FACTOR VII DEFICIENCY DURING PREGNANCY

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SUMMARY

Factor VII deficiency is a genetic disorder of coagulation and inherited as autosomal recessive. Although inherited disorders of coagulation are rare, Factor VII deficiency is the most common among them. Recurrent spontaneous abortions and plasental abruptions have been reported in the pregnant women with Factor VII deficiency. Due to ease of laboratory diagnosis, the clearity of the management and the treatment protocols, Factor VII deficiency should be kept in mind in patients with bleeding diathesis.

In this report, we described a pregnant patient at her 29th weeks of gestation presenting with complaint of vaginal bleeding, thereafter performance of an emergency cesarean section due to placental abruption. The management and the treatment of these patients were discussed.

Key words: *factor VII deficiency, placental abruption, pregnancy, pregnancy loss, replacement therapy*

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GEBELİKTE FAKTÖR VII EKSİKLİĞİ

ÖZET

Faktör VII eksikliği otozomal resesif geçiş gösteren bir klinik tablodur. Kalıtsal koagülasyon bozuklukları nadir görülse de, Faktör VII eksikliği bu grup içinde en sık görülenidir. Literatürde, gebelikte Faktör VII eksikliğinin erken gebelik kayıpları ve plasenta dekolmanı ile ilişkili olduğu bildirilmiştir.

Laboratuar tanısındaki kolaylık, takip ve tedavi protokollerinin belirlenmiş olması nedeniyle, kanama diyatezi olan gebelerde Faktör VII eksikliği akılda bulundurulmalıdır.

Bu yazıda, Hacettepe Üniversitesi Tıp Fakültesi Kadın Hastalıkları ve Doğum Anabilim Dalı'nda takip edilen, 29 haftalık gebe iken vajinal kanama ile başvurup, plasenta dekolmanı ön tanısı ile acil şartlarda sezaryen doğum uygulanan bir gebe sunuldu. Faktör VII eksikliği olan gebelerin takip ve tedavi yöntemleri tartışıldı.

Anahtar kelimeler: *faktör VII eksikliği, gebelik, gebelik kaybı, plasenta dekolmanı, replasman tedavisi*

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INTRODUCTION

Factor VII (FVII) deficiency also known as Alexander disease is an autosomal recessive disorder which is first described in 1951[1]. The disease is characterized by a wide spectrum of mutations occuring in the FVII gene located on the long arm of the 13. chromosome[2]. Among the rare inherited coagulation disorders, this disease is the most frequently encountered with a prevelence of 1/500.000, on the other hand due to asymptomatic individuals in the general population, the actual prevelence is thought to be more frequent[3]. The clinical presentation is very heterogeneous, varies from severe bleeding leading to threatened-life and disability (cerebral, gastrointestinal and articular bleeding) to minor bleeding episodes[3]. Reproductive aged female patients are frequently symptomatic with menorrhagia. Beside this, studies dealing with genotype-phenotype relationship showed that some modifying components result in differences in the expression of FVII deficiency. This relationship reveals the occurence of discordant clinical phenotypes within the carriers of the same mutation of FVII[2]. Surprisingly, 3 to 4% of patients with FVII deficiency also have thrombotic episodes[4].

Laboratory diagnosis of FVII deficiency is simple, prolonged prothrombin time (PT), normal activated partial thromboplastin time (aPTT) and according to plasma Factor VII levels prolonged international normalized ratio (INR) are determined. When FVII level is below 10 IU/dL clinically apparent bleeding diathesis emerges[4]. There are many options of FVII derivatives that are used in clinical practice and fresh frozen plasma are available for patients with a plan of surgery and for symptomatic cases.

CASE

27 year-old G7A5P1Y1 woman at her 15th gestational week of pregnancy admitted to our department for the routine follow-up. She had a diagnosis of FVII deficiency since the age of 15. Her past obstetric history was remarkable with five recurrent abortuses and one live birth. Of those 5 abortuses, 4 were before the 10. weeks of gestation, the remaining one occured at 16. weeks of gestation. All abortuses were accompanied clinically by excessive vaginal bleeding. In her past medical history, she had no complaint other than menorrhagia and frequently recurring gingival bleeding and epistaxis. Her family history was remarkable with her sister's diagnosis of FVII deficiency. Her living child was delivered with cesarean section at 38th weeks of gestation, during delivery and postpartum period she had received fresh frozen plasma replacement for the control of bleeding. Her file examination revealed that she developed pulmonary edema and postpartum cardiomyopathy at the 15. postpartum day. The clinical result was thought to be due to the large amount of fresh frozen plasma replacement.

In her routine antenatal follow-up, second trimester serum biochemical screening, sonographic anomaly screening and 50 g oral glucose challange test performed at 26. weeks of gestation were all normal. FVII level examined at 24. weeks of gestation was 46% (70-130), INR was 1.90 (0.86-1.20), aPTT was 28.3 (27.9-38.1) and PT was 16 sec (10-14 sec).

