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Случај на водене на бременност и раждане при тежок дефицит на фактор XII

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Резюме

Дефицитот на фактор XII е рядко нарушението на крвосоѕирването, коешто теоретично носи ризик од крвенење во резултат на намалени коагулациони фактори или ризик од тромбоза во резултат на намалена фибринолитична активност. Честотата на дефицит на фактор XII е односно ниска – 1 на 1 000 000 души.

Целта на докладаваниот случај е да се подчертае значението на мултидисциплинарниот пристап при воденето на бременоста и раѓањето при жени со тежок дефицит на фактор XII.

Жена со тежок дефицит на фактор XII беше успешно лекувана по време на двете си бремености и раѓања. Вички тестови за коагулација беа извршени со стандартни реактиви на Siemens на коагулометар Dade Behring BCS XP. Тест за тромбоцитна агрегација за проследување на лечението со аспирин беше извршен на Siemens Innovation PFA-200 со стандартен тестов патрон за колаген/епинефрин на Siemens.

По време на двете си бремености жената со тежок дефицит на фактор XII е проследувана редовно во Центарот по хемофилија кај Институтот по трансфузиона медицина. Според коагулационните истражувања при првата бременост е лекувана со нискомолекулен хепарин во следродилниот период, но при втората бременост се е наложило лечение во први и трети триместар, како и во следродовниот период. Предотвратувањето на крвенење поради раѓање се извршува со транексамова киселина. Две бремености беа успешно завршени со естествено раѓање без крвенење или тромботични компликации.

Редовното проследување по време на бременост е неопходно за жени со нарушенија на крвосоѕирването во Центарот за комплексно лечение на хемофилија. Мултидисциплинарниот пристап е од решаващо значеније за успешното лечение на нарушенија на крвосоѕирването.

Клучови зборови: дефицит на фактор XII, бременост, раѓање, мултидисциплинарен пристап

Case report for management of pregnancy and delivery in severe factor XII deficiency

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Abstract

Factor XII deficiency is rare bleeding disorder and theoretically may carry either bleeding risk as a result of reduced coagulation factors or thrombosis risk as a consequence of reduced fibrinolytic activity. The incidence of factor XII deficiency is relatively low at 1 in 1,000,000 people.

The aim of reported case is to emphasise the importance of multidisciplinary approach in the management of pregnancy and delivery in the women with severe factor XII deficiency.

A woman with severe factor XII deficiency was successfully treated during her two pregnancies and deliveries. All coagulation tests were performed with standard Siemens reagents on the coagulometer Dade Behring BCS XP. A test for platelet aggregation for follow up of Aspirin treatment was performed on Siemens Innovance PFA-200 with standard Siemens collagen/epinephrin test cartridge.

During her two pregnancies, the woman with severe factor XII deficiency was regularly followed up in the Center for haemophilia in the Institute for Transfusion Medicine. According to coagulation tests in the first pregnancy she was treated with low molecular weight heparin in the postpartum period, but in the second pregnancy it was necessary to be treated in the first and third trimester, as well as in the postpartum period. Bleeding prevention due to delivery was performed with tranexamic acid. Two pregnancies were successfully finished with vaginal delivery without any bleeding or thrombotic complications.

Regular follow up during pregnancy is necessary for women with bleeding disorders in Comprehensive Haemophilia Treatment Centre. Multidisciplinary approach is crucial for successful bleeding disorders care.

Keywords: factor XII deficiency, pregnancy, delivery, multidisciplinary approach

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Introduction

Factor XII (FXII) is an essential physiological mediator of hemostasis, inflammation, the complement system and fibrinolysis. Typically it is diagnosed incidentally when an isolated prolonged activated partial thromboplastin time (aPTT) is observed during preoperative evaluation [1-3]. First described by Davie and Ratnoff in 1955, deficiency of FXII, also known as the Hageman factor, is one of the rare abnormal in vitro coagulation defects that can be hereditary (i.e. autosomal recessive) or acquired [2-4]. The causes of acquired XII deficiency include nephrotic syndrome, sepsis and disseminated intravascular coagulation and its incidence is relatively low at 1 in 1,000,000 people [4]. The index case was described in 1953 when patient John Hageman had surgery due to duodenal ulcer without bleeding complications. Hageman had no history of bleeding problems previously due to appendectomy and tooth extraction, too. In 1968 he died from pulmonary thromboembolism as a complication due to pelvic fracture [5]. FXII deficiency is rare bleeding disorder and theoretically, may carry either bleeding risk as a result of reduced coagulation factors or thrombosis risk as a consequence of reduced fibrinolytic activity [6].

Material and methods

A case report is described of a woman with severe factor XII deficiency who was successfully treated during her two pregnancies and deliveries. Laboratory for Thrombotic and Haemorrhagic Disorders is a part of the Institute for Transfusion Medicine. All coagulation tests were performed with standard Siemens reagents on the coagulometer Dade Behring BCS XP. A test for platelet aggregation for follow up of Aspirin treatment was performed on Siemens aggregometer Innovance PFA-200 with standard Siemens collagen/epinephrin test cartridge.

