The Turkish Journal of Pediatrics 1996; 38: 257-260

FATAL INTRACRANIAL HEMORRHAGE IN A NEWBORN WITH FACTOR VII DEFICIENCY*

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SUMMARY: Üçsel R, Savaşan S, Çoban A, Metin F, Can G. (Department of Pediatrics, İstanbul University Faculty of Medicine, Çapa-İstanbul, Turkey). Fatal intracranial hemorrhage in a newborn with factor VII deficiency. Turk J Pediatr 1996; 38: 257-260.

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 seven-day-old, male, full-term newborn who was admitted with the diagnosis of sepsis. Hematological tests revealed prolonged prothrombin time and a factor VII level of five percent. After antibiotic therapy and fresh frozen plasma replacement his clinical status improved but the prothrombin time continued to be prolonged. On the 14th day, just before the end of antibiotic therapy, the infant died of sudden intracerebral hemorrhage. In this article, the clinical features and management of factor VII deficiency are discussed. *Key words: factor VII deficiency, newborn, intracerebral hemorrhage.*

Factor VII (F VII) is a vitamin K-dependent glycoprotein, which is essential for coagulation activation by the extrinsic pathway. Its deficiency is expressed in different ways and leads to various clinical pictures[1-3]. F VII deficiency, along with hemophilia, vitamin K deficiency, disseminated intravascular coagulation and protein C deficiency, is one of the rare causes for intracranial hemorrhage during the newborn period[4-6]. Here we report a newborn with F VII deficiency who developed fatal intracranial hemorrhage after therapy for sepsis.

Case Report

A seven-day-old baby boy was brought to the neonatology unit with the complaints of jaundice, bloody stool and bloody vomiting. He was born vaginally to a 24-year-old mother (gravida 1, para 1) at 38 weeks of gestation. The parents were wirst cousins. His birth weight was 3100 g (50^{th} - 90^{th} percentile); Apgar scores were 8 and 10 at 1 and 5 minutes, respectively. The jaundice started on day three of life, but the baby was brought to the hospital after bloody stool and vomiting began. The physical examination revealed hypotonia and jaundice. Laboratory results were as follows: hematocrit 27 percent, white bood cells 8,200/mm^3 (72% neutrophils, 14% band forms, 14% lymphocytes), and

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erythrocyte morphology was normal. Reticulocyte count was four percent; direct Coombs test was negative. There was no blood group incompatibility between the mother and baby. Total bilirubin was measured as 10.5 mg/dl. Hematological test results showed a platelet count of 313,000/mm^3, prothrombin time (PT) 34 sec. (control 13 sec.), partial thromboplastin time (PTT) 31 sec. (control 30-40 sec.), and bleeding time as one minute 25 sec.

The blood culture obtained on admission grew coagulase-negative staphylococci, and the infant was given ampicillin + cephotaxime for a total of 14 days. Cerebrospinal fluid examination was normal. Head ultrasonography was unremarkable.

Fresh frozen plasma (FFP), packed red blood cells and vitamin K were administered to correct the anemia and prolonged PT. Although PTT was within normal limits (32-38.6 sec.), PT remained prolonged (56.5-40.5 sec.) despite the above treatment. Activated PTT was one minute 35, and the fibrinogen level was 320 mg/dl. Factor XIII was positive, and the F VII level was five percent. Based on these findings, a factor VII deficiency was considered[7], and FFP replacement was suggested during symptomatic periods.

Because of the mother's history of mucosal bleeding, consanguinity, and autosomal recessive inheritance of F VII deficiency, the parents' F VII levels were also obtained. The father's and mother's F VII levels were 50 percent and 40 percent, espectively. These results indicated the parents as carriers.

After the antibiotic therapy, FFP and packed red blood cell administration, the clinical status of the infant became stable. However, on the 14^{th} day of the antibiotic therapy (day 21 of life), the patient suddenly deteriorated. Cerebral ultrasonography (Fig. 1) and computerized tomography showed a large intraparenchymal hemorrhage on the right side. The baby was immediately placed on mechanical ventilation, but he did not respond to the therapy and died the next day.

