CASE REPORT

Successful Pregnancy Outcome in a Case of Protein S Deficiency

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Received: 25 September 2009 / Accepted: 24 May 2012 / Published online: 5 February 2013
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Introduction

Protein S deficiency is a rare inherited thrombophilia often associated with fetal losses in pregnancy. It is seen in approximately 1 in 500 to 1 in 3,000 people. Homozygous Protein S deficiency in neonates manifests as a catastrophic and fatal thrombotic complication termed Purpura Fulminans (PF).

Case Report

A 24-year-old 3rd gravida with two neonatal deaths in the past, presented to us in April 2006 for preconceptional counseling. Her first pregnancy in 2002 ended in a preterm Cesarean section at 35 weeks of gestation in view of preterm premature rupture of membranes with prolonged labor. She delivered a female baby weighing 2.3 kg with prominent, black skin lesions all over the body. In the NICU, the neonate had necrosis and peeling of the skin by the third day and died on the

fifth day. The cause of death could not be determined from the history. Her second pregnancy in 2004 was also uneventful till 38 weeks of gestation, when she had antepartum hemorrhage followed by an emergency LSCS. She delivered a female baby with similar prominent black-colored skin lesions. Similarly, this neonate had necrosis and peeling of the skin and died on the fifth day in the NICU. Again the cause of death was not known. The patient had no other postoperative complications and was discharged with contraceptive advice. The investigations carried out on her in the interval period revealed Lupus anticoagulant (LAC) positive, CMV IgG, HSV IgG and Rubella IgG, +ve, ACL IgG and IgM negative, Anti ds DNA, ANA and VDRL negative, and normal sugars and parental karyotyping. The couple was then referred to the dermatology unit to identify a possible dermatological cause for the neonatal losses. They suggested that neonatal PF secondary to Protein S or Protein C deficiency could have been the possible cause of the neonatal losses. Hence, a Thrombophilia profile of both the parents was performed. Thrombophilia profile of the father was normal. Thrombophilia profile of the mother showed deficiency of Protein S–55 % (Normal range = 70–140 %), with normal Protein C, Antithrombin III, and Factor V Leiden levels. The couple was counseled about the autosomal dominant nature of Protein S deficiency. The patient was advised periconceptional folic acid supplementation for 6 months and early antenatal registration with thromboprophylaxis in next pregnancy.

She conceived for the third time in September 2008, and registered at the antenatal clinic of NWMH at nine weeks of gestation. Her baseline complete blood count and

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coagulation profile were within normal limits. In view of Protein S deficiency with positive Lupus Anticoagulant in pregnancy, the patient was started on low dose Aspirin (75 mg) once daily and unfractionated Heparin (UFH) 5000 IU SC BD till 20 weeks. The doses of heparin were increased to 7500 IU SC BD from 20 weeks till 32 weeks, and afterward to 10,000 IU SC BD till delivery. The patient was monitored weekly with APTT levels and platelet counts during pregnancy. She was given two intramuscular doses of Betamethasone at 28 weeks for lung maturity in anticipation of her past history of preterm delivery. Color Doppler at 32 weeks showed good interval growth with normal Doppler flows. She had weekly NST and Biophysical profile from 32 weeks onward for antepartum fetal surveillance. Aspirin was stopped at 34 weeks. At 36 weeks, the patient complained of decreased fetal movements. NST was non-reactive and urgent biophysical profile showed sluggish fetal movement with fetal tachycardia. Heparin was stopped immediately, and 12 h later, an emergency LSCS was performed under spinal anesthesia. She delivered a female child of 2.8 kg with good Apgar scores on August 21, 2009. The neonate was evaluated by the pediatrician and thrombotic profile of the baby was advised. The mother was restarted on UFH 10,000 IU SC bd on the second postoperative day and also started on warfarin 1 mg od. The warfarin doses were stepped up and adjusted up to 5 mg OD with daily monitoring of PT/INR values. Heparin was discontinued once the INR levels were in the range of 2–3. The patient was advised to continue warfarin 5 mg OD for 6 weeks on discharge.

Discussion

Protein S deficiency is a rare inherited thrombophilia with autosomal dominant inheritance [1]. Protein S is a 69,000 MW vitamin-K-dependent natural anticoagulant protein. It functions as a cofactor to facilitate the action of activated protein C on factors Va and VIIIa. Neonatal PF is a manifestation of homozygous Protein S or Protein C deficiency. It is a lethal syndrome of disseminated intravascular coagulation with rapidly progressive hemorrhagic necrosis of the skin due to dermal vascular thrombosis [2].

Pregnant women with Protein S deficiency are typically heterozygous. Partners of women with these defects should be offered screening to identify neonates who may be homozygous or carry combined defects, in whom prenatal diagnosis can be considered. Women with genetic or acquired thrombophilias are at very high risk of antenatal and postpartum venous thromboembolism and should receive thromboprophylaxis during pregnancy and puerperium [3, 4]. Subcutaneous unfractionated or low molecular weight heparins (LMWH) are the anticoagulants of choice. Heparin does not cross the placenta, and thus there is no risk of teratogenesis or fetal hemorrhage. LMWH is the drug of choice because of a better side-effect profile, (reduced risk of osteopenia and thrombocytopenia) good safety record for mother and fetus, and convenient once-daily dosing for prophylaxis. Warfarin is associated with teratogenic effects and should be avoided in pregnancy. Regional analgesia is avoided for at least 12 h after the last dose of LMWH [3]. Postpartum after 24 h, women should resume warfarin with LMWH overlap until the INR is in the pre-pregnancy therapeutic range [3, 4]. Heparin and warfarin can be safely administered to nursing mothers [1, 4]. In conclusion, thrombophilia screening might be justified in women with recurrent pregnancy loss [5], and adequate and appropriate thromboprophylaxis is an important part of the management of pregnant women with inherited thrombophilias [4].

References

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