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Pregnancy and Behcet's Disease: Obstetric Outcomes of 33 Patients

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ABSTRACT:

Pregnancy and Behcet's Disease: Obstetric outcomes of 33 patients

Objective: Behcet's Disease is a chronic multisystemic inflammatory vasculitis and presents with relapsing-remitting oral and genital ulcers accompanied by iridocyclitis. Although Behcet's Disease affects people worldwide, it is seen commonly in Mediterranean, Middle East and Far East.

Material and Methods: We retrospectively reviewed 33 cases of Behçet's disease with antenatal follow-up and deliveries performed between January 2012 and May 2017 in the department of obstetrics and gynecology, division of perinatology of our hospital.

Results: We observed that 27.2% of patients did not need treatment, while 72.8% of patients had colchicine, azathioprine, prednisolone, interferon-alpha, adalimumab and combination of these drugs as medical treatment. Only 8 of the 33 patients (24.2%) had relapse during follow-up period. Mean gestational age at time of delivery was 38.5±2.6 weeks of gestation and the mean birth weight was 3244±681 grams. Preterm delivery rates before 37 and 34 weeks of gestation were observed in 9% and 3% of patients, respectively. Intrauterine growth restriction (IUGR) was observed in three cases (9%) and there was only one case (3%) of preeclampsia.

Conclusions: Behcet's Disease is not associated with unfavorable outcomes in pregnancy in most of the cases. Disease is in remission stage in most of the cases. Adverse effects of the medications on fetus, used to treat Behcet's Disease were not observed. Hence, Behcet's Disease affect women of childbearing age, it will continue to be an issue in pregnancy. Large-scale prospective controlled studies where information is based on more robust bases are needed to determine the pregnancy outcomes in Behcet's Disease.

Keywords: Behcet's Disease, pregnancy, vasculitis

ÖZET:

Behçet Hastalığı ve gebelik: 33 olgunun gebelik sonuçları

Amaç: Behçet hastalığı tekrarlayan oral ve genital ülserlere eşlik eden iridosiklit ile prezente olan multisistemik kronik inflamatuar bir vaskülittir. Behçet Hastalığı tüm dünyada görülse de bazı bölgelerde özellikle Akdeniz bölgesinde, Orta Doğu'da ve Uzak Doğu'da daha sık görülmektedir.

Gereç ve Yöntemler: Hastanemizin kadın hastalıkları ve doğum anabilim dalı perinatoloji bilim dalında Ocak 2012-Mayıs 2017 tarihleri arasında antenatal takipleri ve doğumları gerçekleştirilen 33 Behçet hastalığı olgusu retrospektif olarak irdelendi.

Bulgular: Gebelerin %27.2'sinde tedavi gereksinimi yok iken %72.8'sine medikal tedavi uygulandığı saptandı. Medikal tedavi olarak kolşisin, azatioprin, prednizolon, interferon alfa, adalimumab ve bunların kombinasyonunun kullanıldığı görüldü. Olguların 8 tanesi (%24.2) gebelik sırasında atak geçirdi. Ortalama doğum haftası 38.5±2.6 ve ortalama doğum kilosu 3244±681 gram olarak saptandı. Otuz yedi ve 34 gebelik haftasından önceki doğum oranları sırasıyla %9 ve %3 olarak tespit edildi. Üç olguda (%9) FGK ve 1 olguda (%3) preeklampsi geliştiği gözlendi.

Sonuçlar: Behçet hastalığı gebelikte genellikle olumsuz obstetrik sonuçlara neden olmayan selim seyirli bir hastalıktır. Hastaların büyük bir çoğunluğunda hastalık remisyonda veya sessiz seyreder. Hastalığın remisyonu için kullanılan ilaçların fetus üzerinde olumsuz etkisine rastlanılmamıştır. Görülme yaşı itibari ile gebe popülasyonda karşımıza çıkmaya devam edecektir. Bilgilerin daha sağlam temellere dayandığı geniş ölçekli prospektif kontrollü çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Behçet Hastalığı, gebelik, vaskülit

