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Case Report

Combined protein C and protein S deficiency with pregnancy

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ABSTRACT

A 35 year old female patient, married since 8 years, G6P1L1SA4 was registered with our unit since 8th week of gestation. She was a known case of protein C and protein S deficiency diagnosed 7 years ago (thrombotic profile- protein C: 70% normal: 70-100%, protein S: 55% normal: 70/140%, AT-III: 116% normal 70/140%, factor V leiden: no mutation detected) which was detected on evaluation for her bad obstetric history. ACLA was also positive. She was started on injection low molecular weight heparin 0.6 mg s/c OD, in addition to continuing Tb. Aspirin 75 mg which had been started when the pregnancy was registered. Foleys induction was done at 39 weeks of gestation in view of previous LSCS with pre-eclampsia. Emergency LSCS was done in view of previous LSCS with non-progress of labour. Male child weighing 2.4 kg was born which is doing well. A patient having combined deficiency of both factors protein C and protein S is very rare. Anticoagulation therapy is the cornerstone in the management of patients with inherited coagulation defects.

Keywords: Protein C deficiency, Protein S deficiency, Recurrent miscarriage, Deep vein thrombosis

INTRODUCTION

Acquired or hereditary thrombophilia occur in almost two-thirds of women presenting with recurrent miscarriages, preeclampsia, intrauterine growth restriction, abruption placentae, or stillbirth, which are associated with microvascular thrombosis in placental blood vessels. Protein C and protein S deficiencies are associated with a variably increased risk of thrombosis and are inherited independently in an autosomal dominant trait. Combined deficiency of protein C and protein S is rare and only few confirmed cases with genetic decoding has been reported.^{1,2} Here we report such a rare case of combined protein C and protein S deficiency with a successful maternal and fetal outcome.

CASE REPORT

A 35 year old female patient, married since 8 years, G6P1L1SA4 was registered with our unit since 8th week

of gestation. She was a known case of protein C and protein S deficiency diagnosed 7 years ago (thrombotic profile- protein C: 70% normal: 70-100%, protein S: 55% normal: 70/140%, AT-III: 116% normal 70/140%, factor V leiden: no mutation detected) which was detected on evaluation for her bad obstetric history. She had 4 consecutive spontaneous abortions at 1 and 1/2 months which were followed by check curettage. In her 5th pregnancy. She was diagnosed with protein C and protein S deficiency at 20 weeks of gestation during evaluation of her bad obstetric history. ACLA was also positive. She was started on injection low molecular weight heparin 0.6 mg s/c OD, in addition to continuing Tb. Aspirin 75 mg which had been started when the pregnancy was registered. Elective LSCS was done in view of precious pregnancy and a female baby weighing 2.3 kg was born which is doing well. On post-operative day 12, she developed myoclonic seizures of left upper limb and was admitted in this tertiary care institute. CT scan brain showed superior sagittal sinus thrombosis for which she

was given heparin and warfarin overlap and was discharged after 8 days on Tb. Warfarin 10 mg BD and advised regular INR monitoring. She was also started on Tb. Carbamazepine and Tb Eptoin.

This pregnancy was a spontaneous conception. Warfarin was stopped at 6 weeks as soon as pregnancy was diagnosed and antenatal registration was done. Injection enoxaparin 0.6 mg s/c OD was started along with continuing aspirin 150 mg OD. She was regular with follow up. Congenital anomaly scan revealed no abnormalities. She was admitted at 34 weeks with high BP readings in antenatal OPD and started on tablet alphasoda and subsequently discharged with her BP under control and all investigations from PIH point of view under normal limits. Foleys induction was done at 39 weeks of gestation in view of previous LSCS with pre-eclampsia. Emergency LSCS was done in view of previous LSCS with non-progress of labour. Male child weighing 2.4 kg was born which is doing well. Her post-operative course was uneventful.

DISCUSSION

Protein C and protein S deficiencies are associated with a variably increased risk of thrombosis and are inherited independently in an autosomal dominant trait. The protein C gene resides on chromosome 23 while the protein S gene is located on chromosome 3.4. It has been found that over 160 different mutations on the protein C gene can lead to absence, or a defective form, of protein C and over 90 different mutations of protein S gene.^{5,6} Incidence of clinically symptomatic protein C deficiency lie between 1:16 000 to 1:32 000 persons while that of symptomatic protein S deficiency is 1:20 000.^{2,7} Incidence of severe protein C deficiency presenting as inherited homozygous or compound heterozygous state is very rare, occurring in 1:500 000 to 1:750 000.⁷ Combined protein C and protein S deficiencies are still rare and few cases have been reported in the literature. Anticoagulant therapy is the cornerstone in the management of these patients.

The cerebrovascular system may be primarily involved in young adults suffering from anticoagulants deficiency.⁸ Considering the importance of prothrombotic state, especially caused by deficiency of protein S, any patient presenting with features of cerebrovascular accidents should be thoroughly investigated for any natural anticoagulants deficiency, in whom no other etiologic factors can be determined.⁹ Hence, thrombophilia screening might be justified in women with pregnancy loss, and treatment with low molecular weight heparin might be considered for those with pregnancy loss and thrombophilia.¹⁰ Women with thrombophilia are also more prone to venous thrombo embolism in pregnancy and puerperium.¹¹ Many women with a history of Recurrent miscarriage are at greater risk of preeclampsia, IUGR and intra-uterine fetal death, which suggests that these adverse pregnancy outcomes represent a spectrum

of disorders which share a common origin.¹² Special care and precautions should be taken in post-partum/post-operative period to prevent the catastrophic event of venous thromboembolism which could lead not only to major morbidity but also mortality.

CONCLUSION

In conclusion, patients with protein C or S deficiency may remain asymptomatic or present with thromboembolic incidents, but with combined deficiency of protein C and S the risk of thrombosis is high and occurs early in life. Long term anticoagulant prophylaxis should be considered weighing the risk of bleeding to thrombotic recurrence.

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