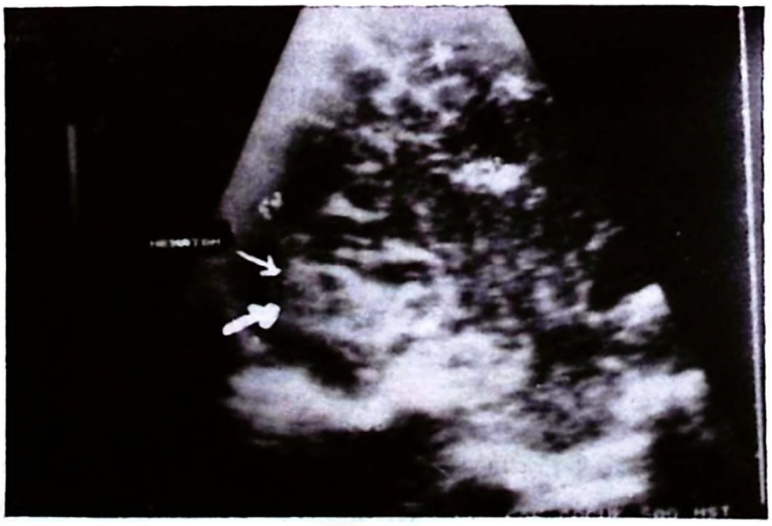

Fig. 1: Cerebral ultrasonography showing intraparenchymal hemorrhage on the right side. There is also a shift towards the left side.

Discussion

F VII deficiency is a rare, autosomal-recessive, hereditary disorder of which different immunological and genetic types have been described[1]. This illness is characterized by normal PTT and prolonged PT. Definitive diagnosis requires a specific F VII assay. In congenital F VII deficiency, bleeding can occur during any period of life. Most commonly, menorrhagia and metrorrhagia occurs in females and hemarthrosis in both sexes[1, 8, 9]. Central nervous system hemorrhages are not uncommon, and may develop during the newborn period or early childhood[5, 6]. The bleeding problem occurs generally in homozygotes. Insignificant non-life-threatening hemorrhages have also been reported in heterozygotes with a wide range of F VII levels[10].

Our patient's mother occasionally, experienced mucosal bleeding, and her F VII level was found to be 40 percent. The father, whose F VII level was 50 percent, was also a possible carrier, but he did not have a bleeding problem.

Currently, in classical hemophilia (F VIII deficiency), prophylactic replacement therapy is being discussed[11]. However, the same prophylactic replacement strategy has not been considered for F VII deficiency. The explanation for this may be that this coagulation disorder is very rare and symptoms are very variable. According to reports in the literature of newborns with hemorrhage problems, replacement therapy should be started during the peripartum period in infants born to a homozygotic mother or to heterozygotic parents[12]. Administration of FFP or F VII concentrates to pregnant women with F VII deficiency should also be considered[13, 14]. In our patient, after the diagnosis of F VII deficiency, FFP replacement was continued until the symptoms of hemorrhage subsided. He also responded well to antibiotic therapy. However, afterwards, during a clinically stable period, intracerebral hemorrhage suddenly developed. We can not relate the hemorrhage in our patient only to the F VII status. The last FFP administration was five days earlier, and the half-life of F VII is five hours. Thus, the F VII level should already have decreased to its previous level, which would have led to hemorrhage earlier. Actually, in patients with a bleeding tendency, the quality of the protein plays a significant role in addition to the F VII level[2]. Sometimes in people with low F VII levels, although coagulation test results may be in the normal range, arterial thrombosis may develop due to the high guality of protein[15]. Since the clinical picture of F VII deficiency is very heterogenous, in newborns with abnormal coagulation tests and/or in the presence of predisposing factors to hemorrhage, e.g. sepsis, replacement therapy should be administered until the risky period is over.

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