Case Report

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Congenital Afibrinogenemia Diagnosed During Pregnancy

Gebelikte Tanı Alan Konjenital Afibrinojenemi Olgusu

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ABSTRACT

Congenital afibrinogenemia is a rare hemorrhagic diathesis with autosomal recessive inheritance characterized by absence of fibrinogen or very low fibrinogen values below detectable levels. While spontaneous hemorrhage risk is common, the patients who have dysfibrinogenemia also carry the risk for thrombosis. In this paper, a patient who was admitted with widespread cutaneous ecchymosis and poor general condition and diagnosed with congenital afibrinogenemia at 24th gestational week is presented.

Key words: Afibrinogenemia, hemorrhage, pregnancy

ÖZET

Konjenital afibrinojenemi otozomal resesif kalıtım özelliği gösteren nadir bir kanama diyatezi olup serum fibrinojeninin olmaması veya belirlenebilecek düzeyin altında çok düşük fibrinojen düzeyleri ile karakterizedir. Spontan kanama riski yaygınken, disfibrinojenemisi olan hastalar aynı zamanda tromboz riski de taşımaktadır. Bu yazıda gebeliğin 24. haftasında cillte yaygın ekimoz ve genel durum bozukluğu ile başvuran ve konjenital afibrinojenemi tanısı alan olgu sunulmuştur.

Anahtar kelimeler: Afibrinojenemi, kanama, gebelik

INTRODUCTION

Congenital afibrinogenemia is a rare hemorrhagic diathesis which influences the amount (afibrinogenemia, hypofibrinogenemia) or the quality of the circulating fibrinogen (dysfibrinogenemia). There is a strong relationship between the fibrinogen activity levels and the severity of hemorrhage. Spontaneous intramuscular or intra-articular hemorrhage may occur in afibrinogenemia. Patients with hypofibrinogenemia are usually asymptomatic however posttraumatic hemorrhage risk is high. Patients with dysfibrinogenemia are under the risk for spontaneous hemorrhage and thrombosis.1,2 Hemorrhagic diathesis is present since childhood and the amount of hemorrhage varies from minimal hemorrhage to life-threatening hemorrhage. Herein, we presented a patient who was detected to have afibrinogenemia during pregnancy and lost her baby.

CASE

The 25-year-old female patient who was being followed up at another center was admitted to our hospital with complaints of spontaneous widespread ecchymosis and poor general condition at 24th week of her pregnancy. Her medical history was unproblematic with regard to hemorrhagic disorders, she did not have the history of trauma, she did not have the family history of hemorrhagic diathesis. On her initial examination, her general condition was poor, she had pallor, her blood pressure was 80/50 mmHg, heart rate was 110 bpm, no obstetric problems were detected on her examination done by the gynecology and obstetrics specialist. The fetus morphology was normal on ultrasonographic examination and fetal heart sounds were normal. On her laboratory examination, activated partial thromboplastin time (aPTT) and prothrombin time (PTT), D-dimer values were elevated, fibrinogen could not be detected. Hemoglobin was 9 gr/dL, hematocrit was 27%, mean corpuscular volume (MCV) 78 fL, platelet count was 500x103/µL. She was administered fresh frozen plasma (FFP), fibrinogen and antibiotic treatment with pre-diagnosis of disseminated intravascular coagulation and her coagulation parameters were seen to improve. However the patient was re-evaluated by the obstetrician due to emergence of vaginal hemorrhage followed by an abortion and rest curettage was performed. Her treatment continued in intensive care unit due to abruptly decreasing oxygen saturation and tachycardia, hypotension. Fibrinogen support continued after her general condition improved, her coagulation parameters improved except for fibrinogen. She was discharged as hemorrhage did not recur. She has been followed up asymptomatically since one year with aPTT>160 sec, PTT-INR>11 sec, fibrinogen <0.80 gr/L.

DISCUSSION

Hereditary afibrinogenemia is a rare coagulation disorder with autosomal recessive inheritance, its incidence is 1/1.000.000.2,3 Although this is a hereditary disorder, we could not get a family history in our patient; however we made the diagnosis based on the laboratory and clinical findings as her laboratory values stayed elevated in the absence of precipitating factors.

Afibrinogenemia is suggested to arise from a problem in fibrinogen synthesis or a pathology in fibrinogen molecules. Therefore plasma fibrinogen either cannot be detected or is very low.4,5,6 We could not detect fibrinogen in our patient.

Clinical findings vary from minimal hemorrhage to severe hemorrhage. Bleeding may occur from umbilical cord or mucosa during delivery.1,7 Congenital fibrinogen abnormalities include dysfibrinogenemia, hypofibrinogenemia and afibrinogenemia. While spontaneous hemorrhage risk is common, the patients with dysfibrinogenemia also have the risk for thrombosis. Fibrinogen in plasma and platelets either may not be detected or is minimal.1 Our patient had cutaneous ecchymosis and developed spontaneous vaginal hemorrhage. Fibrinogen level was too low to be detected.

The maintenance of hemostatic balance and vascular integrity throughout pregnancy has been established as critical to normal development and successful maternal and fetal outcomes. Fibrinogen plays an important role both in the process of coagulation and its ultimate reversal-fibrinolysis. Recently several studies which can shed light on the role of fibrinogen in implantation and placentation have been published. Several cases of pregnancies in afibrinogenemia patients have been reported, most resulting in early spontaneous abortions. A few cases have been recently reported in which

successful outcomes were achieved using fibrinogen replacement therapy throughout gestation.8

Treatment usually includes cryoprecipitate and fibrinogen concentrates however fibrinogen is recommended due to contamination risk in cryoprecipitate use.9,10 Fibrinogen replacement therapy was generally effective in preventing or treating bleeding in doses adequate to achieve and maintain fibrinogen activity above 50-100 mg/dL (non-surgical and obstetric use) or 100-200 mg/dL (surgical prophylaxis). Increased fibrinogen clearance was observed with massive hemorrhage, major surgery, and advanced pregnancy. Obstetric outcomes were optimized when fibrinogen replacement was initiated prior to conception.11 Hemorrhage of our patient could be controlled with fibrinogen replacement and fresh frozen plasma. Unfortunately fetal loss occurred despite adequate and prompt medical treatment. She has been followed up without medical treatment due to the absence of hemorrhage on her outpatient clinic follow ups.

In conclusion, although afibrinogenemia is not usually diagnosed and treated in primary care, we wanted to emphasize that primary care physicians should kept in mind hemorrhagic diathesis in patients who present with hemorrhage, elevated aPTT, PTT as severe cases may be life-threatening. aPTT and PTT should be examined in patients who would undergo major, even minor surgery.

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