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Cerebral Sinus Thrombosis During Pregnancy Associated with Protein S Deficiency: Report of a Rare Case

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Abstract
Hereditary thrombophylic mutations are seen in 10% of the general population and many cases are diagnosed as a result of complications that occur during pregnancy. Of these, Protein S deficiency is a rare hereditary trombophilia with severe thrombogenic features. Pregnancies accompanying protein S deficiency often result in loss of fetus. In this paper, we present the case of a protein S deficiency patient who eventually had a live birth despite the cerebral sinus thrombosis in the 30th week of her pregnancy and discuss the case with references to the relevant literature.
Key Words: Protein S Deficiency; Hereditary Thrombophilia; Cerebral Sinus Trombosis; Pregnancy.

Gebelite Protein-S Eksikliği İle İlişkili Serebral Sinüs Trombozu: Nadir Bir Olgu Sunumu

Özet
Herediter trombofilik mutasyonlar genel popülasyonun %10'unda görülür ve bir çok olgu gebelik sırasında ortaya çıkan komplikasyonlar sonucunda tanı alır. Bunlardan Protein S eksikliği nadir görülen ve şiddetli trombojenik özellikte bir herediter trombofiliadır. Protein S eksikliği eşlik eden gebelikler genelde fetal kayıpla sonuçlanır. Bu yazıda canlı doğumla son bulan gebeliği sırasında, 30. gebelik haftasında serebral sinüs trombozu geçiren ve tetkiklerinde protein S eksikliği saptanan bir olgu sunularak konu literatür bilgileri eşliğinde tartışıldı.
Anahtar Kelimeler: Protein S Eksikliği; Herediter Trombofilia; Serebral Sinüs Trombozu; Gebelik.

INTRODUCTION

Synthesised by PROS-1 and PROS2 genes in the third chromosome, Protein S (PS) is the cofactor of Protein C, an anticoagulant protein (1). PS is primarily synthesized by hepatocytes and, with Protein C, it participates in the inhibition of activate factor 5 and factor 8 showing anticoagulant properties (1). The main role in anticoagulant activity is played by free PS. Apart from its free form, the form it gets when linked to the complement C4 protein is inactive. PS deficiency is an autosomal dominant inheritance and seen in every 1/500-1/3000 (2). Because homozygous PS deficiency is usually lethal in the neonatal period, the PS deficiency in adults is heterozygous (3). Besides it also increases the risk of abortus in pregnancy, growth retardation, preeclampsia, placental ablation, and stillbirth (4).

In this article, we would like to present a rare case of a PS deficiency patient who underwent cerebral sinus thrombosis treatment in her 30th gestational week and the follow-up process.

CASE REPORT

A 41 years old female patient applied to our clinic in her 16th gestational week for follow-up with an obstetric history of G4, P3, and L3. There was no remarkable findings in her obstetric history or family history. The patient had chronic hypertension that had been followed. The examination showed TE: 140/90, pulse 90/min, and 17-week-old single fetus with vertex presentation in obstetric sonography. The patient was asked to attend the routine follow-ups. In the 30th week, she presented with numbness and tingling sensation in the face, numbness in the left arm, and speech impairment. The obstetrical examination showed no abnormal findings and the single fetus was alive and in its 30th week; so we consulted the patient to the neurology department. As a result of neurological examination, she was diagnosed with left central facial paralysis. The MR angiography the patient underwent with cranial pathology prediagnosis showed absence of current in the left transverse, sigmoid sinus, and jugular vein which was interpreted in favour of the thrombosis (Figure 1).

The cranial MRI revealed hyperintense areas consistent with venous infarction in the bilateral periventricular deep white matter, on T2 sequence. The coloured Doppler examination of the lower extremity was normal.

After informing the patient and her relatives about the situation, we hospitalised the patient and started a daily dose of 6000x2 low molecular weight heparin (enoxaparin sodium). Keeping in mind the possibility of an accompanying thrombophilic mutation, we also asked for the patient's thrombophilia panel. The mutation scans for Factor V Leiden, MTHFR, and prothrombin

20210-A were negative. Having measured PS level as 31.5 u/ml (60-130) and 19 u/ml (60-130), respectively, in two consecutive tests, we diagnosed the patient with PS deficiency.

