

Case Report

Successful Pregnancy Outcome in a Patient with Protein S Deficiency: A Case Report

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Abstract

Protein S is a vitamin K-dependent anticoagulant and has a central role in the regulation of coagulation. The mechanism of action of protein S has been one of the least understood amongst the vitamin K-dependent coagulation proteins. A deficiency of protein S predisposes to recurrent thromboembolism and fetal loss. Here we report a case of protein S deficiency in a 28-year-old pregnant woman, who had a history of complete abortion at 22 weeks of gestation and her 2nd pregnancy was managed properly with a successful fetal outcome.

Key words: Protein S deficiency, pregnancy outcome

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Introduction

Protein S deficiency is a rare inherited thrombophilia with autosomal dominant inheritance.¹ It has a prevalence rate of 0.03-0.13% in normal population. Protein S is a 69,000 MW vitamin-K-dependent natural anticoagulant. It functions as a cofactor to facilitate the action of activated protein C on factors Va and VIIIa.² About 60% of protein S in the plasma is inactive and remains bound to a binding protein. Protein S deficiency is associated with increased risk of thrombosis.³ Both quantitative and qualitative abnormalities of protein S have been identified. Protein S deficiency can also be acquired due to vitamin K deficiency, treatment with warfarin, systemic sex hormone therapy, pregnancy, liver disease and certain chronic infections like HIV. Mild protein S deficiency may occur in pregnancy and

treatment needs consideration regarding bleeding complication. Here, we describe a case of pregnancy with protein S deficiency where treatment related complication was successfully managed with good fetal outcome.

Case Report

A 28-year-old non-diabetic, normotensive housewife, a known case of protein S deficiency, presented on 10th November 2014 at her 31⁺ weeks of pregnancy with the complaints of ecchymosis in her lower abdomen and thigh for 5 days. History revealed that it was her 2nd pregnancy and her 1st pregnancy ended at 22 weeks of gestation with complete abortion. Following that abortion investigations were carried out and she was diagnosed as case of protein S deficiency. Her serum protein S level was 37% (Normal range = 70–140 %) with normal Protein C and anti-thrombin III levels. The couple was counseled about the autosomal dominant nature of Protein S deficiency. The patient was advised peri-conceptional folic acid supplementation for 6 months. She was on regular antenatal care (ANC). In this pregnancy her last menstrual period (LMP) was on 3rd April, 2014 and accordingly her expected date of delivery (EDD) was on 10th January, 2015. She was also a known case of polycystic ovarian syndrome (PCOS) and was on treatment with metformin. For her protein S deficiency she was on prophylactic aspirin 75mg daily since 10th weeks of gestation and low molecular weight heparin (LMWH)

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40IU sub-cutaneous daily from her 20th weeks of gestation.

On examination she was hemodynamically stable. On per-abdominal examination, there was a single fetus with longitudinal lie and cephalic presentation, liquor volume was adequate and fetal heart rate (FHR) was 142/min. There were multiple ecchymosis on hypogastrium and umbilical region and on both thigh. On investigation her baseline complete blood count and coagulation profile were within normal limits (Prothrombin time: patient 12.7 second and control 12.0 second, INR-1.04, APTT-32 seconds). She had dyslipidemia (Total cholesterol- 421mg/dl, triglyceride-335mg/dl, HDL-36mg/dl and LDL-318mg/dl) and altered liver functions (serum bilirubin-0.5mg/dl, serum ALT-241 IU/L).

A medical board was formed consisting of medicine specialist, gynecologist, hematologist and decision was taken to stop LMWH and metformin. Aspirin 75mg was continued and patient was given urso-deoxycolic acid 150mg bid, injection vitamin-K orally for 3 days. Plan was to continue pregnancy at least up to 34 completed weeks and follow up pregnancy with non-stress test (NST) on every alternative day, along with liver function, lipid profile and coagulation profile every 3rd day. For fetal lung maturation injection dexamethasone was given.

Gradually, patient was improving, ecchymosis disappeared, liver function and lipid profile became normal. But at her 35⁺ wks of pregnancy ALT was gradually increasing (from 91IU/L up to 119IU/L). For gradual rising of ALT elective lower uterine caesarean section (LUCS) was done on 15th December 2014 at her 36⁺³ weeks of gestation. On LUCS liquor was mildly meconium stained, a healthy male baby weighting 2.8kg was delivered. Her post-operative period was uneventful and her liver function tests, lipid profile, coagulation profile at 5th POD was within normal limits.

Discussion

Protein S deficiency is an autosomal dominant condition, which means one altered copy of the PROS1 gene in each cell is sufficient to cause mild protein S deficiency. Individual who inherent two altered copies of this gene in each cell have severe protein S deficiency. Mild protein S deficiency is estimated to in approximately 1 in 500 individual.⁴ Severe protein S deficiency is rare.

Individual with mild protein S deficiency are at risk of developing deep vein thrombosis which occurs in the deep veins of arms and legs.⁵ In this case her protein S deficiency was diagnosed during this pregnancy.

Pregnancy is associated with profound alteration in the coagulation and fibrinolytic system to minimize postpartum blood loss. Such as factor I, II, VII, VIII, IX, XII increase and protein S decrease and inhibit fibrinolysis. In diagnosed case of protein S deficiency prophylactic LMWH may be used in asymptomatic patient but timing is controversial. Most of the obstetrician prefer LMWH from mid trimester to 6 weeks after delivery.⁶ In this case we prophylactically started aspirin at 10th weeks and LMWH at 20th wks of gestation.

Subsequently she developed superficial bleeding manifestation in the form of ecchymosis with unexplained alteration of liver function that improved after stopping LMWH and adding ursodeoxycolic acid and vitamin-K. Probably this was because of the LMWH which was not mandatory in this case.

Conclusion

Pregnancy with protein S deficiency is a high risk pregnancy. But over-enthusiastic management may cause adverse effect. Mild protein S deficiency may not cause abnormal clotting disorder. So, proper judgment to initiate treatment and frequent monitoring is essential for good pregnancy outcome.

Conflict of interest: None

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