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A Successful Outcome in Pregnancy in a Patient with both Antiphospholipid Antibody Syndrome and Protein S Deficiency

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Abstract: ***Antiphospholipid syndrome (APS) is known to be associated with poor fetal outcomes. Although the evidence is inconclusive, inherited thrombophilias, including protein S deficiency, also contribute to poor pregnancy outcomes. Protein S is a vitamin K - dependent anticoagulant that plays an important role in regulating clotting. Protein S deficiency can cause thromboembolism and recurrent miscarriages. We present a case study of a woman with a history of two abortions who was diagnosed with both antiphospholipid antibodies and protein S deficiency and was treated with aspirin and low - dose hydroxychloroquine. After treatment, the woman became pregnant and delivered a healthy male baby at 36 weeks of gestation. This case describes the pathogenesis and treatment of APS and protein S deficiency in the setting of recurrent miscarriage, focusing on clinical and clinical management.***

Keywords: Antiphospholipid syndrome, Protein S deficiency, Recurrent miscarriage

1. Introduction

Antiphospholipid antibody syndrome (APS) is an autoimmune disease caused by the production of antibodies to cell membrane phospholipids, leading to a hypercoagulable state in blood vessels and a risk of thrombosis. It is characterized by obstetric complications such as recurrent miscarriage, intrauterine growth restriction (IUGR), preeclampsia, and postpartum maternal thrombosis. APS can occur as primary APS when present in healthy individuals, or as secondary APS when associated with an autoimmune disease such as systemic lupus erythematosus (SLE, Sjogren syndrome, mixed connective tissue disorder). In addition to its effects on pregnancy, APS has also been associated with cardiovascular events. The mere presence of antiphospholipid antibodies (aPL) without clinical complications does not necessarily indicate a diagnosis of APS, as there are asymptomatic aPL - positive patients for long periods of time. Protein S deficiency is a rare thrombophilia with somatic chromosomal dominant inheritance. Protein S works as a cofactor that increases the ability of activated protein C to inhibit factors Va and VIIIa, thereby controlling thrombosis. Protein S deficiency is associated with an increased risk of thrombosis. Protein S deficiency should be administered with caution due to concerns about bleeding risk during pregnancy. This article describes the case of a pregnant woman with both APS and protein S deficiency who had a good feto - maternal outcome. Management of these conditions involves many disciplines to reduce the risks associated with hypercoagulable states and increase the frequency of pregnancy.

2. Case Report

A 25 year - old woman experienced two first - trimester miscarriages at weeks six and eight of pregnancy, both of which occurred without treatment. After these losses, she was diagnosed with antiphospholipid antibody syndrome and protein - S deficiency. There was no history of arterial or venous thrombotic events. The diagnosis of lupus anticoagulant (LA) was confirmed by a DRVV (diluted Russell's viper venom) screening time of 48.9 seconds (normal range: 31.36 - 40.44 seconds) and a high DRVV screen value. Baseline APTT (thromboplastin half - time) was 69 seconds (normal range: 21.5 - 32.6 seconds) and INR (international normalized ratio) was 3.19; which was also higher than normal therapeutic range. Serum antiphospholipid antibody (IgG) value was 7.14 and cardiolipin antibody (IgG) value was 12.44, both of which were below the critical value. Antinuclear antibodies were positive. Serum protein S concentration is as low as 27% (normal range: 55 - 123%). The activity of plasma antithrombin and protein C operates within normal limits. She became pregnant three months after starting treatment. Low molecular weight heparin (LMWH) was started, but vaginal bleeding occurred at 13 weeks of gestation, which caused temporary discontinuation. After the bleeding subsided, LMWH was restarted, but genital bleeding recurred. At this time, her platelet count was 129 x 10^9/L and her APTT was 41 seconds. It was decided to stop LMWH while continuing aspirin and hydroxychloroquine treatment. The patient's pregnancy proceeded without any significant complications. At 34 weeks, she was given dexamethasone to stimulate fetal growth in preparation for birth at 36 weeks. Aspirin was stopped a week before planned surgery. She delivered a healthy 2.8 kg baby. After surgery, she received low - molecular - weight heparin for 7 days and continued to receive hydroxychloroquine. She was restarted on low - dose aspirin and made an appointment with a rheumatologist 2 months after birth where subsequently she was diagnosed as Sjogren's syndrome and was stabilised on low dose steroids, hydroxychloroquine and sulfasalazine.

3. Discussion

The primary antiphospholipid antibody syndrome is defined as APLA associated with vasocclusive events in the absence of an underlying disease[1]. The clinical criteria of APLA include evidence of thrombosis, such as supplemental gangrene caused by venous arterial or small vessel thrombosis and fetal loss that occurs repeatedly before 10 weeks or after 10 weeks without explanation. Anticardiolipin antibodies (IgG or IgM isotype in medium to high titers), Lupus anticoagulant, β2 - glycoprotein, and prolonged aPTT (actuated partial thromboplastin time) on two or more occasions 12 weeks apart are among the investigative criteria[2]. Obstetric complications include unexplained fetal death or stillbirth, intermittent pregnancy loss - three or four spontaneous abortion with no further than one live birth, unexplained fetal second or third trimester fetal death, severe pre - eclampsia at less than 34 weeks gestation, and unexplained severe pre - eclampsia at lower than 34 weeks gravidity, unexplained severe IUGR, chorea gravidarum[3]. How APLA causes thrombotic events, isn't completely understood. Deep vein thrombosis of the legs is the most common incarnation being in 30 to 55 percent of patients[3 - 5]. Other manifestations include thrombocytopenia and haemolytic anaemia. Gestation in APLA pattern cases presents with increased threat for fetal loss. Multiple infarctions of the placenta due to micro thrombi is a frequent finding in APLA cases, if placental infarction is extensive, it may cause severe growth deceleration of the fetus leading to repeated gestation losses[6]. Pre - eclampsia is also generally seen in similar cases. APLA can precipitate thromboembolic events at any time of the gestation or during the immediate postpartum period as gestation is a hypercoagulable state [7]. Low molecular - weight heparin is the anticoagulant of choice in the treatment of pregnant women with the APLA pattern[8]. Protein S insufficiency is a rare inherited thrombophilia, autosomal dominant frequently associated with fetal losses in gestation. It's seen in roughly 1 in 500 to 1 in 3, 000 people. Homozygous Protein S insufficiency in neonates manifests as a disastrous and fatal thrombotic complication - Purpura Fulminans (PF). Women with inheritable or acquired thrombophilia are at veritably high threat of prenatal and postpartum venous thromboembolism and should receive thromboprophylaxis during gestation and puerperium[10, 11]. Low molecular weight heparins (LMWH) are the anticoagulants of choice. Heparin doesn't cross the placenta, and therefore there's no threat of teratogenesis or fetal hemorrhage. Recurrent fetal loss is a well - established complication of the APLA pattern. Inherited thrombophilias are also linked to adverse pregnancy outcomes. Women with APLA and inherited thrombophilias has a two - fold advanced risk of first and alternate trimester loss and a five - fold advanced risk of late third trimester loss than women without thrombophilia[12]. Consensus guidelines recommend screening women with unexplained intermittent gestation loss for APLA.1[2] Testing for inherited thrombophilia is controversial. It isn't routinely recommended unless the results will affect management.

4. Conclusion

The coexistence of APLA and protein - S deficiency during pregnancy is exceptionally uncommon and poses significant challenges for both healthcare providers and patients alike. A multidisciplinary approach is crucial, necessitating collaboration among senior obstetricians, rheumatologists, neonatologists, and skilled nurses to achieve a successful outcome.

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