Congenital Hypofibrinogenemia: A Newborn Infant with Cord Bleeding

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ABSTRACT

The genetic disorders causing decreased fibrinogen synthesis may be caused by heterozygous (hypofibrinogenemia) or homozygous (afibrinogenemia) deficiency. The consequences of the disorders are gastrointestinal bleeding, cord bleeding, eccymoses, subcutaneous hematomas and hemarthroses especially due to traumatic delivery in the neonatal period. Laboratory evaluation of the patient with hypofibrinogenemia reveals prolongation of thrombin time, partial thromboplastin time, prothrombin time and decreased fibrinogen level. We report a 21 days old, congenital hypofibrinogenemia case with cord bleeding.

Key Words: Congenital hypofibrinogenemia, Cord bleeding, Newborn.

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INTRODUCTION

Coagulation system of newborn infant differs from older children and adults in terms of many characteristics and it also changes with gestational age[1-4]. In term babies, acquired bleeding disorders are more frequent than genetic congenital disorders[5]. Congenital hypofibrinogenemia is a very rare heterozygous deficiency causing decreased fibrinogen synthesis. We describe a newborn infant with cord bleeding, a positive family history, clinical and laboratory features of hypofibrinogenemia.

CASE REPORT

A 21 days old newborn infant was admitted to our clinic for evaluation of cord bleeding. He was healty for the first three days and developed massive cord bleeding on the fourth day. After whole blood transfusion, his cord bleeding stopped. Four days later, bleeding started again and fresh plasma and 1 mg vitamin K were given but bleeding kept on. The patient was the product of a consanguineous marriage. He was born to a healty mother, gravida 6, para 3. A female term baby was born dead, reason was not investigated and a male baby from gravida 4 died because of cord bleeding when he was three days old. Three sis-

ters and maternal uncles were healty.

On admission, he had fever 37.4°C, blood pressure of 45/28 mm Hg and a regular heart rate of 160 per minute. His weight was 3750 g (75-90 percentile), height 55 cm (>90 percentile). Physical examination revealed a pale skin, cord bleeding and palpable liver 2 cm below the ribs.

Laboratory investigation showed hemoglobin of 8.3 g/dL, leukocyte count 14500/ mm^3, platelets count 561000/mm^3. A peripheral blood smear was normal. Bleeding time was 2 minutes (by ivy method), clotting time was longer than 15 minutes, protrombin time (PT) was 44 seconds, partial tromboplastin time (PTT) was 43 seconds and plasma fibrinogen was 25 mg/dL. Blood urea nitrogen, electrolytes, hepatic enzymes, bilirubin levels, CRP were within the normal limits. Any sign of infection was not observed. Cranial ultrasonography was normal. Fresh plasma and fibrinogen with cryoprecipitate were transfused and bleeding stopped. On the day after, PT was 15 seconds, PTT was 30 seconds and plasma fibrinogen level was 118 mg/dL. After one week, while PT was 21 seconds and PTT was 36 seconds; plasma fibrinogen level was 25 mg/dL. Levels of the parents' plasma fibrinogen were normal. This findings with family history suggested congenital hypofibrinogenemia. He was discharged on the tenth day of hospitalisation and the parents were warned that it is a genetic disorder and there is recurrence risk in their new babies. One month later, plasma fibrinogen level was again 25 mg/dL. He is now three months old and observed as an outpatient.

DISCUSSION

Evaluating a newborn baby with bleeding is different from older children and must include a careful history of family bleeding, perinatal period, maternal illnesses (especially for infection), neonatal and maternal drug administration and vitamin K administration at birth.

Observations on physical examination such as localized or diffuse bleeding, healty or sick appearance of the baby is very important for the classification of hemorrhagic diseases. Infants appear very sick if there is disseminated intravascular coagulation (DIC) and bleeding is diffuse from several sites[5,6]. Infants with isolated platelet disorders, vitamin K deficiency or inherited coagulation defects generally seem healty. Severe congenital factor commonly present with bleeding from cord, from mucous membranes, peripheral blood sampling sites, after circumcision and into the subcutaneous tissue and the scalp[5,6]. Cord was the primary bleeding site in our patient and as there is a history of death of a sibling due to cord bleeding and a consanguineous marriage of the parents we think it is a congenital coagulation defect. As the baby appeared well, we did not think DIC or infection.

Laboratory evaluation revealed decreased plasma fibrinogen level. Although the plasma fibrinogen level increased after replacement with fresh plasma and cryoprecipitate, three days and one month later it was again low and we thought it to be a congenital fibrinogen deficiency.

Fibrinogen deficiency is a rare inherited coagulation defect. In medline research including 62 publications, seven of 226 babies with congenital coagulation defect were found to have fibrinogen deficiency. Five of them had cord bleeding, one with hematoma and two were following circumcision[5].

Fibrinogen deficiency may be as hypofibrinogenemia or afibrinogenemia. Plasma fibrinogen normal level is 150-400 mg/dL. In afibrinogenemia, trace amount of fibrinogen, less than 5 mg/dL, can be detected[7]. The fibrinogen level was 15 mg/dL in this case and it is thought to be hypofibrinogenemia.

This disorder is transmitted by an autosomal inheritance and gene is located on chromosome 4 (q26-q28)[7]. Familial inheritance is also reported[8]. As there is a sibling died due to cord bleeding and consanguineous marriage of healty parents, disorder is caused by an autosomal inheritance in this case.

Bleeding can be treated with fibrinogen consantrate, cryoprecipitate and fresh or fresh frozen plasma replacement[5,9]. Half life of fibrinogen is aproximately 3-5 days and minimum haemostatic

level is 50-100 mg/dL; for this reason the dosage should be given to reach this level[5].

In conlusion, we report a rare genetic disorder congenital hypofibrinogenemia and should be remembered in newborn infants with cord bleeding.

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