Congenital factor X deficiency - An unusual cause of Intracranial hemorrhage

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Abstract

Congenital factor X deficiency is a rare autosomal recessive disorder that usually presents with variable bleeding tendency, prolonged prothrombin time and partial thromboplastin time. Therefore, it may be misdiagnosed as hemorrhagic disease of the newborn. We describe a patient with factor X deficiency who had recurrent haematomas with intracranial hemorrhage.

Key Words: Factor X deficiency, Prothrombin time, Partial thromboplastin time, Intracranial haemorrhage
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Introduction

Factor X deficiency is an extremely rare autosomal recessive inherited coagulation disorder in children. It occurs with a frequency of one per 2,000,000 individuals and so far only fifty cases have been reported worldwide [1]. It has a varied presentation ranging from small hematomas and hemarthroses to life threatening intracranial haemorrhage. Diagnosis is confirmed by prolongation of prothrombin time (PT) and activated partial throm-boplastin time (aPTT) with decreased levels of Factor X antigen and activity. We report such a case with recurrent haematomas and intracranial haemorrhage.

Case Report

A twenty days old male child developed swelling of the right thigh following traditional oil massage. The swelling was aspirated at a local hospital and was followed by profuse bleeding. The procedure was abandoned and he was rushed to our hospital for further treatment. He was a full term baby born to first degree consanguineous parents at local hospital by spontaneous vaginal delivery. Birth weight was normal and the antenatal period was uneventful. Family history was negative for any form of hereditary or acquired bleeding disorder. Injection vitamin K was not given at birth.

On examination the neonate was markedly pale with active bleeding. The neonate was resuscitated with intravenous fluids, packed cell transfusion and Injection vitamin K. The bleeding from the thigh stopped and a clinical diagnosis of hemorrhagic disease of newborn was made. On the same day the neonate had two episodes of multifocal clonic seizures with intermittent posturing with tense anterior fontanel. Intracranial hemorrhage was suspected and he was transfused with two units of 10ml/kg fresh frozen plasma. The seizures were controlled with anticonvulsants. Pre transfusion hemoglobin was 5.2 gm%, total leucocyte count was 12,200 and differential count revealed N 40%, E 03% and L 57%. Prothrombin time was 28.5 secs (control 15 secs), aPTT was 46.3 secs (control 27.7 secs) and the platelet counts was normal. Liver function tests revealed serum total protein of 4.8gm/dl, albumin of 2.9 gm/dl, bilirubin 6.6mg/dl, (direct 2.8mg/dl), ALT 90 IU/L, AST 142 IU/L and alkaline Phosphate of 468 IU/L. CT scan showed retro occipital subdural haematoma with out any mass effect. Subsequently the child did not have seizures and the sensorium improved and there were no further bleeds. Anticonvulsants were tapered and stopped. Post transfusion hemoglobin was 10.2gm%, repeat liver function tests were normal and the neonate was discharged with advice to follow up after one month for further evaluation of his bleeding problem.

However, he promptly came back at fifty days of life with swelling in his left thigh, with fever and pallor following DPT vaccination. On examination, he had a 3×2 cm indurated tender swelling at the injection site. There was however no active external bleeding .He was given antibiotics, packed cell transfusion and injection Vitamin K. Investi-gations revealed hemoglobin of 4.2gm% platelet count of 229,000/cu.m. Total leucocyte count was 13,400.PT 24.6 secs (control 10.8 secs) aPTT was 46.3 secs (control 27.7 secs), thrombin time was 5.3 mts (control 5.9 mts). Since platelets were normal and PT, aPTT were both prolonged and not being corrected with vitamin K, deficiency of common factor pathway was suspected. A mixing test was done which revealed a prolonged PT and aPTT on mixing with adsorbed plasma but getting corrected with aged serum. This was confirmed by performing a repeat test with factor x deficient plasma which revealed prolongation of PT and aPTT. Factor X assay was performed and it was less than 10%. The infant was again transfused with a unit of 10ml/kg of fresh frozen plasma. The repeat CT scan showed the resolution of the subdural haematoma and post transfusion hemoglobin was 9gm%. With antibiotics and plasma the swelling subsided and the infant was discharged. Parents were counselled regarding the nature of the illness and adviced to use 27g needle for immunization and to avoid unnecessary intramuscular injections. The need for frequent transfusions and danger signs to watch for were explained to the parents. His further immunization visits were uneventful.

