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# Successful Delivery of Fetus with Fetal Inherited Thrombophilia After Two Fetal Deaths

Josip Juras, Marina Ivanišević, Slavko Orešković, Slobodan Mihaljević, Goran Vujić and Josip Đelmiš

University of Zagreb, University Hospital Centre Zagreb, School of Medicine, Department of Obstetrics and Gynecology, Zagreb, Croatia

## ABSTRACT

*A pregnant woman with inherited thrombophilia (factor II mutation – 20210A) had two late pregnancy losses. The first pregnancy was not well documented, but the second pregnancy was complicated by fetal thrombophilia and umbilical artery thrombosis, proven after fetal death. During the third pregnancy enoxaparine was introduced in the therapy and early amniocentesis was performed. Fetal thrombophilia was proven again. Early delivery was induced and performed with no complications, resulting in a live healthy infant. A history of miscarriages or recurrent fetal loss should raise suspicion of thrombophilia as a potential cause. It is debatable whether amniocentesis in pursuit of fetal thrombophilia should be performed and whether this will lead to a better perinatal outcome. When fetal thrombophilia is diagnosed, an earlier induction of delivery should be considered, taking into account the fetal extrauterine viability. The aforementioned approach of early delivery in cases of inherited fetal thrombophilia could be a possible solution for better perinatal outcomes.*

**Key words:** *inherited thrombophilia, umbilical cord thrombosis, fetal death, amniocentesis, delivery*

## Introduction

Fetal inherited thrombophilia is a condition whose occurrence and risk for a subsequent adverse perinatal outcome is hard to predict. Thrombosis of the umbilical artery is a frequent occurrence, and carries a great risk of perinatal mortality<sup>1</sup>. In the presence of vessel thrombosis a higher fetal mortality could be expected. Although there are reports on umbilical cord thrombosis and perinatal outcomes, there are no data on the fetal inheritance of thrombophilia and its effect on the course of pregnancy. Moreover, there are no guidelines for the management of such pregnancies.

## Case Report

A thirty-seven-year-old patient with inherited thrombophilia (heterozygote for factor II mutation) was admitted to the hospital for preconception evaluation, due to the history of two fetal deaths, both in the 38<sup>th</sup> week of pregnancy. The past history of the patient was documented at admittance. Perinatal asphyxia was stated as the cause of fetal death of the first fetus in 2009. Two years later, the autopsy of the second fetus showed

thrombosis of umbilical artery, suprarenal glandular hemorrhage, and pleural and heart ecchymoses. During the autopsy a skin sample was taken and fetal DNA isolated from fibroblasts. The DNA analysis revealed an inherited heterozygous factor II mutation (20210A). Basic laboratory tests and an ultrasound examination were performed. Apart from the history of two fetal deaths, there were no other pathological findings. The blood tests for thrombophilia from the previous hospitalization revealed the heterozygous mutation of factor II (20210A).

One year later the patient came to the hospital reporting six weeks and four days of amenorrhea. After taking blood samples for laboratory tests and a cervical smear for microbiological tests, clinical and ultrasound examinations were performed. The concentration of HCG was 34808 IU/L. The ultrasound examination revealed a normal pregnancy consistent with the duration of amenorrhea (6 weeks and three days). The patient was released from the hospital to home care with the recommendation of strict rest. Enoxaparine was introduced as prophylactic therapy for thrombophilia (6000 IU subcu-

taneous). The patient's next pregnancy follow up visit was one month later, and in the 11<sup>th</sup> week of pregnancy she was hospitalized again. The ultrasound examination showed no fetal abnormalities. The patient was advised to continue with strict rest, and low molecular weight heparin therapy was continued. During the 21<sup>st</sup> week of pregnancy (20 weeks and two days) amniocentesis was performed with the aim of taking a sample for testing for thrombophilia. The heterozygous factor II (20210A) mutation was revealed. At the beginning of the 24<sup>th</sup> week of pregnancy an oral glucose tolerance test showed no gestational diabetes mellitus (GDM)<sup>2</sup>. The patient was evaluated monthly and the last ultrasound examination with positive vital fetal signs was performed at full 36 weeks. At that time the ultrasonographically approximated fetal mass was 2600 g, with cephalic presentation and no anatomical abnormalities.

