Recurrent Placental Abruption with Methylenetetrahydrofolate Reductase C667t Heterozygosity: A Case Report

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Placental abruption although uncommon, can result in high rate of maternal and fetal morbidity and mortality. Several studies suggest abnormal placental vasculature, thrombosis and reduced placental perfusion in pathophysiology. Genetic variations may predispose to these problems.
Case: A thirty year old 28 weeks pregnant women underwent cesarean section with the diagnosis of placental abruption, intrauterine dead fetus and previous cesarean section in our clinic. It was learned that she had a cesarean section due to placental abruption 1 year ago. In the postoperative period trombophilia markers, methylenetetrahydrofolate reductase , Factor V leiden and Prothrombin gene polymorphism, homocystein, folate and vitamin B12 levels and genetic karyotyping were evaluated. The only pathology was the metylenetetrahydrofolate reductase gene heterozygosity for the C to T substitution at nucleotide 677.
Risk of recurrence is high in patients with a history of placental abruption. Antenatal care and delivery after fetal lung maturation is advised since the perinatal mortality is high with placental abruption.

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Key Words: Placental abruption, Thrombophilia, Methylenetetrahydrofolate reductase

Introduction

Placental abruption is defined as the premature separation of the placenta from the endometrium. The clinical hallmarks are vaginal bleeding and pain. It's a serious complication with maternal and fetal risks and occurs in about 1 of 100 pregnancies.[1] Maternal risks associated with abruption include massive blood loss, disseminated intravascular coagulopathy, renal failure and less commonly maternal death. The perinatal mortality rate associated with abruption is nearly 12%, which is 15 times more than the mortality among other pregnancies.[2] Fifty five percent of perinatal deaths with abruption are found to be due to preterm birth. But even after controlling for the preterm birth and fetal growth restriction, the high risk of perinatal death associated with abruption still exists.[2]

The primary cause of placental abruption is not known. Trauma, short umbilical cord, sudden uterine decompression, uterine anomaly or tumor, pregnancy induced or chronic hypertension, cocaine abuse, smoking, history of previous abruption, previous cesarean delivery, advanced maternal age, multiparity, prolonged rupture of membranes, chorioamnionitis are the suggested risk factors.[3]

There is a strong relationship between fetal growth restriction and placental abruption. It's stated that fetal growth restriction can be taken as a risk factor for placental abruption. [2] This suggests a placental pathology starting from second and even first trimester in the pathogenesis of abruption. The risk of abruption also increases with a previous history of placental abruption. Genetic variations can be responsible from placental pathology and recurrence of abruption.

We present a case of recurrent placental abruption with methylenetetrahydrofolate reductase gene heterozygosity.

Case Report

A thirty year old, gravida: 2, parity: 1 living: 0, 31 week pregnant women admitted to the emergency department of our hospital with complain of pelvic pain and vaginal bleeding. On examination maternal blood pressure was 150/100 mmHg, pulse rate was 76/ minute. The physical examination of the patient revealed a contracted uterus and a vaginal bleeding, dark red in color. Fetal heart rate could not be heard by the portable hand doppler. Twenty-eight week intrauterine dead fetus and placental abruption was diagnosed after the sonographic examination. The laboratory findings of the patient were: Hemoglobin: 12.1 g/dl, hematocrit: 35.8 %, platelet: 140.000 /µL, SGOT: 32 U/L, SGPT: 11 U/L LDH: 528 U/L, spot protein in urine: 100 mg/dl. From her patient files, it was learned that she had a cesarean section with the diagnosis of 34 week pregnancy with intrauterine dead fetus, hellp syndrome and placental abruption and stayed in the intensive care

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unit due to disseminated intravascular coagulopathy for 2 weeks in the postoperative period in our hospital. She underwent cesarean section and a 1600 gr dead male fetus was born. Intraoperatively total placental abruption with couvelaire uterus was diagnosed (Figure 1). The patient didn't have a history of smoking, substance abuse, trauma, preterm premature rupture of membranes or chorioamnionitis. The only risk factor in her first pregnancy was hellp syndrome. In her second pregnancy, the risk of previous cesarean section and history of placental abruption were added. In the postoperative period trombophilia markers, methylenetetrahydrofolate reductase , Factor V leiden and Prothrombin gene polymorphism, homocystein, folate and vitamin B12 levels and genetic karyotyping were evaluated. Thrombophilia markers, homocystein, folate and vitamin B12 levels were found to be in normal range. The result of karyotyping was 46 XX. Factor V leiden and Prothrombin genes were normal for the FV G1691A Leiden and PTH G20210A mutations respectively. The only pathology was the metylenetetrahydrofolate reductase gene heterozygosity for the C to T substitution at nucleotide 677.