Discussion

Factor X deficiency is a rare autosomal bleeding disorder which was first described in two patients independently and hence the factor is also known as Stuart Prower factor after these individuals. It is a Vitamin K dependent glycoprotein which is changed to its active form as a serine protease both by factor VII and calcium, with tissue thromboplastin in the extrinsic pathway. Factor IX with Factor VIII; Calcium and platelet Factor 3 in the intrinsic pathway activate it. Factor Xa is also involved in the macromolecular complex formation with its cofactor Va, phopholipid surface and calcium to convert prothrombin to thrombin [2]. Factor X deficiency results from either a deficiency of factor X or a qualitative defect in the protein [3]. Acquired deficiencies of factor X may occur with anticoagulant therapy, liver disease, Vitamin deficiency and secondary to drugs like phenytoin. The gene-controlling factor X production is primarily located on the long arm of chromosome 13. Factor X deficiency is known to cause mucocutaneous bleeds as well as post-traumatic Bleeds [4]. However, there are few cases reported of the association of factor X deficiency with intracranial bleeds [5].

The diagnosis is suspected when PT and aPTT are pro-longed which is corrected with aged serum but not with adsorbed plasma. Russell viper venom test is prolonged and the definitive diagnosis is by factor assay with a minimum haemostatic level of 20 – 30 U/dL[6].Though factor x is a vitamin K dependent factor, congenital factor x deficiency is not corrected with vitamin K. In this case, our first impression was late hemorrhagic disease of new born as the initial liver function test was deranged with prolonged PT and clinical bleeds. However since the bleed was not responsive to vitamin K and repeat liver function test being normal, we had to revise our diagnosis and the infant was reinvestigated. Since PT and aPTT were both prolonged with a prolonged clotting time and normal bleeding time, common pathway factor deficiency was suspected, which was later confirmed by Factor X assay.

Fresh frozen plasma has been the mainstay of therapy for Factor X deficiency.

Half life of Factor X is 40hrs. The need for frequent use of large volumes of Fresh frozen plasma is a problem in small children. Prothrombin complex concentrates have also been used with some success [7]. However the degree of elevation for Factor X is extremely variable with added risk of thromboembolic complications and development of inhibitors [8]. The advantages of Prothrombin complex over FFP is reduction in volume infused and decreased chance of infection as they are all heated and paesturized. Prophylactic administration of Factor X to prevent recurrent intracranial haemorrhage was reported by Sandler G et.al [9]. However the clinical experience of using Prothrombin complexes or the prophylactic administration of Factor X to prevent intracranial haemorhage is very limited in factor X deficiency which is otherwise a very rare disorder.

References

1. Barik S, Budhraja A, Bhalla M, Diwan S. Inherited Factor X deficiency in two brothers. Indian J Pathol Microbial 1997; 40:63-65.
2. Mammen EF. Factor abnormalities. Semin Thromb Hemost 1983; 9:31-33.
3. Montgomery RR, Scott JP. Hemostasis: Diseases of the fluid phase. In: Nathan DG, Oski F (eds). Hema-tology of Infancy and Childhood. 4th edn, Philadel-phia, W.B Saunders, 1993; pp 1629-1630.

4. Roberts HR, White GC JR. Inherited disorders of Prothrombin conversion. In Volman RW, Hirsh J, Marder VJ (eds): Hemostasis and Thrombosis: Basic principles and clinical practice. 4th edn, Philadelphia, Lippincott, Williams & Wilkins, 2001, pp 839-853.
5. Ramdas J, Ole D, Warrier RP. Factor X deficiency: An unusual cause for spontaneous intracranial bleeding. Indian Pediatr 2000; 6:656-659.
6. Bauer KA: Rare Hereditary Caoagulation factor Anormalities. In: Nathan DG, Orkin SH, Ginsburg D, Look AT (eds). Nathan and Oskis Hematology of in-fancy and childhood. 6th edn, Philadelphia, WB Saun-ders, 2003; pp 1579-83.
7. Kalla S, Menon NS. Neonatal Congenital Factor X deficiency. Pediatr Hematol Oncol 19991; 8: 347-354.
8. Oleary DS, Ruymann FB, Conrad ME. Therapeutic approaches to Factor X deficiency. J Lab Clin Med 1971; 77: 23-32.
9. Sandler G, Gross S. Prevention of recurrent intracranial hemorrhage in a Factor X deficient infant. Am J Pediatr Hematol Oncol 1992; 14: 163-165.

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