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Fibrinogen Deficiency: A Case Report

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ABSTRACT

Congenital fibrinogen deficiency is a rare autosomal recessive bleeding disorder characterized by absent or reduced levels of functional fibrinogen. It presents variably in childhood, often with umbilical stump bleeding, mucocutaneous hemorrhages, or life-threatening bleeding episodes. Early diagnosis and treatment are essential to prevent complications. We report a case of a 5-year-old boy with a history of recurrent bleeding since infancy, including umbilical stump hemorrhage and easy bruising. He presented with spontaneous massive anterior epistaxis that was difficult to control. Laboratory tests revealed severe anemia, prolonged prothrombin time (PT >100 sec), activated partial thromboplastin time (APTT >180 sec), and critically low fibrinogen levels (48 mg/dL).He was diagnosed with congenital hypofibrinogenemia and managed with cryoprecipitate, packed red blood cells, and tranexamic acid. His bleeding resolved and coagulation parameters normalized. Two months later, he was readmitted with gum bleeding, which was successfully treated with repeat cryoprecipitate transfusion. This case highlights the importance of recognizing congenital fibrinogen deficiency in pediatric patients with unexplained or recurrent bleeding. Prompt coagulation testing, including fibrinogen assay, is critical for diagnosis. Cryoprecipitate remains an effective and accessible treatment in resource-limited settings. Long-term follow-up, family education, and preventive strategies are essential to improve outcomes and prevent bleeding-related morbidity.

Keywords: Fibrinogen deficiency, epistaxis, pediatric bleeding, cryoprecipitate.

INTRODUCTION

Fibrinogen deficiency in children is a serious hematological condition that affects the body's ability to form stable blood clots, which is crucial for stopping bleeding. This condition can be inherited or acquired, with congenital forms resulting from genetic mutations that impair fibrinogen production or function and a rare autosomal recessive.

Fibrinogen is a soluble plasma protein produced by the liver, and it is essential for the final stages of blood coagulation. When a blood vessel is injured, fibrinogen is converted into fibrin by the enzyme thrombin. Fibrin then forms a mesh-like structure that stabilizes the platelet plug and prevents further bleeding. In fibrinogen deficiency, this process is disrupted, leading to an increased risk of bleeding.[1]

Children with fibrinogen deficiency may present with a range of symptoms depending on the severity of the deficiency. Symptoms often include spontaneous bleeding, excessive bleeding from minor injuries, easy bruising, frequent nosebleeds, and heavy or prolonged menstrual bleeding in older girls. In severe cases, bleeding can occur into the muscles, joints, or internal

organs, leading to complications such as hemarthrosis (bleeding into joints) or hematomas.[2]

The diagnosis of fibrinogen deficiency involves a combination of clinical assessment and specialized laboratory tests. Initial evaluations typically include a complete blood count, prothrombin time (PT), activated partial thromboplastin time (aPTT), and specific fibrinogen assays. These tests help determine the level of fibrinogen in the blood and assess its functionality. In congenital cases, genetic testing may also be performed to identify specific mutations.[3]

Treatment for fibrinogen deficiency focuses on managing bleeding episodes and preventing complications. This often involves fibrinogen replacement therapy, which can be administered through intravenous infusion of fibrinogen concentrate. Additionally, supportive measures such as antifibrinolytics, which help stabilize clots, may be used. Regular monitoring and follow-up are crucial to adjust treatment plans and address any emerging issues.[4] Early recognition and intervention are essential in managing fibrinogen deficiency. With appropriate treatment and care, children with this condition can lead relatively normal lives, though they may require ongoing medical supervision to manage their bleeding risks effectively.[5]

CASE PRESENTATION

A 5-year-1-month-old boy was admitted to the Pediatric Emergency Unit of Dr. M. Djamil General Hospital, Padang, in May 2024, with a chief complaint of nose bleeding. The bleeding began spontaneously one day prior to admission and was described as continuous. The family reported no history of trauma, and initial attempts to stop the bleeding at home and at a regional hospital were unsuccessful. The patient had previously received tranexamic acid, vitamin K, and supportive therapy at the Pasaman Barat Regional Hospital before being referred.

