CASE REPORT

SPONTANEOUS INTRACEREBRAL HEMATOMA: THINK OF THE FACTOR VII DEFICIENCY

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INTRODUCTION

Congenital factor VII (FVII) deficiency is a rare autosomal recessive coagulation disorder whose clinical manifestations can range from simple epistaxis to cerebral hemorrhage.¹,² Its prevalence is estimated at approximately 1 per 500,000, accounting for approximately 0.5% of all inherited coagulation disorders, and equal among males and females.² FVII deficiency is known to be associated with an increased intracranial bleeding tendency.³ Premature death may occur from severe bleeding. The treatment is based on replacement therapy by the administration of FVII concentrate. We report a case of an infant hospitalized at the age of 4 months for spontaneous intracerebral hematoma whose exploration has concluded a severe congenital factor VII deficiency. Through this observation we describe the clinical, biological and therapeutic characteristics of this bleeding disorder.

CASE REPORT

A 4 months old baby girl was admitted for consciousness disorders sudden onset. Her parents are consanguineous first degrees. There was no family history of bleeding apart a history of bleeding at the circumcision of her father. The beginning was three days before admission by the spontaneous ecchymotic tasks in the back, elbow and thigh, followed two days later by the appearance of unexplained and incessant crises. That day, the infant presented disorders of consciousness with tonico-clonic seizures affecting hemibody left. Clinical examination at admission objectified an infant eutrophic (weight = 7 kg, height = 64 cm), head circumference at 43 cm, afebrile at 37.2° C, hypotonic, unconscious (Glasgow score = 11), pale, with some ecchymotic spots at the trunk and limbs, and bulging anterior fontanel, the rest of the physical examination was normal. Cerebral CT scan revealed a right frontal intraparenchymal hematoma measuring 52x40x35 mm with a massive subarachnoid hemorrhage responsible for deletion of cortical sulci with mass effect on the ipsilateral ventricle, a deviation of the midline to the side left indicating a commitment under falcoriel (figure 1).

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ABSTRACT

Inherited factor VII deficiency is a rare bleeding disorder, with recessive autosomic transmission and a bleeding tendency of variable severity, in which premature death may occur from severe bleeding. We report a case of severe factor VII deficiency revealed by spontaneous intracerebral hematoma in a 4 months old girl through which we describe the clinical, biological and therapeutic characteristics of this deficiency.

Keywords: Factor VII deficiency, Intracranial hemorrhage, Congenital coagulopathy
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Figure 1: Cerebral CT scan: right frontal intraparenchymal hematoma with a massive subarachnoid hemorrhage and mass effect on the ipsilateral ventricle with commitment under falcoriel.

Figure 2: Cerebral CT scan follow-up control: right fronto-parietal ischemic lesions sequelae with a passive triventricular hydrocephalus.

The biological investigations revealed normocytic normochromic anemia with a hemoglobin level of 9 g/dl and thrombocytosis (833,000 elements/mm³), prothrombin time (PT) at 14% with an activated partial thromboplastin time (APTT) at 34 seconds (control: 32 seconds). Liver function tests were within normal limits.

Baby required initially repeated transfusions of fresh frozen plasma (FFP) and vitamin K for 48 hours; with a phenobarbital bolus followed by a relay of sodium valproate for the seizures. FVII deficiency was suspected because of the parental consanguinity, the hemorrhagic syndrome with a low PT and a normal APTT. The dosage of the FVII showed a rate of 1.5%. The dosage in parents showed moderately reduced rate of FVII (48% in mother and 38% in father) which corresponds to a heterozygous status. Genetic study was not performed because of lack of financial means. The patient was given recombinant activated FVII (rFVIIa) at a dose of 30 µg/kg every 6 hours for 5 days with good clinical and radiological improvement. Cerebral CT scan control showed a regression of the right frontal intraparenchymal hematoma, a disappearance of the subarachnoid hemorrhage; with the presence of right fronto-parietal ischemic lesions sequelae and a passive triventricular hydrocephalus (figure 2).

One month later, the infant was admitted to the emergency room for macroscopic hematuria, the urine culture was sterile and abdominal ultrasound showed no abnormalities of the urinary tract. The infant has evolved favorably after 3 days of administration of rFVIIa. Two months later, the patient was readmitted for the right knee hemarthrosis which regressed after administration of rFVIIa for 2 days.

At the age of 10 months, the infant is admitted for incessant cries with vomiting, clinical examination did not objectify exteriorized hemorrhagic syndrome. Recurrence of cerebral hemorrhage was suspected, cerebral CT scan was performed and showed a massive left subarachnoid hemorrhage (figure 3) having evolved favorably after the administration of rFVIIa at a dose of 30 µg/kg every 6 hours for 7 days.

