Deep vein thrombosis in pregnant women with heterozygous factor-V Leiden mutation: a case report

Heterozigot faktör-V Leiden mutasyonu olan gebede derin ven trombozu: Olgu sunumu

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Deep vein thrombosis during pregnancy is an important risk factor increasing maternal morbidity and mortality. Factor V Leiden mutation is the most frequent one among many hereditary and acquired thrombophilic risk factors during pregnancy. In a 23-year-old woman who had been pregnant for 11 weeks and applied to hospital with sudden onset pain, swelling, and erythema in her left lower extremity, a thrombus from left main iliac to superficial femoral veins was detected via Doppler ultrasonography. She was hospitalized and low molecular-weight heparin (enoxaprine sodium) was initiated with a dosage of 12000 IU/day. She showed a rapid healing clinically and was followed up with enoxaprine and varsity sock until delivery. After labor, the dosage of enoxaprine was halved and withdrawn after six weeks, and oral warfarin sodium was started. The patient is still continued to be followed up without any problems.

Key words: Deep vein thrombosis; enoxaprine; factor V Leiden mutation; pregnancy.

Gebelikte ortaya çıkan derin ven trombozu, maternal mortalite ve morbiditeyi artıran önemli bir faktördür. Gebelikte hiperkoagülabiliteye yol açan edinsel ve kalıtsal birçok trombofilik risk faktörleri içerisinde faktör-V Leiden mutasyonu en sık karşılaşılanıdır. Sol alt ekstremitede ani başlayan ağrı, şişlik ve kızarıklık yakınmasıyla başvuran 23 yaşında 11 haftalık gebe hastanın venöz Doppler ultrasonografik incelemesinde sol ana iliyak venden, yüzeyel femoral vene kadar uzanan trombüs tespit edilmesi üzerine, yatırılarak düşük molekül ağırlıklı heparin (enoksaparin sodyum 12000 IU/gün) tedavisine başlandı. Klinik olarak hızla düzelme gösteren hasta normal doğum yapana kadar enoksaparin ve varis çorabı ile izlendi. Doğumdan sonra enoksaparin dozu yarıya indirilip altı hafta kullanıldıktan sonra kesilerek oral warfarin sodyum başlandı. Hasta halen kontrollere gelmekte ve sorunsuz izlenmektedir.

Anahtar sözcükler: Derin ven trombozu; enoksaparin; faktör V Leiden; gebelik.

Pregnant women have a five-times higher risk of venous thromboembolism than their non-pregnant peers.[1] Like pulmonary embolisms, the thromboembolic complications are also one of the most important reasons of the death among women during pregnancy and the peripartum period. Deep vein thrombosis (DVT) occurring during pregnancy is one of the factors increasing maternal mortality and morbidity, and determining the appropriate treatment for this condition can also be problematic.[2]

There are many acquired and hereditary thrombophylic factors causing hypercoagulability during pregnancy. Again, during pregnancy, certain changes occur in the plasma concentrations and activities of some proteins that participate in the coagulation and fibrinolytic system. These changes trigger a coagulation, decrease anticoagulation and suppress the fibrinolytic system.[2]

Thrombophylic risk factors have been identified in $^1/_3$ of the women who experienced a pregnancy-related DVT. Heterozygous factor-V Leiden mutation, which is characterized by an activated protein-C resistance, is the most common one among the hereditary thrombophylic risk factors.[3,4] In this article, we present our diagnostic and treatment approach for a pregnant woman who developed a DVT and in whom a heterozygous factor-V Leiden mutation was detected.

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CASE REPORT

A 23-year-old female patient in the 11th week her first pregnancy was admitted to our hospital with pain, swelling and blotches in her lower left extremity. The family of the patient, whose complaints suddenly started five days ago and gradually increased until she was hospitalized, also had a history of DVT. In the physical examination of the patient, edema, sensitivity and blotches were detected in the lower left extremity. The left distal pulse was weak. In the immediate color Doppler ultrasonographic examination that followed, findings consistent with a thrombus during the acute-subacute period were detected in the left main and external iliac veins, the main and surface femoral veins and the saphenous vein. The laboratory values were as follows: Hgb: 10.6 gr/dl, Hct: 32%, WBC: 12.000/mm^3, Plt: 134.000/mm^3, D-dimer: 9382 ng/ml, the sedimentation speed: 85 mm/min. Besides these biochemical values, the protein-C and S values were also normal. The activated protein-C could not be measured. However, a heterozygous factor-V Leiden mutation was detected in the patient using the DNA sample obtained from the peripheric blood and examined using the polymerase chain reaction technique.

After the patient was admitted to our clinic, a low molecular weight heparin (enoxaparin sodium 12000 IU/day, 2 subcutaneous doses) treatment was started and leg compression was applied. During the two weeks she stayed in our hospital, the patient's health rapidly improved and she was discharged after being prescribed the same dose of enoxaparin and elastic stockings. The patient monitored through regular control visits, reached full term and gave birth to a healthy male baby by a normal vaginal delivery. After the delivery, the enoxaparin dose was reduced by $^1/_2$ and continued for six more weeks. After this, the enoxaparin treatment was ended and the oral warfarin sodium treatment began at the necessary dose to keep the International normalized ratio (INR) value at 2.5. The patient still comes for follow-ups and she is problem-free.

DISCUSSION

Hereditary thrombophylic diseases are among the most important causes of the increasing mortality and morbidity in pregnant women and they might cause negative pregnancy complications such as fetal losses in the second or third trimesters, severe intrauterine growth retardation and severe early pre-eclampsia.[4] Women having a factor-V Leiden mutation are under a high risk in terms of maternal thromboembolic diseases. Hence, routine anticoagulant application is suggested during pregnancy and for postnatal DVT prophylaxis for this patient group.[4,5] The most efficient and reliable method of providing prophylactic anticoagulation during pregnancy is using unfractioned heparin or low molecular weight heparin. Since with low molecular weight heparin, there is less need for monitoring and the risk of thrombocytopenia, hemorrhage and osteoporosis are lower, using low molecular weight heparin is more advantageous than using unfractioned heparin.[4] Furthermore, it was also shown that low molecular weight heparin prophylaxis had more positive effects in terms of fetal deaths.[5] In our case with a heterozygous factor-V Leiden mutation, we preferred to use low molecular weight heparin for the DVT treatment and we applied it until the delivery. We planned to complete the treatment in six months by applying oral warfarin for prophylaxis after the anticoagulation therapy with heparin. Preventing the development of DVT will be a much more efficient and also far less risky method than applying treatment after the development of the disease. Unfortunately, genetic diseases like factor-V Leiden mutation are often detected after the development of a DVT. Thus, it might be useful for women of reproductive age with a history of venous thrombosis in their families to be scanned for factor-V Leiden mutation.

In conclusion, using low molecular weight heparin is safe in the treatment and prophylaxis of a DVT that may occur during pregnancy in women with a factor-V Leiden mutation. In pregnant women under known hereditary risk, thromboprophylaxis might be useful even when there is no history of thromboembolism or a symptomatic DVT.

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