An analysis of 8 cases of factor X deficiency

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Abstract

Background Factor X deficiency is a rare coagulation defect. There are occasional reports of factor X deficiency from India. Difficulty in accurate diagnosis and non-availability of ideal treatment is discussed.

Methods Eight cases of factor X deficiency, diagnosed from 1992 to 2007 are reported here

Results Seven were male while one was female. Seven patients were symptomatic from early childhood. One patient became symptomatic from 18 years of age. Factor X assay was done in 4 patients, 3 had severe deficiency and one had mild deficiency. One patient had associated factor IX deficiency. Three patients had repeated bleeding episodes requiring multiple transfusions. Two patients had intracranial bleed and one had umbilical cord bleeding at birth. There was no mortality. No patient received prophylactic transfusion.

Conclusions Factor X deficiency is a rare coagulation defect. Hereditary deficiency should be distinguished from acquired deficiency. CNS, joints and skin are the common sites of bleeding.

Keywords Factor X deficiency · Stuart factor · Multiple factor deficiency · Vitamin K · Prothrombin complex concentrate · Fresh frozen plasma

Introduction

Factor X deficiency is an autosomal recessive disorder with moderate to severe bleeding manifestations. Males and females are equally affected [1]. Clinical manifestation of factor X deficiency is related to the functional level of factor X and genetic mutation [2]. In severe deficiency, (factor X level less than 1% of normal), patient bleeds spontaneously as well as following trauma [3, 4]. Primary sites of bleeding are joints, soft tissue and mucous membrane. In moderate (factor X level: 1–5 %), mild (factor X level: 6–30%) deficiency and in carriers (heterozygote), bleeding usually occurs after trauma, or during or after surgery [3, 4]. Prevalence of factor X deficiency is 1 in 1–2 million.

Factor X is involved in common pathway of coagulation cascade. Prothrombin time (PT) and activated partial thromboplastin time (APTT) are increased in factor X deficiency. APTT or PT is corrected with addition of normal plasma and aged sera as both supply factor X. APTT is not corrected with adsorbed plasma and Factor X deficient plasma as they are deficient in factor X. Aged serum contain factor XII, XI, X, IX and VII. Adsorbed plasma contain factor XII, XI, VIII, V and I. Factor X assay is helpful in confirmation of the diagnosis and to know severity.

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Materials and methods

This retrospective analysis was done using patients' records from 1992 to 2007 who attended the haematology clinic. During this period, 357 patients had hereditary bleeding problem and 287 had acquired bleeding problem. Blood collection, processing and analysis of samples for coagulation tests were done according to the standard methods as described by Dacie and Lewis [5].

Correction study was done to find/exclude factor deficiency. Four part patient's plasma and one part control / aged sera / adsorbed plasma / factor deficient plasma were taken. PT and APTT based correction study were done in one and seven patients respectively. In one patient PT based correction was done as APTT was only marginally prolonged.

Adsorbed plasma was prepared in plastic tube. 5 ml blood from three healthy normal adult persons was taken in 10 mg of ammonium or potassium oxalate in three different test tubes. Platelet poor plasma (PPP) was prepared and then pooled. 100 mg BaSO₄ was added in 1 ml pooled plasma and then mixed on vortex for 30 seconds. PPP was spun at 3000 RPM for 5 minutes and PT was performed from the supernatant. PT should be more than 2 minutes.

Aged sera were made in glass tubes. 3 ml blood was collected from 3 normal healthy adult donors in three different test tubes. Blood was allowed to clot, kept at 37°C for 8 hours and then at room temperature for 16 hours. Aged sera were preserved at $\leq -18^{\circ}\text{C}$ in aliquots of 100 μl . [5].

Factor Assay was done by one stage PT based clotting method. Liver function test and sonography abdomen was done in all the patients to exclude liver disorder. Injection vitamin K was given to all the patients to exclude vitamin K deficiency and to document vitamin K response in hereditary factor X deficiency.

