Congenital Factor VII Deficiency Presenting With Isolated Recurrent Hematuria: A Case Report

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Abstract- Factor VII deficiency is a rare congenital coagulopathy disorder. In most cases, this disorder is diagnosed in childhood. Common symptoms of congenital factor VII deficiency are different and consist of cutaneous, mucosal hemorrhage, gastrointestinal bleeding, and joint bleeding. CNS hemorrhage is a fatal and severe complication of congenital factor VII deficiency. The incidence of gross hematuria is a rare symptom of factor VII deficiency. Isolated presentation of hematuria is rarer and usually is accompanied by bleeding in other sites. The patient reported here is a 6-month-old girl who was diagnosed with congenital Factor VII deficiency following episodes of isolated gross hematuria. We decided to report this case to demonstrate if there is no other organic cause in the investigation of a child with recurrent hematuria, we should also consider a coagulation factors deficiency. Since isolated hematuria is a rare symptom in the coagulation factors deficiency, the coagulation tests may be of less interest.
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Keywords: Hematuria; Congenital factor VII; Children; Coagulation factors

Introduction

Factor VII deficiency is a rare congenital coagulopathy disorder. The incidence rate of this inherited autosomal recessive hemorrhagic disease is one in 500,000 populations (1,2). In most cases, this disorder is diagnosed in childhood (3). Although prolonged prothrombin time (PT) with normal partial thromboplastin time (PTT) can demonstrate factor VII deficiency, assessing the specific factor level is needed for establishing the diagnosis. Factor VII is a Vitamin K-dependent coagulation factor produced in the liver and has a short circulating half-life of 3-4 h (4-5).

Common symptoms of congenital factor VII deficiency are different and consist of cutaneous, mucosal hemorrhage, gastrointestinal bleeding, and joint bleeding (6). CNS hemorrhage is a fatal and severe complication of congenital factor VII deficiency. The important issue is that clinical bleeding can differ widely and does not necessarily correlate with the level of factor VII activity in the plasma (7). The incidence of gross hematuria is a rare symptom of factor VII deficiency. Isolated presentation of hematuria is rarer and usually is accompanied by bleeding in other sites (8). Based on our reviews, only a 23-year-old young man with congenital Factor VII deficiency was reported with only recurrent episodes of isolated hematuria (9). The patient reported here is a 6-month-old girl who was diagnosed with congenital Factor VII deficiency following episodes of isolated gross hematuria.

Case Report

A 6-month-old girl born of non-consanguineous marriage with normal birth and without developmental delay was referred to the emergency department of Ali Asghar Children Hospital because of gross hematuria without clots. She had no fever and restlessness during urination. In her past medical history, she had a history of hematuria 40 days prior to this visit which lasted two days

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and resolved without any action. There was no history of any febrile disease preceding these episodes. She had no history of rash, oral ulceration, and other sites bleeding since birth. There was no history of drug intake, including any anticoagulant medication. There was not any history of bruise formation. Also, the family history of any bleeding disorder was negative.

On examination, she was hemodynamically stable. The systematic examination was unremarkable. Full blood count showed hemoglobin of 8.3 g/dL, total leukocyte counts of 11700, platelet count of 505000, blood urea of 10 mg/dL, serum creatinine of 0.7 mg/dL, total bilirubin of 0.7 mg/dL, direct 0.2 mg/dL, alanine aminotransaminase (ALT) of 22 U/L, aspartate aminotransaminase (AST) of 33 U/L.

Urinalysis revealed severe hematuria with plenty of red blood cells (RBCs) with no RBC casts or any evidence of dysmorphic RBCs; there was no proteinuria. Urine culture and urine for malignant cytology were negative. The patient's PT was elevated to 38.6 with an international normalized ratio of 5.4. His activated partial thromboplastin time (APTT) was normal. Further investigations revealed that the PT could be corrected with normal plasma, suggesting an inherent clotting factor deficiency. Ultrasound showed no calculus or mass lesions. Clotting factor assay (i.e., factor VII activity) was suggestive of factor VII deficiency with levels of less than 2%. Factor VII assays of both parents, however, showed normal levels.