Because of the recurrence of severe hemorrhagic syndrome, we proposed to the patient prophylactic treatment of FVIIa, but parents were unable to follow this prophylaxis because of lack of financial resources.

Figure 3: Cerebral CT scan: massive left subarachnoid hemorrhage with right fronto-parietal ischemic lesions sequelae.

DISCUSSION
FVII clotting or proconverting is a glycoprotein of blood synthesized in the liver and secreted as a single-chain glycoprotein of 48 kD. This factor is vitamin K-dependent. It is involved in the extrinsic pathway of coagulation and has a short circulating...
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half-life of 3-4 hours. It has the shortest half-life of all pro-coagulant factors, being the first to decrease when there is a problem in synthesis. The activated form of FVII (FVII a) interacts with cofactor tissue factor to play a critical role in initiating blood coagulation. FVII deficiency was first described in 1951 by Alexander et al. It is transmitted as an autosomal recessive trait, and causes a bleeding disorder of variable severity owing to a decreased level of this vital trigger of blood clotting. More than 100 heterogeneous mutations, mostly missense mutations, have been identified in the FVII gene located on the long arm of chromosome 13 (band 13q34). Only homozygous or compound heterozygous patients may have a hemorrhagic syndrome, heterozygous subjects are asymptomatic. Homozygous patients have a major deficit, with a rate of FVII below 10%. Three levels of severity were distinguished according to the depth of the deficit: FVII less than 5%, between 5 and 20%, and greater than 20%. Symptomatology ranges from asymptomatic to severe hemorrhagic problems without clear-cut correlation between circulating FVII level and the clinical manifestation reflecting the existence of immunological variants of FVII deficiency that could be related to the different second FVII mutated allele.

Of all factors evaluated, clinical history appears to be the best predictor of bleeding risk. The disease can occur as early as the neonatal period, during a fall hemorrhagic cord or be later in the fall of teeth, or the age of puberty in girls with menorrhagia abundant. However, the deficit may remain unnoticed and is diagnosed on the occasion of trauma, surgery or a family survey.

The hallmark of FVII deficiency is prolonged PT with a normal APTT. The diagnosis is confirmed by isolate deficiency of FVII activity. FVII deficiency is considered to be associated with bleeding only in moderate to severe deficiency, and it is known to be associated with an increased intracranial bleeding tendency as in our patient who had a recurrence of spontaneous cerebral hemorrhage. Patients with moderate deficiency (FVII activity 5-15%) typically present with mucosal bleeding such as epistaxis, menorrhagia, hematuria. These features are attributable to the role of the FVIIa-tissue factor complex in generating prothrombinase activity to provide thrombin for platelet activation. The early onset in the first months of life often reflects a severe form of the disease as in our case. Most severe cases of FVII deficiency are diagnosed during childhood, often during the first 6 months of life. The severe hemorrhagic problems such as hemarthrosis or intracerebral hemorrhage are encountered mostly in severe deficiency (< 1%). Mortality is related to severe bleeding, most often resulting from cerebral hemorrhage.

Management of acute hemorrhage primarily consists of FVII replacement therapy with plasma-derived products (FFP, prothrombin complex concentrates, and FVII concentrates). If available, FVII concentrates are preferred over untreated plasma. The administration of FFP is least effective because of its low factor VII, leading at the transfusion of large volumes with an inherent risk of pathogen transmission. Prothrombin complex concentrates (PPSB) is less used because of the risk of tromboembolic complications, particularly with repeated administration. rFVIIa is not derived from human blood, it was originally developed to treat patients with hemophilia with factor inhibitors and has been authorized for inherited FVII deficiency treatment. It is characterized by excellent effectiveness and very good tolerance. Levels of more than 10% are usually considered hemostatic, although higher levels may be advisable in the event of a severe bleeding episode. Repeat treatment may be necessary in all except minor bleeding episodes because FVII has a short half-life. The dose depends on the indication. The recommended dose is 15 to 30 µg/kg every 4-6 hours until the bleeding is controlled. When surgery is planned, prophylactic injections are given, 20 to 30 µg/kg of FVII administered preoperatively and 5 to 10 µg/kg every 4 to 6 hours postoperatively for 5 to 10 days. In case of serious and repeated bleeding, a long-term treatment with 2 injections per week is proposed. This has been proposed to our patient because of the recurrent and severe hemorrhagic syndrome but the parents didn’t have the financial means to ensure treatment.

CONCLUSION

Congenital FVII deficiency is a rare bleeding disorder characterized by a wide genetic heterogeneity and a poor relationship between FVII activity levels and severity of the hemorrhagic diathesis. It should be suspected in a healthy bleeding child presenting in infancy when platelets and APTT are normal with a prolonged PT. In its severe form, it may involve the functional and vital prognosis which remains bound to the risk of occurrence of serious bleeding especially cerebral hemorrhage.

REFERENCES