Results

The presenting age varied from 6 months to 18 years. Except one patient, who presented at the age of 18 years, all others were symptomatic from early childhood. All the patients except one were male. The female patient's sister also was suffering from factor X deficiency. Table 1 lists complaints of the patients. Two patients had intracranial bleed and one had umbilical bleeding at birth. Six patients received blood/blood component transfusion for bleeding episodes. Three patients had repeated bleeding episodes requiring multiple transfusion support. Two patients required transfusions for joint bleeds and one for menorrhagia. Average blood/blood component transfusion was 72.15 units (range 0–514).

Table 1 Patient complaints

Sites	Patients (%)
Joint (Knee, shoulder, ankle)	3 (37.5)
Skin	2 (25)
CNS	2(25)
Nose	1(12.5)
Muscle (Gluteal)	1(12.5)
Umbilical cord	1(12.5)
Scalp	1(12.5)
GI tract	1(12.5)
Menorrhagia	1(12.5)
Hematuria	1(12.5)
Gum	1(12.5)

Factor X assay was done in four patients, three had severe deficiency and one had mild deficiency. One patient had associated deficiency of factor IX. There was no mortality although six patients had multiple bleeding episodes and two had life threatening bleeding episodes.

Discussion

There are sporadic publications of factor X deficiency from India [3, 4, 6]. Factor X deficiency was diagnosed on the basis of prolong PT, APTT, correction with normal plasma and aged sera and no correction with adsorbed plasma. Factor X assay could not be done in all the patients either due to non-availability of the test or for economical reasons. Associated deficiency of factor IX, VII and II could be picked up only by doing factor assay or correction study with respective factor deficient plasma [7]. One of our patients had associated factor IX. Deficiency of factor VII, IX and II along with factor X is reported in the literature also [7, 8].

One 6-month-old male patient had correction of PT and APTT following vitamin K injection. Since he was 6 month old, differential diagnosis included haemorrhagic disease of newborn, chronic liver disease and hereditary factor X deficiency. He was lost to follow-up and hence firm diagnosis could not be established. Transient response to vitamin K is known to occur in some patients of hereditary vitamin K dependent factor deficiency and hence hereditary factor X deficiency could not be excluded [8].

One of our patients, 2-year old male with 9 % factor X level had subdural hematoma and convulsion at the age of 1 month. There was no history of trauma or difficult delivery. Life threatening spontaneous bleeding is very uncommon in mild deficiency; however injury at the time of birth can't be completely excluded. He remained asymptomatic after that. Another patient also had intracranial bleeding at one month

of age and umbilical cord bleeding at birth. Intracranial bleeding is also reported previously, particularly in infants [9]. Herrmann FH et al reported high incidence (21%) of intracranial bleeding in homozygotes as well as heterozygotes [2]. Our series also has very high incidence of intracranial bleeding (2 out of 8 cases, 25%). Umbilical cord bleeding is more commonly seen in factor I and XIII deficiency, but it can occur in factor X deficiency also.

Seven out of eight patients were symptomatic from early childhood while only one patient had late presentation. This patient presented at the age of 18 year. He denied any history suggestive of bleeding problem in the past. His investigations were not suggestive of liver disorder and amyloidosis.

All the patients received whole blood or fresh frozen plasma. Only two patients used prothrombin complex concentrate (PCC) intermittently as it is not easily available and is very costly. Some patients, who resided in small cities or villages, used whole blood, as components were not available. Minor and moderate bleeding episodes could be treated with FFP, as haemostatic level in factor X deficiency is 10 % [10].

Three patients required multiple transfusions. The female patient required transfusions due to bleeding per rectum and menorrhagia. Her menorrhagia could not be controlled with anti-fibrinolytic drugs and hormonal therapy. Prophylactic factor X infusion is recommended to reduce bleeding episodes and resultant morbidity but it was not possible in our patients due to non-availability and economical reasons [11].

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