Umbilical bleeding

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Umbilical bleeding: a presenting feature for congenital afibrinogenemia

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Congenital afibrinogenemia is a very rare inherited coagulation disorder characterized by absence of plasma fibrinogen (factor I). There are only about 250 cases reported in the world literature. We describe a case of congenital afibrinogenemia which presented as an umbilical cord bleeding. *Blood Coagul Fibrinolysis* 26:834–835 Copyright © 2015 Wolters Kluwer Health, Inc. All rights reserved.

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Introduction

Congenital afibrinogenemia is a rare blood disease that occurs due to low levels of fibrinogen [1], and is defined as plasma levels below 10 mg/dl. This is presented in the form of bleeding from different parts of the body such as umbilical cord or gastrointestinal system. Spontaneous bleeding is rare in this condition. Fresh frozen plasma (FFP), cryoprecipitate, and fibrinogen concentrate could be used in treatment of these patients. Prophylaxis is not recommended in this patient.

Case presentation

A 9-day-old baby, born out of consanguineous marriage by cesarean section, with birth weight of 2700 g and gestational age of 39 weeks, was admitted to our hospital with history of bleeding from the umbilical cord of 2 days' duration. No significant history of trauma, fever, jaundice, or previous blood transfusions was recorded. The mother had a history of abortion. There was no certain disease during and before pregnancy, and she had no history of medication use. No family history of similar illness was present. On examination, the child was well nourished. There were no petechiae, purpura, and ecchymosis. Systemic examination was essentially normal with no organomegaly. Investigations revealed hemoglobin of 12.1 g/dl, and white cell count of 13 000/μl, with normal differential counts. Platelet count was 513 000/μl. Prothrombin time (PT) (>120 s, control 12 s), PT/international normalized ratio (INR) (>10 s, control 1 s), activated partial thromboplastin time (PTT) (>180 s, control 33 s), and thrombin time (>240 s, control 17 s) were all abnormally prolonged. Liver function tests (LFTs) and renal function tests were normal. Peripheral blood film did not reveal any evidence of microangiopathy, hemolysis, infection, or thrombocytopenia. Factor X level was 73 mg/dl (normal 70–120 mg/dl) and level of factor XIII was abnormal. Absolute fibrinogen level was below 10 mg/dl (normal 200–400 mg/dl). The patient received vitamin K and FFP and cryoprecipitate without blood transfusion. Finally, after definitive diagnosis, fibrinogen concentrate was injected. The results of the tests that were conducted immediately following the injection of fibrinogen concentrate included: PT (12 s, control 12 s), PT/INR (1 s, control 1 s), and PTT (49 s, control 33 s). The patient was discharged with instructions of avoiding aspirin-containing compounds and for the measures to be taken in the future in the event of trauma, injuries, or operations. The baby's mother was asked for regular visits for fibrinogen injection.

Discussion

Congenital afibrinogenemia is a rare coagulation disorder that is inherited by an autosomal recessive gene located on chromosome 4 (q26–q28) [2]. Our patient's siblings and parents had apparently normal hemostatic mechanism. This disease is characterized by the complete absence or extremely reduced levels of fibrinogen in patients' plasma. Partial deficiency of fibrinogen (hypofibrinogenemia) is a milder disorder. Afibrinogenemia occurs in the homozygous state, whereas hypofibrinogenemia occurs in the heterozygous state [2].

Clinical manifestations range from minimal bleeding to serious hemorrhage [3]. Bleeding may occur in the newborn period manifesting as hematomas from delivery, and may also present with hematemesis, melena, or bleeding from the umbilicus. Other manifestations include bleeding in soft tissues and mucosa. Hemarthrosis is uncommon (20%) [4]. Awasthy *et al.* [5] reported a 6-year-old female child with history of bluish spots around the eyes and thighs of 1-month duration. In another study, Gopakumar *et al.* [2] reported a congenital afibrinogenemia case with presentation of intracranial bleeding. Despite having nonclotting blood, these patients normally did not have severe spontaneous bleeding that could be attributed to the von Willebrand factor (vWf), which binds to

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the glycoprotein complex on platelets and provides a mechanism for platelet aggregation, but the case identification is important to prevent more severe bleeding following injuries or surgery [6]. Although our case had spontaneous bleeding from the umbilicus, bleeding from the umbilical cord can be caused by a deficiency of factor XIII [7] as shown by Rashida *et al.* [8]. Plasma level of factor XIII in our patient was normal.

Coagulation tests which depend on clot formation, such as clotting time, PT, PTT, and thrombin time, may be prolonged, and abnormalities of platelet function such as bleeding time, adhesion, and aggregation may usually exist.

Afibrinogenemic patients have undetectable levels of fibrinogen (<10 mg/dl; normal 200–400 mg/dl). In the absence of consumptive coagulopathy, an unmeasurable fibrinogen level is diagnostic of the condition [9]. Bleeding in fibrinogen deficiency is most significant when the plasma level is less than 50 mg/dl [10]. The value in our patient was below 10 mg/dl, and fresh bleeding was noticed.

Bleeding episodes can be effectively treated with FFP or cryoprecipitate. Theories regarding aim levels for treatment of bleeding, range from 50 mg/dl [11], to 100 mg/dl fibrinogen [12], and therapy with 100 mg/kg fibrinogen prepares a hemostatic level. In our patient, bleeding stopped when cryoprecipitate was used. We can also use fibrinogen concentrate, and because the half-life of fibrinogen is 3–5 days, frequent infusions are usually not necessary [5]. We also used fibrinogen concentrate, and the results of the tests conducted immediately following the injection of fibrinogen concentrate was normal.

Prophylactic treatment with regular infusions of cryoprecipitate has been advocated by some [13], but the majority do not recommend it because they believe that spontaneous bleeding is very rare and mild, and moreover, there is a danger of acquiring infections with regular blood product infusion. Antibodies may also form against fibrinogen with consequent thromboembolic complications, especially pulmonary embolism; so a prophylactic infusion of cryoprecipitate is not done in recurrent hemorrhage, but because of our experience in lethal bleeding due to lack of fibrinogen prophylaxis, in recent patients, we did prophylaxis with fibrinogen (200 mg + 50 ml distilled water infused within 20 min).

Conclusion

Afibrinogenemia should be considered as a differential diagnosis in patients with bleeding from any part of the body, which in congenital type could show itself as bleeding from the umbilicus. Although less spontaneous bleeding has been reported, its occurrence is not impossible. In afibrinogenemia, coagulation tests are abnormal and a definitive diagnosis can be achieved with levels of fibrinogen below 10 mg/dl. FFP, cryoprecipitate, and fibrinogen concentrate can be used for treatment. Finally, we recommend prophylaxis with fibrinogen to prevent possible serious bleeding.

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Conflicts of interest

There are no conflicts of interest.

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