bleeding disorders. He was well until the age of 12 days when after separation of umbilical cord, he started to bleed from the umbilical stump. He was taken to a private hospital where he received vitamin K but with no response. He was then taken to special baby care unit in a regional hospital where he was found to be pale and anemic together with normal coagulation profile and biochemical screening. He was given vitamin K and blood transfusion. He improved and was discharged home two days later.

At 14 months of age, he had small cut in the chin following trauma requiring stitches but continued to ooze blood from the wound for two weeks. He had a history of gum bleeding during teething. At the age of 18 months, he was admitted to the surgical department with swelling in the scalp and vomiting for five days after banging his head on the wall in a fit of anger. The scalp swelling started one day after trauma and progressively became larger. He was investigated with a CT scan of the head which showed diffuse sub-aponeurotic hemorrhage, more on the left side without any intracranial hemorrhage (Fig. 1). His CBC showed a Hb of 80 gm/l and the coagulation profile (platelets, PT, PTT) was normal. He was given

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Fig. 1: Computerized tomography of the head showing diffuse bilateral sub-aponeurotic hemorrhage without any intracranial bleeding

blood and was seen by a pediatrician who advised further evaluation in our pediatric department to rule out coagulation disorder. But parents could bring the child to our department only one month later when he started to bleed from a cut wound on the tongue together with a bruise on the right groin following trauma in the swimming pool.

On admission, the child was conscious, alert, and active with bleeding from cut wound on the tongue, multiple bruises over the lower limbs, and bruises and hematoma in the right groin. His height and weight were on 25th centile. No organomegaly was noticed and he was not circumcised. Investigations showed: Hb 108 gm/l, MCV 69 fl, WBC $8.2 \times 10^9/l$ with normal differential count, platelets $431 \times 10^9/l$. Biochemical screen was normal. Bleeding time, PT, INR and APTT were normal.

In view of the history of recurrent delayed bleeding tendency since birth together with normal coagulation profile, congenital factor XIII deficiency was suspected and was confirmed by positive fibrin clot solubility in 5M urea and "1% monochloroacetic acid" and very low factor XIII in the blood (Factor XIII level $< 12.5\%$, N = 70-140). He was treated with cryoprecipitate successfully and was discharged home on cryoprecipitate prophylaxis every three weeks. He had a successful circumcision under cryoprecipitate cover without any problem at the age of two years and three months. He remains well on two units of cryoprecipitate prophylaxis every three weeks and is developing normally with no further bleeding diathesis

DISCUSSION

Despite a high index of suspicion for a bleeding disorder in this case, the diagnosis was not made until the age of one year and seven months on his

third hospital admission. We attribute this to many factors : First, in factor XIII deficiency primary coagulation study is normal; second, factor XIII deficiency is a rare bleeding disorder and needs high index of suspicion^[5] and lastly the transfusion of blood, plasma and other blood products before collecting investigations can be especially problematic in the interpretation of coagulation tests^[1]. The clinical features and investigation results in factor XIII deficiency had been reviewed in recent publications^[2,3,5,6]. Our patient had indeed the typical presentation. He presented in the neonatal period with delayed cord separation followed by umbilical stump bleeding not responding to vitamin K injection but to blood transfusion. He then continued to have recurrent delayed bleeding tendency following teething and traumas. Bleeding tendency in factor XIII deficiency can be spontaneous, post surgery or post trauma, even a minor injury^[3]. Contrary to hemophilia, joint bleeding is rare^[3]. Good history is very important to reach a proper diagnosis. Delayed bleeding tendency with normal coagulation profile is very suspicious of factor XIII deficiency. The diagnosis then is to be confirmed by clot solubility test and factor XIII assay. Whole blood, fresh frozen plasma, stored plasma and cryoprecipitate have all been used successfully in the treatment of factor XIII deficiency and are adequate sources of factor XIII^[2]. Plasma-derived pasteurized factor XIII concentrate under the name of Fibrogammin P is now available. Recombinant factor XIII is now being tested in experimental animals^[2]. Our case was indeed treated successfully with cryoprecipitate at the time of bleeding and is now doing well under regular cryoprecipitate prophylaxis every three weeks without any bleeding problem and with normal growth and development. Because of long half life of factor XIII, three weekly prophylaxis is quite adequate.

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