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Factor VII Deficiency: A Rare Cause of Severe Bleeding Disorder in a Newborn

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Abstract

Factor VII deficiency is rare. It is an autosomal recessive inherited disease with an estimated prevalence of 1/1,000,000. We report the case of a newborn male from first-degree consanguineous parents admitted at 15 days of life due to a hemorrhagic syndrome. Hemostasis tests showed low prothrombin time (PT) and normal activated partial thromboplastin time (aPTT). A coagulation panel revealed isolated factor VII deficiency. In this case, we highlight the clinical, biological, and therapeutic aspects of this condition during the neonatal period.

Keywords

Congenital Deficiency, Factor VII, Hemorrhage

1. Introduction

Factor VII, or proconvertin, is a blood glycoprotein synthesized by the liver. It is vitamin K-dependent and plays a role in the extrinsic coagulation pathway. Congenital factor VII deficiency is an extremely rare condition. Clinical presentation can be variable, ranging from asymptomatic conditions to severe and potentially fatal bleeding [1] [2]. Coagulation tests are the first step in the diagnostic workup of pediatric bleeding, but the crucial point is that clinical bleeding can vary greatly and does not always correlate with the level of factor VII activity in the plasma [3].

In this study, we describe a case of isolated factor VII deficiency in a newborn. This case highlights the features of this rare deficit. This condition needs to be considered by clinicians when faced with challenging patients presenting with bleeding disorders.

2. Clinical Observation

We present the case of an 8-day-old male newborn, born to first-degree consanguineous parents. The mother was 24 years old, 0 Rh-positive, a primigravida, and a primipara. The pregnancy was carried to term, and the delivery was conducted vaginally at the maternity unit. The birth weight was 3100 g, and the Apgar score was 10/10. The newborn received vitamin K shortly after birth and was in good health until day 8 when he had a minor umbilical cord hemorrhage, treated as an outpatient with vitamin K. On day 15, he developed scalp bleeding with active epistaxis, leading to his admission to our department. There were no similar cases in the family. Clinical examination at admission revealed a conscious, pale, alert newborn with good hemodynamic and respiratory status. Cutaneous and mucosal examination showed ecchymoses on the right hand (**Figure 1**) and the left lower limb (**Figure 2**), active epistaxis, and gingival bleeding (**Figure 3**) with active scalp bleeding.

The rest of the physical examination was unremarkable. Laboratory tests indicated normochromic normocytic anemia with a hemoglobin level of 6.9 g/dL and a normal platelet count of 349,000 platelets/mm^3. Hemostasis testing showed a PT of 11% (70% - 100%), and a normal aPTT, with a normal fibrinogen level.

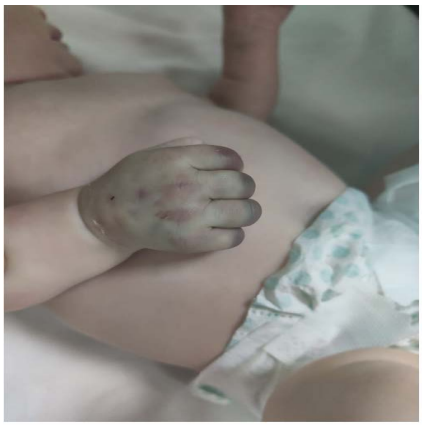

Figure 1. Ecchymoses on the right hand.

Figure 2. Ecchymoses on the left lower limb.

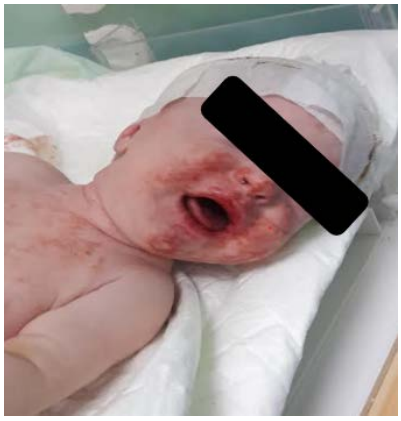

Figure 3. Active epistaxis and gingival bleeding.