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INTRODUCTION

Behcet's Disease is a chronic multisystemic inflammatory vasculitis, presenting with relapsing-remitting oral and genital ulcers accompanied by iridocyclitis. This classical symptom triad was originally described by Hippocrates, but in 1908 it was redefined by Blüthe (1,2). However, after being defined in 1937 as a separate clinical entity by Hulusi Behçet, (3) a Turkish dermatologist, it was named as Behçet's Disease. In addition to the initial definition, arthritis, thrombophlebitis, erythema nodosum, gastrointestinal lesions, central nervous system lesions, epididymitis, vascular injuries and hypercoagulability have also been observed to be associated with different patterns of illness. In 25% of patients, the effect on the vascular system is in both the arterial and venous pattern, whereas the pulmonary vascular system is affected in 5% of the patients (4,5).

Although the etiology is not completely known, it is histopathologically characterized by vasculitis and vasculitis is present in all affected organs. Autoimmune agents, microbial origin and human leukocyte antigen HLA-B51-related immunogenetic predisposition are the mechanisms suggested for the pathology of the disease (4,6). Although Behçet's disease is seen all over the world, it is more common in some regions, especially in the Mediterranean region, Middle East and Far East. The prevalence in Turkey is at the highest level with a rate of 80-370 in 100,000. The prevalence in Japan, Korea, China, Iran, and Saudi Arabia is 13.5-20 in 100,000, while the prevalence in Western countries is even lower. In the United States, the prevalence is 0.12-0.33 in 100,000 (6). Behçet's disease is often seen in the third decade of life and twice as often in men than in women. Familial cases have been reported very rarely, suggesting that genetic factors do not play an important role in the development of the disease (4).

In the literature, Behçet's disease and data associated with the progression in pregnancy are based on observational studies, and in addition, the data are restricted and conflicting. The aim of our study is to investigate the maternal and fetal outcomes, to investigate the effect of pregnancy on the course of Behçet's disease and to evaluate the prognostic factors affecting the obstetric outcomes.

MATERIAL AND METHOD

We retrospectively reviewed 33 cases of Behçet's disease with antenatal follow-up and deliveries performed between January 2012 and May 2017 in the department of obstetrics and gynecology, division of perinatology of our hospital. Behçet's disease was diagnosed according to 1990 International Study Group criteria. In addition to oral ulcers, patients with at least two of the following factors such as genital ulcers, the typically identified eye lesions and positive pathergy test, were included in the study (7).

The demographic characteristics of the patients, obstetric history, age of diagnosis, duration of illness, number of attacks, drug use, arterial blood pressure follow-up, complete blood count and biochemistry parameters, umblical artery doppler parameters were extracted from medical records. As outcomes of pregnancy, delivery type, preterm delivery, presence of intrauterin growth restriction (IUGR), preeclampsia and fetal losses were evaluated. Data was obtained from the medical records of the newborns.

Preeclampsia was defined as the proteinuria (>300 mg/day) and hypertension occuring after 20th weeks of pregnancy; IUGR as the birth weight to be below the 5th percentile; premature birth as births before the 37th gestational week; and fetal loss as intrauterine fetal deaths after 22 weeks of gestation. The exacerbation of Behcet's disease was defined as the presence of new symptoms or the increase in the frequency of symptoms in a way that would cause a change in the treatment approach.

The study was conducted following the approval of the local ethics committee. Analysis of data was performed using SPSS statistical program package, version 17.

RESULTS

Clinical features of the cases are shown in Table-1. The mean age of the patients was 31.6±5.1 years and the nulliparity rate was 21.2%. One, two and three or

Table-1: Clinical features of the cases

Klinik özellikler	n= 33	%
Age (Mean±sd)	31.6±5.1	
Nulliparity	7/33	21.2
Abortus story		
1	9/33	27.2
2	1/33	3
≥3	2/33	6
Smoking	5/33	15
Age at diagnosis	24.8±4.8	
Duration of disease (years)	6.4±2.9	
Patients with an attack during pregnancy	8/33	24.2
No treatment	9/33	27.2
Colchicine	12/33	36.3
Prednisolone	3/33	9
Azathioprine	4/33	12.1
Colchicine+Azathioprine	2/33	6
Prednisolone+Colchicine	1/33	3
Colchicine+IFN alpha	1/33	3
Adalimumab	1/33	3

Table-2: Obstetric and perinatal outcomes of the cases

Obstetric and perinatal outcomes	n= 33	%
Gestational age at birth (Mean±sd)	38.5±2.6	
Birth weight (Mean±sd, gr)	3244±681	
Cesarean delivery	13/33	39.3
Low birth weight	3/33	9
Preeclampsia	1/33	3
Preterm birth		
<37 weeks	3/33	9
<34 weeks	1/33	3
Fetal loss	1/33	3

more previous abortions were observed in 27.2%, 3% and 6% of the patients. The mean age of diagnosis and duration of the disease was 24.8±4.8 years and 6.4±2.9 years for patients with Behçet's disease.