The patient had a notable history of recurrent bleeding episodes since the neonatal period. At 3 days old, he experienced prolonged umbilical stump bleeding that required transfusion with four units of packed red cells. At 6 months of age, he was hospitalized again due to a febrile seizure and pallor, during which he received an additional three units of PRC. His history was also significant for frequent bruising after minor trauma and prior hospitalizations for unexplained bleeding, including an episode in July 2023 involving persistent epistaxis and abnormal coagulation profiles. However, the family was unable to pursue further hematologic evaluation due to financial constraints. There was no known family history of bleeding disorders; however, the patient's mother reported a history of multiple miscarriages. There is no history of consanguineous marriage.

On physical examination, the child appeared moderately ill but was alert and interactive. Vital signs were stable: blood pressure 100/60 mmHg, heart rate 108 bpm, respiratory rate 26/min, temperature 36.7°C, and oxygen saturation 100% on room air. Anthropometric measurements indicated undernutrition: body weight 13 kg (weight-for-age 72%), height 100 cm (height-for-age 91%), and weight-for-height 81%. Clinical findings included pale conjunctivae, anterior nasal tampon in situ without active bleeding, and no hepatosplenomegaly or lymphadenopathy. Chest and cardiac auscultation were unremarkable. Capillary refill time was less than 3 seconds with warm extremities.

Initial laboratory investigations revealed severe anemia (hemoglobin 5.3 g/dL, hematocrit 16%) with normal leukocyte and platelet counts. Coagulation studies showed markedly prolonged activated partial thromboplastin time (APTT >180 seconds) and prothrombin time (PT >100 seconds). Reticulocyte count was elevated at 2.36%, indicating a bone marrow response to blood loss.

The working diagnosis was massive anterior epistaxis, severe anemia secondary to bleeding, suspected congenital hypofibrinogenemia, hyponatremia likely due to decreased intake, undernutrition. Initial management included packed red cell (PRC) transfusions at 7 and 10 mL/kg body weight, cryoprecipitate transfusion (2 units), and intravenous tranexamic acid. Consultations were made to the ENT department for anterior nasal tampon placement. The patient was monitored in the High Care Unit (HCU).

On follow-up, bleeding had ceased and coagulation parameters improved significantly: PT and APTT normalized to 12.7 seconds and 24 seconds, respectively. The patient's clinical condition stabilized, and he was discharged after four days with instructions to return for outpatient hematology follow-up.

In May, 2024, outpatient fibrinogen testing confirmed hypofibrinogenemia at 48 mg/dL (reference range: 210–456 mg/dL). A diagnosis of congenital fibrinogen deficiency was established, and the family was counseled regarding bleeding precautions, emergency care access, and the importance of prompt cryoprecipitate transfusion during bleeding episodes.

Two months later, on August 20th, 2024, the patient was readmitted with active gum bleeding and swelling of the left cheek. The bleeding had started five hours prior to admission. Physical examination revealed active gingival bleeding. Laboratory investigations again showed prolonged PT and APTT, with hemoglobin at 9.2 g/dL and hematocrit at 27%. He was treated with three units of cryoprecipitate, intravenous tranexamic acid. Clinical improvement was observed within days, and the bleeding resolved completely. The family was educated the importance of early medical intervention during any future hemorrhagic episodes.

DISCUSSION

Congenital fibrinogen deficiency is a rare autosomal recessive disorder that disrupts the final and critical phase of the coagulation cascade, resulting in impaired fibrin clot formation. Fibrinogen, also known as coagulation factor I, is synthesized by hepatocytes and serves as the precursor to fibrin, the structural backbone of a stable blood clot. It is also essential for platelet aggregation and wound healing.[6] The disorder manifests in various clinical forms, namely afibrinogenemia, hypofibrinogenemia, dysfibrinogenemia, and hypodysfibrinogenemia, each with varying degrees of quantitative or qualitative abnormalities in fibrinogen levels or function.[7]

In this case, the patient demonstrated classic clinical features of congenital fibrinogen deficiency, specifically hypofibrinogenemia, which is characterized by low but detectable levels of functional fibrinogen. The early onset of symptoms—such as umbilical cord bleeding at day 3 of life—should raise suspicion for a congenital coagulopathy, particularly when coupled with a history of frequent bruising and mucosal bleeding during early childhood. The presence of massive anterior epistaxis in this patient reflects the vulnerability of mucosal surfaces to bleeding in fibrinogen-deficient states.

