CASE REPORT

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A 39 Year-old Female Patient with Hypofibrinogenemia Diagnosed Incidentally in the Preoperative Period

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ABSTRACT Hereditary fibrinogen diseases are rare. Congenital afibrinogenemia is characterized by the absence of fibrinogen.Circulating fibrinogen levels below 150 mg/dl are called hypofibrinogenemia. Although hypofibrinogenemia is estimated to be more common than afibrinogenemia, most of the affected individuals are asymptomatic. Congenital fibrinogen disorders result from several mutations in FGA, FGB, or FGG. Their epidemiology is not well known. We aimed to present a case of a 39 year-old female patient diagnosed with hypofibrinogenemia in the preoperative period. In the patient, the homozygous frameshift mutation in the FGG was detected. Congenital fibrinogen disorders are rare coagulation diseases. The molecular epidemiology of congenital fibrinogen disorders is complex and the identification of new mutations will help shed light on this complex molecular structure. Therefore, we recommend a genetic analysis for at-risk patients.

Keywords: Afibrinogenemia; fibrinogen; blood coagulation disorders; inherited

Hereditary fibrinogen diseases are rare. Prevalence of afibrinogenemia is 1: 1,000,000 Hypofibrinogenemia is estimated to be more common than afibrinogenemia, but as it is asymptomatic, it is difficult to determine the true prevalence since there is no hospital admission.[1] Fibrinogen disorders can be divided into numerical (quantitative) and functional (qualitative). Quantitative fibrinogen disorders are afibrinogenemia and hypofibrinogenemia. Afibrinogenemia is inherited autosomal recessively, there is no fibrinogen production and obstetric complications may progress with bleeding and rarely with thrombosis. Circulating fibrinogen levels below 150 mg/dl are called hypofibrinogenemia. Hypofibrinogenemia may be genetic or acquired. Qualitative fibrinogen disorders can be classified as dysfibrinogenemia, hypodisfibrinogenemia and cryodisfibrinogenemia.[2]

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A 39 year-old female patient was admitted to our hematology outpatient clinic in February 2019 under the elective conditions, saying that she had an abnormal coagulation test before a surgical procedure. The patient has no complaints (hematemesis, melena, and hematochezia). Physical examination revealed no pe-

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techia, purpura, ecchymosis, hematoma. Hepatoslenomegaly and lymphadenopathy were not detected. She has no any disease or chronic drug use. It was learned that there was no bleeding disorder during the menstruation periods, she had a healthy child and there was no bleeding problem during delivery and her mother and father were first cousins. Laboratory test results were as follows: WBC: 13.170/mm^3 neutrophil: 9390/mm^3 HGB: 14.3 g/dl HTC: 42% MCV: 88.6 fl MCHC: 34 g/dl platelet: 287.000/mm^3 aPTT: >210 sec PT: >120 sec INR: 12 Fibrinogen 100 mg/dl.

There was no pathological finding in peripheral smear. Abdominal USG revealed normal liver and spleen. In pre-operative preparation, the patient was examined by cryoprecipitate replacement. INR was 1.05 APTT: 25sec, PT: 12.5 Fibrinogen 110 mg/dl. The patient was asymptomatic at the outpatient clinic. APTT: 200 sec, INR: 11.82, PT: 150 sec, Fibrinogen: 42 mg/dl (7/22/2019). There were no symptoms in favor of bleeding.

Since the patient was considered to have a quantitative deficiency of fibrinogen as a preliminary diagnosis, mutation analysis and genetic panel were sent from the patient. Homozygous mutation (FGG NM_000509 c123+1 G≥A rs1218450006) was detected in the FGG gene, which is associated with the synthesis of the gamma chain from the FGA FGB FGG genes encoding alpha beta gamma chains in the structure of the fibrinogen.[3] Informed consent was obtained from the patient.

The homozygous mutation of the FGG gene detected in the patient's genetic analysis was classified as pathogenic mutation in the classification on the Varsome pathogenicity prediction platform. There was no record in the Clinvar mutation bank; Omin phenotypic database has been reported to be responsible for the congenital afibrinogenemia with autosomal recessive inheritance.

Our patient lives abroad and continues to be followed up there.

DISCUSSION

According to the World Federation of Hemophilia 2010 report, approximately 7% of rare bleeding disorders are composed of fibrinogen deficiencies. Afibrinogenemia is mostly seen in autosomal recessive and hypofibrinogenemia is seen in autosomal dominant inheritance. It is more common in women than in men. The risk of this disease increases as a result of consanguineous marriages.[1]

The characteristics of the patient in our case were consistent with the literature. The fact that our patient's mother and father had a fourth-degree consanguineous marriage (cousin and uncle's child) confirmed that hypofibrinogenemia was more common in female gender as a result of consanguineous marriages.

Increased fibrinogen degradation such as decreased fibrinogen synthesis or disseminated intravascular coagulation in liver diseases are the causes of acquired hypofibrinogenemia.

Nowadays, the Turkish Society of Anesthesiology and Reanimation has limited the groups of patients with liver disease, coagulopathy diagnosis, and anticoagulant medication to be asked for coagulation tests in the preoperative evaluation guide for 2015.[4]

But our case is outside these groups. In the preop evaluation, coagulation tests were requested with the expert's opinion and a rare disease was diagnosed. So, a perioperative life-threatening condition was prevented.

Routine prophylaxis is not recommended if the patient is asymptomatic in hypo and afibrinogenemia. Fibrinogen concentrate, cryoprecipitate or fresh frozen plasma may be preferred in symptomatic patient or preoperative surgery. Fibrinogen concentrate is recommended in clinical situations where volume of the patient is important. In acute hemorrhages, fibrinogen level of 100 mg/dl is sufficient for hemostasis, whereas in severe cases such as intracranial hemorrhage, fibrinogen level is recommended to be 150-200 mg/dl.[5] In this case report, preop preparation with cryoprecipitate was performed. There were no complications during the operation.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

All authors contributed equally while this study preparing.

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