Results

The patient came in the Center for Haemophilia, Institute for Transfusion Medicine at the 30th gestational age in the first pregnancy because of prolonged activated partial thromboplastin time (aPTT). 120 seconds (sec) was the result for aPTT (normal values 27,9-37,7 sec) and the value was corrected with normal plasma. Severe deficiency of 0,1 % FXII was diagnosed (normal values 50-150%). Bleeding prevention due to vaginal delivery was performed with tranexamic acid (15 mg/kg/BW). In the postpartum period, according to coagulation tests she was treated with low molecular weight heparin (enoxaparin 40 mg, twice daily) for three weeks. No bleeding or thrombotic complications were observed.

After six years, the woman with severe factor XII deficiency started to visit our center again. She was pregnant at 7th gestational week. Ultrasonographic findings of placental lacunae were observed and her gynecologist recommended Dobroston and Aspirin 100 mg every other day. Performed coagulation tests and test for platelet aggregation for follow up of Aspirin treatment in the first trimester are presented in the Table 1.

According to lupus anticoagulant negative result, elevated D dimers and possible bleeding risk, decision was made for discontinuation of treatment with Aspirin and starting treatment with low molecular weight heparin (enoxaparin 40 mg, twice daily). Afterwards, the values of D dimers decreased and the treatment with low molecular weight heparin was suspended. In the second trimester, ultrasonographic finding of placenta maturation grade II was observed and her gynecologist recommended Aspirin 75 mg once a day. Because the result of platelet aggregation test showed no effect from the aspirin treatment, D dimers were in the expected range for gestational age and there was possible bleeding risk, recommendation was made for suspension of treatment with Aspirin and only for follow up (Table 2).

Table 1. Performed coagulation tests and test for platelet aggregation in the first trimester

Date	Plt (150-450x10 ⁹ /L)	Ht (35-50%)	PT (9,8-14,2 sec)	aPTT (27,9-37,7 sec)	TT (16,1-24,1 sec)	FXII (50-150%)	DD (0-500 ngr/mL)	LAC neg screening 25-42 sec	Test for follow up of th with Aspirin (col/epi) 82-150 sec
28 01 2022	242	30.7	11.5	120 (32)	17.1	0.1	5684	Neg 29.8	268
04 02 2022	230	29.4	11.2	120 (34)	17.9	0.1	1246	/	/
14 02 2022	229	28.2	10.7	120 (32)	18.8	0.1	294.7	/	/

Table 2. Performed coagulation tests and test for platelet aggregation in the second trimester

Date	Plt (150-450x10 ⁹ /L)	Ht (35-50%)	PT (9,8-14,2 sec)	aPTT (27,9-37,7 sec)	TT (16,1-24,1 sec)	FXII (50-150%)	DD (0-500 ngr/mL)	Test for follow up of th with Aspirin (col/epi) 82-150 sec
06 06 2022	225	28.1	10.6	105.4 (35)	15.5	0.1	1087	125

At the end of third trimester, due to elevation of D dimers, treatment with low molecular weight heparin (enoxaparin 40 mg, twice daily) was recommended. Bleeding prevention due to vaginal delivery was performed with tranexamic acid (15 mg/kg/BW). Thromboprophylaxis was performed for five weeks in the postpartum period. There were no bleeding or thrombotic complications.

Discussion

The impact of FXII deficiency on pregnancy outcome is still ambiguous and debatable [7]. Recurrent miscarriage, mild postpartum hemorrhage and normal pregnancy have been found in a small series with factor XII deficiency [8]. The patient from our center with severe FXII deficiency had no problematic obstetric history. Two pregnancies were successfully finished with vaginal delivery without any bleeding or thrombotic complications. Risk management is required to improve treatment and prevent possible complications in people with FXII deficiency. Due to the rarity of cases, FXII deficiency is a subject of ongoing research, whereas each case is considered unique [9-12]. In the second pregnancy, at the 27th gestational week, due to negative blood type (B neg), immunohematological tests were performed (indirect antiglobulin test, enzyme test, Selectogen I, II, V, VI, autoagglutinins with Coombs and isoagglutinins with Coombs). Rh-D prophylaxis was recommended because all tests were negative.

Conclusion

FXII deficiency is a rare bleeding disorder and theoretically, may carry either bleeding or thrombosis. Regular follow up during pregnancy is necessary for women with bleeding disorders in Comprehensive Haemophilia Treatment Centre. Multidisciplinary approach is crucial for successful bleeding disorders care. Close and fruitful collaboration between a specialist of transfusion medicine and a gynecologist-obstetrician was basic for successful management of pregnancies and deliveries in our patient with severe FXII deficiency.

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