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Successful outcome of pregnancy with protein c deficiency with bad obstetric history: A rare case report

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Abstract
Protein C is thought to play a key role in the regulation of hemostasis, and its deficiency has been associated with an increased risk of thromboembolism. Protein C-deficient women are at particular risk of developing thromboembolic complications during pregnancy and delivery. The incidence of thromboembolic events is estimated to be 500-1000 times higher than in normal women. We report the case of a 28-year-old woman with previous deep vein thrombosis, PPH, BOH who experienced a successful pregnancy and delivery despite severe congenital protein C deficiency. She was ant coagulated with LMWH (enoxaparin) during the second part of her pregnancy. Our observation suggests that ambulatory full-dose subcutaneous low molecular weight heparin therapy during pregnancy constitutes adequate prevention. However, definite guidelines will require more extensive studies.

Keywords: BOH-bad obstetric history, PC-protein C, PS-protein S, PPH-postpartum hemorrahge

Introduction
The term BOH includes patients with previous 2 or more consecutive spontaneous abortions, stillbirths, intrauterine growth restrictions, early neonatal death, and or congenitally malformed babies. Broadly the causes can be divided into genetic, immunological, hormonal and maternal infections.
Protein C deficiency is rare and can lead to an increased risk for blood clots. Heterozygous Protein C deficiency occurs in 0.14–0.50% of the general population [6, 7]. Based on an estimated carrier rate of 0.2%, a homozygous or compound heterozygous protein C deficiency incidence of 1 per 4 million births could be predicted, although far fewer living patients have been identified [1]. The incidence of protein C deficiency in individuals who present with clinical symptoms has been reported to be estimated at 1 in 20,000 [8].
Activated protein C (APC) is a strong inhibitor of coagulation. The normal concentration of PC in the plasma is approximately 4 microg/ml. Throughout pregnancy, PC activity and antigenic levels show no significant trend and remain within the normal reference range. Several PC point mutations have been documented, including those characterized as type I and II PC deficiencies. These, as well as mutations in Protein S (PS), factors Va and VIIIa, and thrombomodulin, can result in venous thrombosis of various degrees of severity. The relative risk of thrombosis with PC deficiency is 7.3%. In pregnancy, the risk is 3-10% antepartum and 7-19% postpartum. PC deficiency has also been reported to be associated with both non-recurrent and recurrent first, second and third trimester miscarriages, intrauterine fetal death, intrauterine growth retardation, placental abruption and early onset preeclampsia.

Case Report: A 28 year old patient came in our antenatal opd for checkup, with 6 weeks of pregnancy with BOH with previous 1 section with protein C deficiency with spleenomegaly with H/O DVT.
Obstetrics history- G4P1+2L0A2, In 1st pregnancy underwent LSCS, delivered a IUD female baby 5 years back in some private hospital, and went in Post partum hemorrhage, it was not atonic.
In 2nd pregnancy underwent laproscopic removal of unruptured ectopic pregnancy 2 and a half years back.
In 3rd pregnancy had a spontaneous abortion of 2 month gestation, 1.5 yrs back.
Thereafter she was investigated thoroughly and diagnosed as a case of thrombophilia with protein C deficiency.

Her LMP was 16.5.15 with the normal regular menstrual cycle with normal blood flow, so EDD was 23.2.16.

Hopi: She presented with Amenorrhoea of 1 and half month without any complaint, but with BOH with a k/c/o protein C deficiency.

Trimester wise history – uneventful 1st trimester-started with dydrogesteron 10 mg tds, folic acid 5 mg OD, she has not been started aspirin adviced by cardiologist and hematologisti. Her routine antenatal examination was found to be normal. Anomaly scan was WNL.

2nd and 3rd trimester – Started with 40 mg s/c enoxaparin twice a day, with iron and folic acid tablets, received TT immunization. Her target scan was WNL, She was under regular coagulation profile monitoring, antenatal fetal surviellance with fetal growth sacn, biometry and colour Doppler studies.

No any H/O sudden weight gain, haeadache, edema and bleeding per vaginum was found during antenatal visit.

Medical H/O – DVT (documents not avialale), PPH, Protein C deficiency on regular t/t since 2 yrs.

General and systemic examination was normal, per abdominally scar was healthy, 32 weeks cephalic, uterus relaxed, liquor was adequate, no scar tenderness, FHS- 136/min regular.

Investigations: Showed-Blood group- B +ve, Hb -11.3 gm%, hematocrit – 34.9%, WBC – 2200 /cumm, platelets-73000/cumm, LFT – were normal. HIV, HBsAg, VDRL- Non reactive.

APTT- 28.4sec, PTINR-1.1 sec, EGFR-226 mL/min, Creatinine-0.3mg/dl, Planned for elective C section after consulting anesthetist, cardiologist and hematologist, after explaining HR about DVT, PPH, Obstetric hysterectomy, spinal hematoma. Stopped enoxaparin 24 hour before planned elective section, With the arrangement of 2 unit packed cell,1 unit single donor plasma, 4 unit platelet concentrate, she underwent cesarean section with a healthy female of 3 kg. Intraoperatively 20 units of platelets has been transfused.

Post operatively patient has been kept under close observation, and it was uneventfull. Started with thromboprophylaxis again with LMWH for next 6 weeks.

Discussion

Protein C is a protein produced by the liver. It's found in low concentrations in the blood stream. It is inactive until vitamin K activates it. Protein C serves a variety of functions. Its main function is preventing blood from clotting. Higher than normal levels of protein C aren't associated with any known health issues. But it may increase bleeding. Protein C deficiency is found in similar levels in both men and women, and among different ethnicities.

There are no standardized treatment protocols or guidelines for affected individuals. Due to the rarity of the disease, there are no treatment trials that have been tested on a large group of patients. Various treatments have been reported in the medical literature as part of single case reports or small series of patients. Treatment trials would be very helpful to determine the long-term safety and effectiveness of specific medications and treatments for individuals with protein C deficiency.

Many individuals with mild forms of protein C deficiency will not need any treatment, except at times where there is an increased risk of blood clot formation such as during surgery, pregnancy, immobilization, or trauma. Some individuals with a strong family history to developing blood clots may receive preventive therapy (e.g. anticoagulant therapy) [2, 3, 4].

Anticoagulant therapy is the use of drugs like heparin and warfarin that thin the blood and make it harder for the blood to clot. Special care must be taken if warfarin is used because of the risk of warfarin-induced skin necrosis. The duration of anticoagulant therapy varies based upon an individual patient's specific situation.

Homozygous protein C defect constitutes a potentially life-threatening disease, and warrants the use of supplemental protein C concentrates [5].

Liver transplant may be considered curative for homozygous protein C deficiency [5].

In 2007, the US Food and Drug Administration approved the use of a protein C concentrate called Ceprotin for the treatment of individuals with severe protein C deficiency experiencing purpura fulminans or venous thrombosis. Fresh frozen plasma can be used if Ceprotin is unavailable.

In Europe, there is another drug that is a plasma-derived concentrate of protein C. This drug is called Protexel.

Genetic counseling may be of benefit for affected individuals and their families. Psychosocial support for the entire family is essential as well.

Conclusion

Thromboprophylaxis at low doses seems tobe efficacious in improving fetomaternal outcomes in women with previous adverse outcomes and the presence of inherited causes of thrombophilia. Randomized controlled trials are needed to validate these preliminary observational studies.

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