A child with congenital factor VII deficiency

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(Key words: congenital factor VII deficiency, child)

Introduction

Factor VII (F VII) deficiency is a rare autosomal recessive coagulation disorder with quantitative and qualitative defects¹. Incidence is 1:500, 000². Normal levels of F VII range from 50-150%³. Homozygotes have F VII concentrations < 10% whilst heterozygotes have variable levels with a mean 50% of normal³.

Clinical manifestations are variable with poor correlation between circulating F VII coagulant activity and degree of bleeding. Bleeding is frequently of mucocutaneous type. Commonest manifestation is prolonged bleeding following dental extraction. In some neonates bleeding from umbilical stump has been observed. Mild factor VII deficiency patients are asymptomatic and severely affected homozygotes (<1% clotting activity) have bleeding similar to haemophilia¹. Central nervous system bleeding has been reported⁴.

Case report

An eight year old boy, born of a non-consanguineous marriage, presented with repeated attacks of mucocutaneous bleeding from the age of 3 years - after shedding of milk teeth, dental trauma and infrequent ecchymotic patches following minor trauma. His bleeding was controlled with local measures such as applying pressure and an ice pack. There was no past history of liver disease, significant gastrointestinal disease or history of taking oral anticoagulants. He had no family history of bleeding disorders. On examination, he was an averagely grown, otherwise normal, child with a few ecchymotic patches. There was no evidence of anaemia or jaundice and the Hess test was negative.

The haemoglobin was 13.1g/dl, white cell count 14x10⁹/L (N60, L32, E8%) and platelet count 216x10⁹/L. Blood picture was normocytic, normochromic with no abnormal cells. Reticulocyte count was 0.9 %. Bleeding time (BT) was 2 ½ minutes and clotting time 4 ½ minutes. Activated partial thromboplastin time (APTT) was 34 seconds (control 32 seconds) and prothrombin time (PT) 30.7 seconds (control 14.4 seconds). PT was repeated after a 7-day course of vitamin K therapy and was 37.7 seconds (control 14.4 seconds), PT with addition of plasma was 19.4 seconds and with addition of serum 17.9 seconds. Fibrinogen degradation products were <2 µg/ml (normal <10 µg/ml). Serum protein was 8.5 g/dl, SGPT 8 IU/dl (albumin 5.5 g/dl. globulins 3 g/dl) and the serum alkaline phosphatase 243 IU/L. Family screening was normal.

Discussion

Factor VII plays a central role in the initiation of haemostatic response through conceptually divided extrinsic pathway when it forms a complex with tissue factor damaged vessel walls (TF-VIIa)¹. The TF-VIIa initiates thrombin generation by directly activating the Factor X and Factor IX. It also activates Factor VII by an autocatalytic mechanism¹.

Normal APTT and a prolonged PT that is fully corrected by the addition of normal serum or Russell viper venom signify deficient F VII activity². Congenital F VII deficiency must be differentiated from acquired deficiency as may occur in patients with liver disease vitamin K deficiency or those on oral anticoagulant therapy and rarely due to circulating inhibitor³.

A F VII level > 20% is considered haemostatic. Products used in F VII deficiency are fresh frozen plasma (FFP), prothrombin complex concentrate (containing Factors II, VII, IX & X) and a specific F VII concentrate¹. Excessive doses of F VII are potentially thrombogenic. Because of varying clinical manifestations of F VII deficiency, replacement therapy should be individualized and will depend on the nature and severity of the coagulation defect, site of bleeding and type of intervention. A plasma level of 10-20% is sufficient to maintain haemostasis. Infusion of 1 unit

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(Received on 11 April, 2003)
of FVII concentrate / kg of body weight increases circulating F VII level by approximately 2%.

In Sri Lanka FFP is the only source of F VII replacement therapy. The dose of FFP is 10-15 ml/kg and for most bleeding episodes it has to be given 8-12 hourly.

For treatment of bleeding or as cover for minor surgery, a single dose of F VII concentrate has been found to be sufficient. For surgical interventions it is recommended that a plasma level of 20% is maintained for 8-10 days. The maintenance dose should be given at intervals of 12 hours. Whereas Jandl suggests administration of replacement therapy 3-4 times daily, Kankirawatana et al observed that FFP had been effective in treatment as well as prophylaxis of intracranial haemorrhage. For prophylaxis they used FFP 10 ml/kg twice a week.

PT is prolonged with abnormalities of Factors II, X, V or VII, liver disease, vitamin K deficiency or if patient is on oral anticoagulants. APTT is prolonged with deficiencies or inhibitors to one or more of the following factors: XII, XI, VIII, X, V, II or I (but not factor VII). Vitamin K deficiency is usually associated with prolonged PT and APTT. In our patient the normal platelet count, BT, blood picture and negative Hess test exclude the possibility of platelet or vascular disorders. The PT is prolonged but acquired causes are unlikely as there is no history of liver disease, malabsorption or ingestion of oral anticoagulants. Further, his prolonged PT is accompanied by normal APTT and BT indicating that the defect is in F VII, which could be either of F VII deficiency or inhibitors to FVII. The almost complete correction of PT with normal person's serum and plasma excludes the possibility of an inhibitor. Thus a provisional diagnosis of congenital factor VII deficiency was made, confirmation of which requires F VII assay, which is not possible in our country. The patient was treated with FFP and immunized against hepatitis B virus. Future management plan was drawn up and the parents were instructed accordingly.

Acknowledgements

We wish to thank Dr. N. Ekanayake, Consultant haematologist, Teaching Hospital, Kandy for performing the coagulation profile.

References


