

CONGENITAL AFIBRINOGENEMIA

A.C. Biswas, MD, FRCP, FRCPC; M.A.M. Molla, MRCP, MRCPCH;
Khaled Al Moslem, Fachartz; Riyadh Al Khalif, Fachartz

Congenital afibrinogenemia (CAF) is a very rare inherited phase III coagulation disorder, characterized by virtual absence of plasma fibrinogen (factor I). There are about 250 cases¹ in the world literature, mostly with consanguineous parents. Despite having totally incoagulable blood,² these patients normally do not have severe spontaneous bleeding, but the case identification is important to prevent more severe bleeding following injuries or surgery. We report a case of CAF with continuous oozing of blood following circumcision.

Case Report

A five-month-old male Syrian infant was admitted to our hospital with a history of continuous oozing of blood from a circumcision wound he had undergone five days earlier in a private clinic. The infant had not had any investigations to check his coagulation profile before the operation. He was born at 34 weeks of gestation by emergency cesarian section due to antepartum hemorrhage with placenta previa. His birth weight was 2700 g. During the neonatal period, he had moderate to severe hyaline membrane disease and required mechanical ventilation for four days. On the ninth day of life, he started to have fresh bleeding from his umbilical stump and increased bleeding from the puncture sites. He had a full septic screening and coagulation profile and was treated with antibiotics, vitamin K and fresh frozen plasma. His septic screening was negative. Tests for disseminated intravascular coagulation were also negative. Coagulation profile showed prothrombin time (PT) 22.9 seconds (control, 13.5 seconds), activated partial thromboplastin time (APTT) 41.9 seconds (control, 25.9 seconds) and fibrinogen level of 99 mg/dL (control 295 mg/dL). His bleeding stopped with the above treatment and he was discharged home with a diagnosis of congenital hypofibrinogenemia and appropriate advice, which the parents ignored. The parents were first cousins. Their first child, who was female, died at the age of 2 years and 3 months, due to recurrent bruising and

On examination of the studied baby, he was well-looking and well-nourished, with a weight of 6 kg. He was not pale. There was oozing of fresh blood and plasma from his circumcision wound. There were no purpuric spots or bruises anywhere on the body. There was no lymphadenopathy or hepatosplenomegaly, and systemic examinations were normal. On investigations, the baby's hemoglobin was 10.1 g/dL, and white cell count was $13.97 \times 10^9/L$ with normal differential counts. Platelet count was $336 \times 10^9/L$, bleeding time (BT) 10 minutes, clotting time (CT) 18 minutes, and prothrombin time was 60.6 seconds (control 11.8 seconds, normal 23-45 seconds). APTT was 293.20 seconds (control 26.8 seconds, normal 23-45 seconds), fibrinogen was 0 mg/dL (normal 160-350 mg/dL). The patient was treated with a transfusion of fresh frozen plasma and the oozing of the blood stopped immediately. Post-transfusions repeat PT and APTT were 15.8 seconds and 25.6 seconds, respectively. He was discharged home with a diagnosis of congenital afibrinogenemia. The parents were provided with a diagnosis card and clear instructions for the measures to be taken in the future event of trauma, injuries and operations. They were also advised to report to our outpatient clinic with all their children for a family study, which they did not do.

Discussion

Congenital afibrinogenemia is transmitted by an autosomal recessive gene located on chromosome 4 (q26-q28), with normal fibrinogen or hypofibrinogenemia in the heterozygote and afibrinogenemia in the homozygote.³ This variable phenotype expression of unprotected heterozygotes with no more than 2.5 g/L fibrinogen and protected heterozygotes with normal fibrinogen levels is not clear.⁴ CAF patients (homozygous) may present with symptoms of bleeding in the newborn period, with hematomas from the trauma of delivery, hematemesis, melena and bleeding from the umbilicus.³ Although spontaneous bleeding in older children is rare and mild, it may sometimes occur in the skin, muscles and mucous membrane, with epistaxis and gastrointestinal bleeding into joints or the central nervous

system. More severe bleeding occurs following trauma, injuries and surgery.

Our patient had spontaneous bleeding in the neonatal period and prolonged bleeding following surgery at the age of five months. As it is a phase III disorder with the final

From the Department of Pediatrics, Al-Yamamah Hospital, Riyadh, Saudi Arabia.

Address reprint requests and correspondence to Dr. Biswas: P.O. Box 1878, Riyadh 11342, Saudi Arabia. E-mail: saheb121@yahoo.com.

Accepted for publication 27 June 2000. Received 1 August 1999.

bleeding problems. She was investigated but the parents did not know the diagnosis. Four other children (3 boys and 1 girl) were clinically normal.

substrate for formation of the clot missing, results of all screening tests such as clotting time, PT, PTT and thrombin time are abnormal.³ Platelet functions such as bleeding time, adhesion and aggregation are also abnormal, presumably because of absence of fibrinogen, and can be corrected by addition of fibrinogen to the test.⁵ As expected, our patient had prolonged BT, CT, PT and APTT.

Acute hemorrhagic episodes can be treated with either fresh frozen plasma or cryoprecipitate or fibrinogen concentrate (Cohn fraction I). Each cryoprecipitate bag contains 225 to 250 mg of fibrinogen, and therapy with 100 mg/kg of fibrinogen provides a hemostatic plasma level.² The half-life of fibrinogen is 3–5 days and frequent infusions are not necessary. Our patient was treated with a single infusion of fresh frozen plasma 20 mL/kg, with which the hemostasis was achieved with the return of PT and APTT to normal.

Although prophylactic treatment with regular infusions of cryoprecipitate has been advocated by some,⁶ it is not recommended by others¹ for several reasons. First, the spontaneous bleeding is very rare and mild. Second, there is a potential danger of acquiring hepatitis and AIDS with regular blood product infusion. Antibodies have been reported to form against fibrinogen³ and thromboembolic complications, particularly pulmonary emboli, have been reported.^{7,8} We are of the opinion that regular prophylactic treatment should not be given. Such patients can have fresh frozen plasma in the event of any spontaneous bleeding and during any surgical operation.

A family study is essential to identify the unprotected heterozygote for genetic counseling and asymptomatic

homozygote to have prompt therapy as and when necessary. We could not perform this study due to lack of cooperation from the father. This case shows the importance of checking the coagulation profile before any surgical operation.

Acknowledgements

We are grateful to Dr. Mohammad Saleh Al Ghreimil, the hospital director, Al Yamamah Hospital, for his kind permission to report this case. We are also thankful to Mrs. Lerma A. Manalo, medical secretary, for her secretarial help.

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