The pregnant woman had hereditary thrombophilia, and two previous fetal deaths. In the last pregnancy the fetus had the same mutation of factor II like the mother, and the pregnancy was terminated due to umbilical artery thrombosis. Considering all the forementioned facts, we decided to conclude this pregnancy by elective cesarean section, taking into account the fetal extrauterine viability. In the 37<sup>th</sup> week of gestation (36 weeks and two days) a male newborn was delivered, weighing 2640 grams and measuring 46 cm. The Apgar score was 8 and 9 in the 1<sup>st</sup> and 5<sup>th</sup> minutes, respectively. The pH of the umbilical artery was 7.25. The newborn did not need any care out of the usual, and as the further maternal course of the puerperium was unremarkable, both mother and child were discharged from hospital on the 6<sup>th</sup> post-operative day. The therapy of enoxaparine was continued at the same dose for three more weeks.

## Discussion

The history of miscarriages or recurrent fetal loss should raise suspicion of thrombophilia as a potential

cause. Alfirevic et al. described how heterozygous factor II mutation was associated with intrauterine growth restriction, and could be found more often in preeclamptic/eclamptic pregnant women<sup>3</sup>. Although there is no association with stillbirth according to available literature, due to our patient's medical history it seemed reasonable to perform tests for thrombophilia of the fetus. The available literature does not present data about the perinatal outcome in fetuses with inherited thrombophilia. Several studies have shown that thrombosis of the umbilical vein is more common than umbilical artery thrombosis, and its perinatal outcome better<sup>1,4</sup>. In high-risk pregnancies umbilical cord thrombosis is more frequent with an incidence of about 1/250<sup>1,5</sup>. Tests for thrombophilia were not performed in any of the studies reported.

In one case report of umbilical vein thrombosis with non-reassuring fetal heart rate and later occurrence of portal vein thrombosis, tests for thrombophilia were not performed either. The authors of the case report concluded that the perinatal outcome would have been worse if the delivery had not been induced in time<sup>6</sup>.

## Conclusion

It is debatable whether amniocentesis in pursuit of fetal thrombophilia should be performed and whether this will lead to a better perinatal outcome. This case report of two documented fetal deaths, both in the 38<sup>th</sup> week of pregnancy, emphasize the importance of early amniocentesis for diagnosing fetal thrombophilia, especially in confirmed cases of maternal thrombophilia and previous fetal thrombophilia and death. When fetal thrombophilia is diagnosed, an earlier induction of delivery should be considered taking into account the fetal extrauterine viability. The aforementioned approach of early delivery in cases of inherited fetal thrombophilia could be a possible solution for better perinatal outcomes.

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*J. Juras*

*University of Zagreb, University Hospital Centre Zagreb, School of Medicine, Department of Obstetrics and Gynecology, Kišpatičeva 12, 10000 Zagreb, Croatia  
e-mail: josipjuras@gmail.com*

## **USPJEŠNO DOVRŠENJE TRUDNOĆE S DJETETOM S NASLJEDNOM TROMBOFILIJOM NAKON DVIJE FETALNE SMRTI**

### **S A Ž E T A K**

Trudnica s nasljednom trombofilijom (mutacija čimbenika II – 20210A) imala je dva gubitka trudnoće u poodmakloj gestaciji. Tijek prve trudnoće nije detaljno dokumentiran, a druga trudnoća je bila komplicirana trombofilijom fetusa i trombozom umbilikalne arterije, što je ustanovljeno nakon smrti fetusa. Tijekom treće trudnoće trudnica je liječena enoksaparinom te je učinjena rana amniocenteza. Opet je fetus imao nasljednu trombofiliju. Učinjena je prijevremena indukcija porođaja bez komplikacija, što je rezultiralo živim i zdravim djetetom. Pobačaji ili ponavljajuća smrt fetusa trebala bi pobuditi sumnju na trombofiliju kao mogući uzrok. Upitno je je li potrebno izvođenje amniocenteze sa svrhom traženja trombofilije u fetusa i utjecanja na bolji perinatalni ishod. U slučaju prisustva fetalne dijagnoze indukcija porođaja prije termina bi se trebala razmotriti, uvažavajući sposobnost fetusa za život izvan maternice. Spomenuti pristup u slučaju nasljedne fetalne trombofilije bi mogao biti potencijalno rješenje za bolji perinatalni ishod.