The patient was consulted with hematology department and she was proposed to receive replacement therapy when she became symptomatic. Her cardiological examination with echocardiogaphy revealed that an ejection fraction of %54 with diminished left ventricular function, minimal mitral and tricuspit valve deficiency. Close monitoring for cardiac decompensation was recommended.

The patient admitted to labor ward at 29th weeks of gestation with the complaint of sudden onset pelvic pain, abrupt vaginal bleeding. Fetal sonography showed a fetus in breech presentation compatible with its gestational age with positive cardiac activity. Placenta looked heterogenous. Fetal cardiotocography showed frequent uterine contractions accompanying fetal bradycardia and non-reassuring fetal heart rate activity. The clnical diagnosis of ablasio placenta was considered due to severe abdominal pain accompanying profuse vaginal bleeding. An emergency cesarean delivery was performed and 1020 gr weighting male baby was delivered with 1. and 5. minutes Apgar scores of 5 and 6, respectively. The intraoperative clinical examination of the placenta confirmed the diagnosis of ablasio placenta. Intraoperative blood loss was estimated as 900 cc and replacement was performed with approximately 1000 cc of crystalloid and colloid solutions. The patient's Factor VII level was 35% (70-130), INR was 5.88 (0.86-1.20), aPTT was 48.5 (27.9-38.1), PT was 22 sec (10-14 sec) and hemoglobin value

was 8.1 g/dL. The neonate was hospitalized in the Neonatal Intensive Care Unit due to prematurity. The patient was given 8 units of fresh frozen plasma ve 2 units of erythrocyte suspension because of anemia postoperatively. Her vaginal bleeding was in normal limits and no cardiac decompensation developed. She was discharged at home on the 4th postoperative day.

DISCUSSION

Congenital Factor VII deficiency is an autosomal recessive disease with variable penetrance has an incidence of 1/500.000 in the general population[1]. With tissue factor, FVII accelerates the hydrolysis of Factor X in the extrinsic pathway. The ultimate result by providing the conversion of prothrombin to thrombin is the formation of clot[2].

Factor VII level is below 10 IU/dL in homozygous individuals, while heterozygous individulas are reported to have levels between 20-60 IU/dL[4]. Bleeding diathesis is thought to be significant when FVII is below the level of 10 IU/dL[3]. Presence of different phenotypes for the same mutation and discordance of genotype-phenotype can be explained by environmental and/or extragenic factors[2]. The clinical presentation of the disease varies from slight bleeding such as epistaxis, gingival bleeding and menorrhagia to potentially fatal central nervous system and gastrointestinal tract bleeding[2]. Our case was diagnosed as Factor VII deficiency with a complaint of menorrhagia at 15 years old.

By the advancing gestational age, as a possible protective mechanism against postpartum hemorrhage clotting factor levels increase. In the medical literature, it has been reported that this increase in patients with homozygous Factor VII deficiency does not take place and if appropriate replacement is not performed, intraparum and postpartum massive hemorrhage will be encountered[5]. However in heterozygous individuals, there is an increase in the levels of Factor VII and the lack of massive bleeding during and after delivery and no requirement of prophylaxis in those patients has been reported to be related with the rising factor levels[3]. In our case, the lack of bleeding following delivery of her first gestation may be due to the rising factor levels. Excessive bleeding that accompanies early pregnancy loss is thought to be related to the factor levels that increase with advancing gestational ages. The case presented here also had excessive bleeding accompanying recurrent early pregnancy losses.

Today, the treatment protocols for severe end of the spectrum of Factor VII deficiency are determined. Treatment options include antifibrinolytics, fresh frozen plasma, Factor VII concantrates and recombinant Factor VII[2]. However, definitive treatment protocols for mild-moderate forms of the sepctrum do not exist. In such cases, rising levels of Factor VII can be protective enough and prophylaxis is not always required[3]. For this reason, replacement treatment given during or after delivery should be tailored according to the patient's clinical presentation. Possible side effects of the replacement therapy should also be considered. In fact, following the delivery of her first gestation our case developed postpartum cardiomyopathy secondary to great amount of fresh frozen plasma replacement. The case presented here, had an emergency cesarean delivery with the clinical presentation of ablasio placenta, received fresh frozen plasma with INR monitoring for the control of bleeding and has been followed closely for cardiac decompensation due to the previous postpartum cardiomyopathy. In this period, morbidity and mortality have been prevented with a multidisciplinary approach.

CONCLUSION

In patients with Factor VII deficiency the prophylaxis and treatment protocols should be individualized, obstetric emergencies should be considered, such cases should be followed up in multi-disciplinary centers to provide emergency cesarean section and appropriate replacement therapies.

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