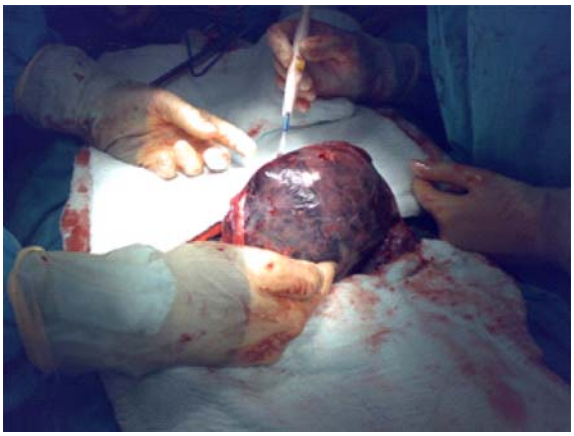

Figure 1: Couvelaire uterus diagnosed intraoperatively

Discussion

The precise etiology of placental abruption is unknown, but the most studies focus on vascular or placental abnormalities. Placental abruption risk significantly increases with hypertensive disorders and smoking which are associated with impaired placental function.[4] Rasmussen et al hypothesized that placental abruption, preterm labor, pregnancy induced hypertension and intrauterine growth restriction share a common etiologic factor or represent a clinical expression of recurrent placental dysfunction.[5] During placental development, spiral artery endothelium is replaced by trophoblast cells leading to vessels free from vasomotor control and creating a low resistance placental vascular bed. Studies indicate that abnormalities in trophoblast invasion are associated with the development of uteroplacental diseases such as preeclampsia and intrauterine growth restriction.[6]

The physiological changes in spiral arteries seem to be influenced by Angiotensinogen Thr235 mutation.[7] It's found that Angiotensinogen Thr235 mutant allele is frequent with placental abruption.[8] Homocysteine is known as an independent risk factor for vascular disease.[9] Hyperhomocyteinemia which is a risk factor for placental vasculopathy is found more frequent in placental abruption than in control group.[10] The cause of hyperhomocysteinemia can be due to deficiency in enzymes involved in metabolism or can be due to folate, vitamin B12 and B6 deficiency. Mutation of Betaine-Homocysteine S-Methyltransferase gene is found to be frequent in placental abruption cases,[11] while Methylenetetrahydrofolate Reductase gene mutation is not found associated with placental abruption. [12] Maternal thrombophilia as a cause of placental abruption has also come under investigation.[13]

In our case we didn't find any abnormalities in thrombophilia markers and homocystein, folate and vitamin B12 levels. There was only a heterozygote mutation in metylenetetrahydrofolate reductase gene for the C to T substitution at nucleotide 677. Although the presence of hellp syndrome in the first pregnancy and the recurrence of the placental abruption suggest a placental pathology we couldn't find any pathological test results suggested as causative factors for the placental pathology. However in a study, it's stated that fetal inherited thrombophilias may also influence the course of late pregnancy outcomes such as severe preeclampsia, intrauterine growth restriction and placental abruption.[14]

Recurrence is 10 times more likely if there is a previous history of abruption.[15] However in a study done in low socioeconomic population recurrence is found as high as 35% and perinatal mortality is found around 33%.[16] Cessation of smoking and prophylactic therapy with heparin and low dose aspirin for those with protein S deficiency, factor V leiden mutation or anticardiolipin antibodies or prophylactic folic acid supplementation to those with mutation in metylenetetrahydrofolate reductase gene offer an opportunity to reduce the risk of recurrence of placental abruption. It's not clear whether antenatal care could have prevented the recurrence of abruption, but it's found that neonatal outcome is more favorable in patients who had antenatal care. Delivery is recommended after the fetal lung maturation is completed, to patients with a history of placental abruption.[16]

Conclusion

Risk of recurrence is high in patients with a history of placental abruption. Antenatal care and delivery after fetal lung maturation is advised since the perinatal mortality is high with placental abruption.

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