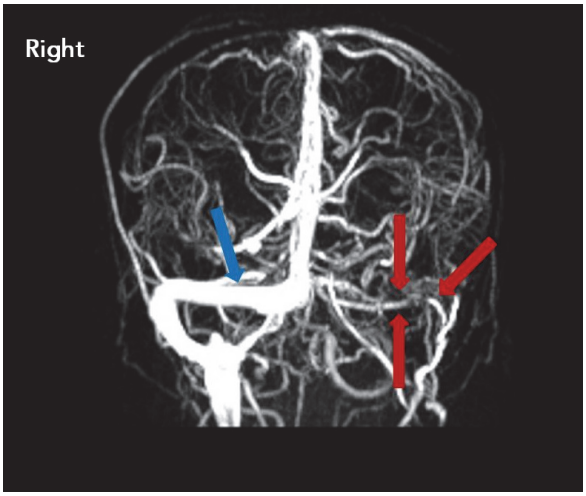

Figure 1. MR angiography image showing normal current in the right cerebral sinuses (blue arrow) and loss of current in the left transverse and jugular vein (red arrows).

After informing the family about the current situation we observed no additional complications and her complaints declined; then the patient returned to the routine pregnancy monitoring at the outpatient clinic as the neurology clinic started the follow-up. The patient had a smooth pregnancy until the 38th week 1 day when she was hospitalised as she was in labor. As the patient developed fetal distress, we delivered the baby with caesarean section. The neonate was a 3160g baby girl and its 1st minute Apgar score was 10.

Following the neurological consultation, the patient continued on the anticoagulant therapy at the same dose in the postoperative period. The control cranial MRI conducted in the postoperative period reported that the acute venous infarct area described in the diagnosis report had changed for the better. As the MR angiography showed, a similar thrombus-compatible view was also observable in the left transverse sinus, sigmoid sinus, and jugular vein. On the postoperative 4th day the patient was discharged and invited to attend the follow-ups at neurology and gynecology outpatient clinics.

DISCUSSION

Hereditary thrombophilic mutations are seen in 10% of the general population and the incidence rate of thromboembolic complications in such patients is 24-37% (1, 5). In patients with weakened anticoagulant capacity due to lack of PS, the most common clinical presentations are vein thrombosis and pulmonary embolism (6). Visceral, cerebral, and superficial venous thrombosis are less common clinical conditions. In this regard, the atypical presentation of our patient is noteworthy.

Due to the fibrinogen, factor 5, factor 7, factor 8, and factor 10 increase in pregnancy along with restricted fibrinolytic activity, women in such conditions are exposed to the risk of thrombosis 6-10 time more compared to non-pregnant women (7). This procoagulant status does not cause any complications in healthy women but it may bring about severe clinical manifestations in women who are thrombophilia mutation carriers. PS deficiency is defined as a severe thrombogenic thrombophilia and in pregnant women it raises the risk of recurrent abortus, fetal growth retardation, maternal thromboembolic complications, early-onset severe preeclampsia, and fetal death (4-6). The case we present in this article is important because there was no deterioration in placental engorgement and the pregnancy ended up with an alive and healthy fetus despite the presence of maternal cerebral sinus thrombosis.

The incidence of cerebral venous thrombosis varies in different societies but the rate is reported to be 0.67-1.32/100,000 (8). Unlike other thromboembolic complications, it is less common and it usually affects young females (8).

It is recommended for females with thrombophilic mutations during pregnancy and those who have thromboembolic complications to start anticoagulation treatment immediately (4). For a better patient compliance and fewer side effects, low molecular weight heparin treatment can be used. The risk of having another episode of attacks during the same pregnancy increases in women who have thromboembolic complications in their medical history. This risk is more pronounced in the later weeks of pregnancy; indeed, it has been reported that the risk of thromboembolic complications is highest during the puerperium. Romualdi et al., in their meta-analysis that compiles the data about 981 patients who underwent thromboembolic complications during pregnancy and puerperium, have reported anticoagulant therapy to be safe during pregnancy and that the dose can be increased in puerperium due to the higher risk rate in postpartum (9). Therefore, anticoagulant therapy should continue throughout the pregnancy and until the end of postpartum. We also used therapeutic doses (2x6000) of low molecular weight heparin for the follow-up. In addition, after the neurological consultation, we have agreed that the patient should continue with the anticoagulant therapy for two years.

As a result, practitioners should keep in mind thromboembolic complications related to hereditary thrombophilic mutations such as PS deficiency in cases when neurological or cardiovascular symptoms are seemingly unrelated to pregnancies. A long-term treatment with an upgraded dosage from prophylaxis dose to therapeutic dose is suitable for the treatment of patients who are having attacks to ensure adequate anticoagulation. As a cause of morbidity and mortality both for mother and fetus, the appropriate treatment of these cases requires a multidisciplinary management.

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