Blood typing revealed O Rh-positive with a negative direct Coombs test. Given parental consanguinity, hemorrhagic syndrome with a low PT and normal aPTT, factor VII deficiency was suspected. Subsequent testing confirmed the diagnosis, with an initial factor VII level of 6% (70% - 140%). (Chronometric technique using STA-Néoplastin CI Plus® reagent on Stago STA R Max 2). A second factor VII testing indicated a low level of 4% with a normal FVII antigen (FVII: Ag). A genetic study confirmed the diagnosis of a severe FVII deficiency with mutation at the level of chromosome 13. These tests were performed before any replacement therapy during the hemorrhagic episode. Parental factor VII levels were within the normal range for PT and aPTT. Radiological assessments included a normal abdominal-pelvic ultrasound and a transfontanellar ultrasound followed by a cerebral computed tomography, which showed triventricular hydrocephalus without visible obstruction and signs of transependymal resorption. The newborn received transfusions of fresh frozen plasma and red blood cell concentrates, which stopped the bleeding but did not prevent active quadri-ventricular hydrocephalus. Intravenous administration of recombinant activated factor VII at a dose of 30 ug/kg led to clinical and biological improvement.

To treat the hydrocephalus, external ventricular drainage was considered, however, the risque of bleeding was a concern. Therefore, periodic lumbar puncture and drainage were performed. The results of lumbar puncture were normal and the patient was under regular factor VII supplementation. Screening for parents has been proposed and they have been informed about the need for implementing substitute treatment in case of hemorrhagic risk. At present, the patient is followed regularly.

3. Discussion

Factor VII deficiency was first described in 1951 by Alexander, with an estimated prevalence of 1/1,000,000 [4]. It is transmitted in an autosomal recessive manner, making it more frequent in consanguineous marriages, as in this case. Only homozygous or compound heterozygous individuals may present with a hemorrhagic syndrome, while heterozygous carriers are asymptomatic. The re-

sponsible gene is located on chromosome 13 [4]. Factor VII, or proconvertin, is a blood glycoprotein synthesized by the liver, playing a role in the coagulation cascade. There are two types of factor VII deficiencies [5] [6]: congenital, inherited from parents, and acquired, resulting from other conditions (malignancies, liver diseases, certain medications, etc.). The correlation between bleeding severity and the level of bleeding is not established. In addition, there is no method to detect the severity, even though the factor VII gene has already been sequenced.

The symptoms also vary case by case. Most often, epistaxis (60%), gum bleeding (34%), easy bruising (36%), and menorrhagia have been reported. Males and females are equally affected; however, due to the symptoms of menorrhagia, females are more likely to have symptomatic disease [7].

The disease can manifest in the neonatal period with umbilical cord bleeding or present later during the shedding of primary teeth. It can also remain asymptomatic and only become apparent with trauma, surgery, or during family investigation. Early onset of symptoms in the first months of life often indicates a severe form of the disease, as seen in this case. Thrombotic events have also been reported in factor VII deficiency carriers [8]. Positive diagnosis relies on laboratory findings, including prolonged quick time PT with normal aPTT. The measurement of factor VII activity using a chromogenic method confirms the deficiency, with normal values ranging from 70% to 140% [9]. Family screening, including testing parents and siblings of affected individuals, is crucial.

Treatment is indicated in cases of acute hemorrhage or prophylactically before surgery. Fresh frozen plasma transfusion is less effective due to its low factor VII content. Prothrombin complex concentrate (PCC) is becoming less common due to the high risk of thromboembolic complications [7]. In contrast, factor VII concentrate is effective and well-tolerated, with a dose of 0.5 ug/kg increasing proconvertin levels by 1%. The recommended dose for bleeding episodes is 15 to 30 ug/kg every 4 to 6 hours until bleeding stops. When surgery is planned, prophylactic injections are recommended with 20 to 30 ug/kg of factor VII preoperatively and 5 to 10 ug/kg every 4 to 6 hours postoperatively for 5 to 10 days [8] [10]. For severe and recurrent bleeding, some authors have proposed long-term treatment with two injections per week [11] [12]. In this case, long-term treatment was not recommended, but parents were informed of the risk of recurrence and the need for replacement therapy in case of bleeding.

According to a review of the medical literature, up to one-third of the episodes documented during the neonatal period had a delayed diagnosis and/or treatment [13]. Pediatricians should be informed about the importance of hemostasis control when a newborn presents with abnormal bleeding.

4. Conclusion

Factor VII deficiency is rare and can present with a wide range of symptoms, from mild epistaxis to severe cerebral hemorrhage. In severe forms, it can affect functional and even life prognosis. It is crucial to perform coagulation factor

testing in cases of significant bleeding before transfusion to avoid delaying diagnosis and subsequent management.

Consent

Written informed consent was obtained from the patient parents for publication of this case report and accompanying images.

Author Contributions

All authors contributed to the conduct of this work. All authors also declare that they have read and approved the final version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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