Because of continuous hematuria, she received ten cc/kg Fresh Frozen Plasma (FFP) in the emergency department, and, consequently, the bleeding stopped. However, after preparing the test results and proving the factor VII deficiency, treatment started with factor VII replacement. The patient was discharged from the hospital and is now on regular follow-up.

Discussion

Congenital Factor VII Deficiency is a rare hemorrhagic disorder inherited in autosomal recessive disorders (1). Factor VII is an essential factor in the external coagulation pathway and has the shortest half-life of 3 to 4 hours (10). In Factor VII deficiency, PT and INR levels increase (11), and factor level is reported below 5%. There is a poor relationship between the bleeding phenotype and factor VII levels (12).

Factor VII deficiency was first defined by Alexander *et al*., (13). Only a few cases (14) have been demonstrated from India. Although Type 1 deficiencies result from decreased production or accelerated clearance, a dysfunctional molecule has been found in type 2 abnormalities. Many different mutations (15-16) have been demonstrated in the factor VII gene located on chromosome 13 (9). Because this disorder is hereditary, the frequency is higher in countries where consanguineous marriage is more common.

It is revealed that isolated hematuria is uncommon as the primary manifestation of Factor VII deficiency (8). In our patient, both parents were non-consanguineous, but there was a similar disorder in her father's cousin.

Although their factor VII levels were normal, this condition is known to have a rather variable expression with a poor correlation between the reported coagulant activity and clinical bleeding tendency. This may well be the explanation for the normal factor VII assay in the parents. Another possibility is that the parents are gonadal mosaics, or, alternatively, only one of them is a gonadal mosaic, with the other mutation occurring spontaneously in the patient himself. Acquired factor VII deficiency may arise due to Vitamin K deficiency, Vitamin K antagonist therapy, or liver disease, none of which persisted in this patient.

Furthermore, in acquired factor VII deficiency, reduced factor VII levels are associated with reduced levels of other Vitamin K-dependent factors. In the index case, other factor assays in the blood were normal. The PT has prolonged factor VII deficiency, and the INR is elevated. The aPTT is within the reference range in isolated factor VII deficiency, as seen in this case.

Factor VII deficiency may be classified into the severe form (factor VIIc <1%) and the mild to moderate form (Factor VIIc 5%-7%) (17). However, the plasma level of factor VII that is required for hemostasis is not demonstrated, and this may contribute to its rather variable expression and poor correlation between reported coagulant activity and clinical bleeding tendency (18).

Management of acute hemorrhage primarily consists of FVII replacement therapy to stop bleeding (4-5). Levels of more than 10% are usually hemostatic, although higher levels are perhaps advisable in the event of a severe bleeding event. As factor VII has a short half-life (3-4 h), continuous treatment in several doses may be necessary in all cases of bleeding, except minor bleeding episodes. Another treatment is fresh frozen plasma (FFP) that is used only when Factor VII is not available. FFP is the least effective choice because of the volume required to provide adequate factor VII replacement. Prothrombin complex concentrates (PCC) contain factors II, IX, and X in addition to factor VII. These agents have a risk of thrombogenic complications, especially with repeated

doses. Maintaining factor VII levels of at least 15%-25% provides adequate hemostasis levels for most surgical procedures.

In conclusion, the presentation of congenital factor VII factor deficiency, as isolated recurrent hematuria, is a rare occurrence. Prolonged PT with normal PTT demonstrates factor VII deficiency. For a definitive diagnosis, the specific factor VII level should be assessed. Management consists of factor VII replacement therapy to treat active bleeding. Since isolated hematuria is a rare symptom in the coagulation factors deficiency, the coagulation tests may be of less interest. Therefore, we decided to report this case to demonstrate if there is no other organic cause in the investigation of a child with recurrent hematuria, we should also consider a coagulation factors deficiency.

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