Factor VII Deficiency: A Rare Case Report

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Received: 7 April 2010 / Accepted: 8 July 2010 / Published online: 6 October 2010
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Abstract Factor VII deficiency is a rare congenital coagulopathy. Prolonged prothrombin time with normal partial thromboplastin time indicates factor VII deficiency. For the definitive diagnosis, the specific factor VII level should be investigated. We report a 20 day old, baby girl, born full-term who was admitted with the diagnosis of sepsis. Hematological tests revealed prolonged prothrombin time and a factor VII level of nine percent. After antibiotic therapy and fresh frozen plasma replacement, her clinical status improved but the prothrombin time continued to be prolonged. On the seventh day of discharge the baby died due to sudden intracranial hemorrhage.

Keywords Factor VII deficiency · Congenital coagulopathy · Intracranial hemorrhage

Introduction

Factor VII is one of the vitamin K-dependent coagulation factors synthesized in the liver and has a short circulating half-life of 3–4 h. Inherited factor VII (FVII) deficiency is a rare autosomal recessive hemorrhagic disorder. We hereby present a 20 day old baby who was diagnosed as congenital factor VII deficiency and died in the neonatal period due to intracranial hemorrhage.

Case History

A 20 day old baby girl was admitted for surgical drainage of breast abscess. The abscess was drained under the cover of appropriate antibiotics and the baby recovered from sepsis during hospital stay. She developed melena and GI bleeds on day 3 of hospital stay. There was no family history of bleeds but, there was a definite past history of intermittent epistaxis. The underlying coagulopathy was investigated.

The investigations revealed normal platelet counts, deranged prothrombin time (PT) with International normalised ratio (INR) of 6.2. Activated partial thromboplastin time (aPTT) was within normal limits. Further investigations revealed factor VII activity of 9%. Other factors assays (factor V and factor X) were normal.

Baby required repeated transfusions of fresh frozen plasma (FFP) to maintain normal INR. This confirmed the diagnosis of congenital factor VII deficiency. Parents were investigated for heterozygosity of factor VII deficiency and found to be normal.

Baby was discharged after appropriate counselling. Seven days after discharge, the baby presented with convulsions. CT brain revealed extensive intracranial bleeds and baby succumbed to the underlying illness.

Discussion

Factor VII deficiency was first described by Alexander et al. [1]. Frequency is higher in countries where consanguineous marriage is more common. Few case reports [2] are reported from India. Type 1 deficiencies result from decreased biosynthesis or accelerated clearance; type 2 abnormalities represent a dysfunctional molecule. More

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than 100 mutations, mostly missense mutations [3, 4], have been identified in the Factor VII gene located on chromosome 13. Acquired FVII deficiency may arise due to vitamin K deficiency, vitamin K antagonist therapy or liver disease. In these conditions, reduced FVII levels are associated with reduced levels of other vitamin K-dependent factors. Acquired FVII deficiency [5, 6] is far more common than inherited deficiency. In the index case, other factor assays in blood were found to be normal.

Clinical bleeding can widely vary and does not always correlate with the level of FVII coagulant activity measured in plasma. Mortality is related to severe bleeding, most often resulting from CNS hemorrhage as was seen in the index case. Most severe cases of FVII deficiency are diagnosed during childhood, often during the first 6 months of life. In infancy, the most common bleeds occur in the gastrointestinal tract or CNS, accounting for 60–70% of bleeds in this age group [7, 8].

The PT is prolonged in FVII deficiency and the INR is elevated. The aPTT is within the reference range in isolated FVII deficiency as seen in the index case. FVII assays are performed by using thromboplastin-dependent one-stage clotting assay. The more sensitive thromboplastins, usually recombinant human thromboplastin, are preferred for measuring FVII activity in the very low range.

Management of acute hemorrhage primarily consists of FVII replacement therapy to treat bleeding [7, 8]. Levels of more than 10% are usually hemostatic, although higher levels may be advisable in the event of a severe bleeding episode. Because FVII has a short half-life (3–4 h), repeat treatment may be necessary in all except minor bleeding episodes. Treatment alternatives include fresh frozen plasma, which is least effective because of the volume required to provide adequate FVII replacement. Prothrombin complex concentrates contain factors II, IX, and X in addition to FVII. These agents carry a risk of thrombogenic complications, particularly with repeated

administration. If available, FVII concentrates are preferred over untreated plasma. Recombinant activated FVII (rFVIIa) was originally developed to treat patients with hemophilia with factor inhibitors. It can be used at lower doses for patients with congenital FVII deficiency. Maintaining FVII levels of at least 15–25% provides adequate hemostasis levels for most surgical procedures.

Conclusion

Congenital Factor VII deficiency is a rare cause of bleeding disorder, which should be suspected in a healthy bleeding child presenting in infancy when platelets and aPTT is normal with a deranged PT.

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