Case report

A case of successful pregnancy after 6 times pregnancy loss and secondary subfertility

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Abstract

Thrombophilia is a disease which predisposes thromboembolism and may be congenital or acquired. The purpose of the study was to evaluate the clinical analysis of a couple with reproductive failure. A couple with recurrent pregnancy loss was referred to us. Among the various investigations, protein C, protein S, factor V Leiden and antithrombin were deficient in the female partner. Clinical and hormonal profile were normal in both the partners. The ultrasound scan of female revealed normal uterus and ovaries. Chromosomal analysis of the couple revealed normal 46, XY in male and 46, XX in female. The female partner was treated with enoxaparin. She conceived and delivered a male baby.

Keywords: Repeated pregnancy loss, subfertility, thrombophilia, congenital or acquired, protein C, protein S

Introduction

Thrombophilia is a hematological disorder which causes hypercoagulable state. It results into arterial or venous thrombotic disorders.[1] It can be genetical or acquired. Acquired is more common. [2]Antiphospholipid syndrome is most aggressive and commonest cause. Genetic thrombophilia includes Factor V Leiden, prothrombin thrombophilia, protein C deficiency, protein S deficiency, antithrombin deficiency, the G20210A mutation of prothrombin gene and homozygosity for *the thermolabile variant of methylenetetrahydrofolate reductase (C677T MTHFR).[3] Factor V Leiden is the commonest among the inherited form. Its prevalence is 3-8% in USA and Europe.[4] Thrombophilia also causes obstetric complications, as first trimester miscarriages, repeated pregnancy losses, abruptio placentae, pre-eclampsia etc. [5]

In reproductive age group, about 1 to 5 percent of women faces recurrent pregnancy loss (RPL).[6] RPL or habitual miscarriage means two or more successive loss of pregnancies before viable age. It can be subdivided into 1st trimester loss and 2nd trimester loss.[7] The causes are idiopathic in about 30 to 50% cases.[8] However, there are also various factors as genetic, endocrine, infective and also thrombophilia.[9] Pregnancy itself is a hypercoagulable state, so thrombophilia in pregnancy may worsen the condition. [10]It impairs blood flow through maternal veins. This may lead to DVT, placental thrombosis and which may result into IUGR and fetal demise.[11,12]

Case report

Mrs. Tahmina, 32 years old lady came to Gynae OPD with history of 6 times first trimester repeated pregnancy losses. Last miscarriage was 6 months before. Physical examination revealed no abnormality. Her weight was 57 kg, BMI was 24.8. she had no history of taking OCP and DVT. She had also no family history of blood clots.

The patient was suggested to investigate the subject and uterine malformations, hormonal abnormalities, chromosomal translocations and infectious causes were excluded. As there were no abnormalities, investigator advised the patient to screen for thrombophilia disorders. The laboratory studies revealed, Protein S activity: 38.7% (normal value: 70% - 120%), Protein C activity: 46.3% (normal value: 70%-140%), Factor V Leiden: 1.13 (2.12-3.02), Antithrombin III: 54.8% (normal value: 70% - 120%), homocysteine: 10.07 micromole/L (normal range: 5.0-14.0 micromole/L), negative ANA and negative lupus anticoagulants (DRVVT and Lupus sensitive APTT).

Rivaroxaban, newer anticoagulant was given before pregnancy for 6 months. After 6 months, she conceived again and it was her 7th pregnancy. Rivaroxaban was changed, as it was teratogenic, and LMWH (enoxaparin) was started daily subcutaneously at a dose of 40mg/0.4ml. Aspirin 75 mg was also added daily. Throughout the antenatal period her pregnancy went uneventful. Compression stockings for legs were given to patient. Fetal growth was also compatible with the expected fetal weight according to gestational age. But at 34 weeks of gestation, she was admitted into the hospital as a diagnosed case of preterm premature rupture of membranes (PROM). As Bishop's score was good, we decided for induction of labor with oxytocin. A male baby was delivered per vaginally in vertex presentation with the aid of episiotomy. Baby's weight was 2.1kg.

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Baby was referred to NICU due to prematurity and it was discharged after 3 days. Both mother and baby were discharged in healthy status. Her postpartum period was also uneventful.

Discussion

In every normal pregnancy, there are some alterations in hemostasis, coagulation and fibrinolytic system. [13] Procoagulant factors as, factor VII, VIII, X, XII and fibrinogen are increased. [14] Coagulation inhibitors are usually declined. So, risks of venous thromboembolism are increased.[15] These changes results from hormonal changes during pregnancy in a purpose to control postpartum hemorrhage.[16] Thrombophilia adversely affects pregnancy outcomes.[17] It is a very known factor to cause repeated pregnancy loss, intrauterine fetal death (IUD), intrauterine fetal growth restriction (IUGR), abruptio placentae, placental infarction, pre-eclampsia, eclampsia, HELLP syndrome DIC and fetal bradycardia.[18] Protein C and Protein S are vitamin K dependent natural anticoagulants, which are synthesized mainly in liver. Protein S also synthesized from endothelial cells and megakaryocytes. Its deficiency is autosomal dominant. Protein C and Protein S maintain the balance between coagulation and anticoagulation. Protein S naturally decreases during pregnancy and 3 months postpartum, so deficiency cannot be diagnosed during these periods.[19] Facto V Leiden mutation can be congenital or acquired, and the congenital one is autosomal dominant. Substitution of arginine with glutamine at position 506 of factor V gene occurs in this condition. This mutation leads to excessive thrombin formation.[20]

In thrombophilia, fetal jeopardies may happen due to excessive thrombosis of the placental vessels, which results into infarction and utero-placental insufficiency. Women with thrombophilia may have history of 1 fetal loss in 20% cases and 2 or more losses in 5% cases. But again, in 30%- 40% cases, cause of recurrent pregnancy loss may be unknown after proper evaluation.[21] These patients have also tendency to deliver at a lower gestational age and to have low birth weight babies, while pregnant.[22]

Gris et al found significant association of recurrent pregnancy loss with protein S deficiency and no association with protein C deficiency. But our patient had both.[23]

LMWH (Low molecular weight heparin) and low dose aspirin are used to prevent placental vascular complications. But only aspirin has no significant value in pregnant women with thrombophilia with previous complications. Aspirin is rather discouraged with LMWH now-a-days, because it crosses placental membrane. In combination with LMWH, aspirin increases the bleeding tendency.[23-25]

On the other hand, a study showed low dose aspirin with LMWH causes improvement in uterine artery flow and utero-placental circulation and significantly raises live birth rate. So, we gave our patient both aspirin and LMWH. Throughout the pregnancy period, close maternal and fetal monitoring were done. And, she had a successful pregnancy & safe delivery despite of thrombophilia.[26]

Conclusion

Thrombophilia is a hidden factor for recurrent pregnancy loss (RPL) and bad obstetric history. So, screening for thrombophilia is mandatory in RPL cases. It is highly recommended to use anticoagulants specially LMWH to prevent miscarriages and maternal & fetal complications.

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