The diagnostic approach to suspected congenital bleeding disorders involves a combination of clinical suspicion, targeted laboratory investigations, and the gold standard for the diagnosis of afibrinogenemia and hypofibrinogenemia is genetic testing DNA Sanger sequencing of the coding portions of FGA/FGB/FGG.[8] In this patient, initial findings included a severely decreased hemoglobin level (5.3 g/dL), indicating significant blood loss. Importantly, both prothrombin time (PT) and activated partial thromboplastin time (APTT) were markedly prolonged (>100 seconds and >180 seconds, respectively), a pattern that suggests a defect in the final common pathway of coagulation.[8] The platelet count was within normal limits, thereby excluding thrombocytopenia as a primary cause of bleeding.[2] In this patient,

we did not perform DNA Sanger sequencing of the coding regions of the FGA, FGB, and FGG genes due to limitations in the diagnostic facilities available at our center.

Fibrinogen quantification subsequently confirmed the diagnosis, with a fibrinogen level of 48 mg/dL—far below the normal range (210–456 mg/dL). Levels below 100 mg/dL, particularly in the context of bleeding, are consistent with hypofibrinogenemia. Further subtyping of the condition through functional and antigenic assays, and ideally molecular genetic analysis of FGA, FGB, and FGG genes, would allow differentiation between hypofibrinogenemia and dysfibrinogenemia. However, such testing was unavailable in this setting.[6]

The differential diagnosis includes other inherited bleeding disorders such as von Willebrand disease (VWD), which can present with mucocutaneous bleeding but typically shows a different pattern of coagulation abnormalities and often includes a family history.[9] Disseminated intravascular coagulation (DIC) could mimic this presentation in acute illness but was unlikely given the patient's stable clinical status and lack of infectious or traumatic triggers. liver disease may elevate the thrombin time, PT and PTT, However, this patient did not exhibit any signs or symptoms of liver disease [10]

The management of this patient was timely and appropriate. Acute bleeding was addressed through transfusion of cryoprecipitate, which is rich in fibrinogen, as well as fresh packed red blood cells (PRC) to correct anemia. Tranexamic acid, an antifibrinolytic agent, was also administered to stabilize formed clots by inhibiting the breakdown of fibrin.[11,12] After therapy, coagulation parameters improved significantly, with normalization of PT and APTT and cessation of bleeding, demonstrating the efficacy of fibrinogen replacement.

Cryoprecipitate remains a cornerstone therapy in resource-limited settings. Each unit contains approximately 250 mg of fibrinogen, and dosing is generally 1 unit per 5–10 kg body weight. Although it carries risks of volume overload and potential viral transmission, it is effective and readily available. In contrast, fibrinogen concentrate is the preferred option in developed countries due to its purity, consistent dosing, rapid administration, and lower immunogenicity. However, it is often expensive and inaccessible in many developing regions.[13]

Notably, the patient had a second bleeding episode (gum bleeding and facial swelling) two months later, highlighting the chronic and relapsing nature of the disorder. Once again, cryoprecipitate was used successfully. This underscores the importance of both on-demand treatment during bleeding episodes and the potential consideration of prophylactic fibrinogen replacement in patients with frequent or severe bleeding. According to the 2019 World Federation Haemophilia Annual Global Survey, which assessed information from 115 countries, fibrinogen deficiencies represent 0.91% of cases of the total number reported 324,648 people, with bleeding disorders being more prevalent in men when compared with women. To date, there have been no reported cases of pediatric patients with fibrinogen deficiency in Indonesia.

Long-term management of congenital fibrinogen deficiency requires a proactive, multidisciplinary approach aimed at preventing recurrent bleeding episodes and minimizing long-term complications. Regular follow-up with a pediatric hematologist is essential to monitor fibrinogen levels, assess bleeding frequency, and guide the need for prophylactic treatment. While on-demand cryoprecipitate transfusions are effective during acute episodes, patients with frequent or severe bleeding may benefit from prophylactic fibrinogen replacement therapy to maintain hemostatic levels and prevent spontaneous hemorrhage.[12] This approach, although potentially limited by cost and availability in resource-constrained settings, has been

shown to improve quality of life and reduce emergency hospital visits.

CONCLUSION

Fibrinogen deficiency, though rare, should be suspected in children with unexplained or recurrent bleeding and prolonged coagulation times. Timely recognition and administration of fibrinogen-containing products such as cryoprecipitate are critical in preventing life-threatening complications.

Declaration by Authors

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