Nine (27.2%) of the patients din't need treatment, while others had colchicine, azathioprine, prednisolone, interferon-alpha, adalimumab and combination of these drugs as medical treatment. Twelve (36.3%) of the cases were treated with colchicine alone. Eight of the cases (24.2%) had attacks during pregnancy. One of the cases who had attack was not getting any treatment during pregnancy and had an arthralgia attack. Three of the other 7 cases had uveitis, and others had vascular attack, gastrointestinal system-associated attack, genital ulcer and arthritis attacks.

The obstetric and perinatal outcomes of the cases are shown in Table-2. Mean gestational age at birth was 38.5±2.6 weeks and mean birth weight was 3244±681 grams. Birth rates before 37 and 34 weeks of gestation were 9% and 3%, respectively. Intrauterine growth restriction (IUGR) in 3 cases (9%) and preeclampsia in 1 case (3%) were observed.

DISCUSSION

Behcet's disease is a vasculitis most commonly affecting ethnic groups in Mediterranean and East Asia, and most commonly seen between the 20-35 age group (8). In our study, the mean age was 31.6 years, which is consistent with the literature. Therefore, it is possible to say as a result that Behçet's disease affects the patients in the reproductive period. Even though there are studies showing that abortus rate increases in the presence of Behçet's Disease, there is no data in the literature to make a definite judgment in this regard and the results are contradictory. These contradictory results can be explained by different number of patients between the studies and different characteristics in the case control groups.

In our study, only two cases (6%) had 3 or more previous abortion. No abortion was observed among patients. The effect of Behcet's disease on abortion is contradictory. The mean age at the time of diagnosis and duration of disease were found to be 24.8 years and 6.4 years, respectively. In a study conducted by Iskender et al. (9) in 2014, the mean age of disease was 21.4 years and the duration of disease was 7.2 years. Our results were in concordance with the literature. Behçet's disease is the problem of women of childbearing age and will continue to be faced during pregnancy.

Even if the prognosis in Behçet's disease during pregnancy is variable, we observed that 24.2% of the patients had an attack during pregnancy. In a study conducted by Uzun et al. (10) with 44 pregnant cases accompanied by Behçet's disease in 2003, 27.3% of the cases were found to be exacerbated. This rate was 8.3% in the study of Iskender et al., whereas it was 15.5% in Jadaon et al.'s study (9,11). In the context of our study, we also believe that Behcet's disease will show a lower rate of exacerbation during the pregnancy, and it will

course in the same way in the majority of patients, or will be under remission.

Studies have shown that Behçet's disease does not cause major obstetric problems such as preeclampsia, intrauterine growth restriction, and neonatal mortality during pregnancy (9,10,12-15). We also found that only 9% of the cases had IUGR and 3% had preeclampsia. When it is considered that preeclampsia is seen in 3-10% and low birth weight newborns are seen in 8% of pregnancies, we can suggest that there was no increase in the adverse obstetric events due to Behcet's disease in our study (16-18).

As in other studies, the most commonly used drug in our study was colchicine. Other medications include steroids and azathioprine. Although colchicine has antimitotic effects, it has been shown to be safe in prospective studies (19). No complications related to the use of azathioprine and steroids was found in other studies and in our study.

In conclusion, Behçet's disease is a disease with mild-course which is not usually associated with adverse obstetric outcomes in pregnancy. In a large majority of patients, the disease is in remission or quiet. Medications used for the remission of the disease are not a serious threat to the fetus. As of the age of onset, it will continue to be confronted in the pregnant population. Large-scale prospective controlled studies are required where information is based on more robust bases.

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