17th World Congress in Fetal Medicine

A successful pregnancy after 10 recurrent pregnancy losses

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Objective

Recurrent pregnancy loss (RPL) is defined as the spontaneous loss of the pregnancy before the fetus reaches viability. This includes the time from conception until 24 weeks of gestation. The diagnosis of recurrent pregnancy loss (RPL) could be considered after the loss of two or more consecutive pregnancies. This includes non-visualized pregnancy losses – biochemical pregnancy losses. Ectopic and Molar pregnancies should not be included in the definition. Recurrent Early Pregnancy Loss (REPL) is defined as the loss of two or more pregnancies before the 10th week of the gestation. RPL affects around 1-2 % of women and is considered a major traumatic life event for the couple with serious psychological and social impacts. The risk factors associated with RPL are: age, chromosomal abnormalities, congenital and acquired uterine malformations, immunological diseases, endocrine misbalances and thrombophilia. We present a case of a 35 years old patient, experiencing 10 previous consecutive miscarriages in a period of four years. After being placed on daily low dose Aspirin and LMWH therapy throughout her pregnancy, she delivered a healthy baby at term.

Methods

This is a case report of a 35-year-old patient referred to the Ob/Gyn Clinic after five consecutive pregnancy losses between the 5th and 7th week of gestation. After the fifth miscarriage, dilatation and curettage (D&C) was performed with no complications. The investigation screen for hormone misbalances, TORCH infections and microbiological swabs was negative. A 3D/4D ultrasound was performed to assess Müllerian duct anomalies with normal results. A hysteroscopy was performed subsequently, detecting a Class U2 partially septate uterus and a hysteroscopic resection of the small septum was done. The patient discontinued the examinations in our clinic and she experienced another five biochemical pregnancy losses. Following the 10th pregnancy loss, a number of routine investigations were undertaken like PAP test, microbiological swabs, thyroid function, screening for thrombophilia including testing for Factor V Leiden gene mutation, Protein C, Protein S and Methylenetetrahydrofolate reductase MTHFR mutation and the antiphospholipid antibodies (lupus anticoagulant and anticardiolipin). The patient was heterozygous for Factor V Leiden and heterozygous for MTHFR mutation and we started daily low dose of Aspirin (100mg), MethylFolate (methylated form of folic acid) and vaginal Progesterone. The screening for genetic factors and parental genetic analysis of the couple, was performed with conventional karyotyping genetic technique, with normal results. We did not perform genetic analysis of the pregnancy tissue as only the fifth pregnancy loss was ended with D&C. In the subsequent pregnancy, for the first time, at the 6th gestational week a fetal heartbeat was detected. The patient was immediately started on low molecular weight heparin LMWH (Enoxheparin, 40mg) and she continued her therapy with low dose Aspirin and LMWH throughout her pregnancy. At 26 weeks, gestational diabetes was diagnosed and the glucose levels were well controlled under diet. The patient developed preeclampsia on the 33rd gestational week and antihypertensive medication was started. The fetal growth showed an EFW on the 15th centile with normal Doppler velocimetry in umbilical and middle cerebral artery. The amniotic fluid was increased with a large vertical pocket of 9. 0 cm. At 36 weeks of gestation an emergency caesarean section was required for fetal distress. A female baby was delivered in good condition, with Apgar score 8/9, weight 2540 g.

Results

Thrombophilia is an inherited or acquired condition of hypercoagulability resulting in excessive blood clotting. Pregnancy itself is considered a hypercoagulable state with elevation of most of the clotting factors (Factor VII, Factor VIII, vW Factor, Platelets, Fibrinogen and D-dimer). The connection between Thrombophilia and RPL is undeniable and can be detected in 40% of the cases. This condition leads to arterial and venous thrombosis at the site of implantation or in the placental blood vessels resulting in multiple placental infarctions causing miscarriages. Thrombophilia is also associated

with advanced pregnancy outcomes like preeclampsia, abruption of the placenta, IUGR and intrauterine fetal death. All of these conditions are caused by abnormal placental vascularization and deficient fetal - maternal circulation. In this case report, the patient has thrombophilia with a heterozygous mutation of Factor V Leiden and MTHFR which have been associated with RPL and preeclampsia. The Factor V Leiden mutation is an autosomal dominant inherited defect producing a mutated Factor V molecule resistant to inactivation by activated protein C, increasing the risk of thrombosis in the affected patient by increasing the persistence of prothrombin activity. The MTHFR mutation leads to an increased homocysteine level which is linked to venous thrombosis, neural tube defects, abruption, preeclampsia and RPL. The patient had ten recurrent pregnancy losses and she acquired mild preeclampsia although she was placed on daily low dose Aspirin and LMWH therapy throughout her pregnancy.

Conclusion

Anticoagulant therapy is an effective treatment against RPL in patients presenting with inherited or acquired thrombophilia. The therapy of choice is low dose Aspirin and low molecular weight heparin LMWH. Patients with RPL due to thrombophilia which are treated with Aspirin and LMWH have a very good prognosis and they have a 70% chance of having a successful pregnancy outcome.