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The relationship between deep vein thrombosis and erythema nodosum in male patients with Behçet's disease

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Abstract. – OBJECTIVE: The pathogenesis of thrombosis in Behçet's Disease (BD) is unknown, however, multiple factors leading to the disease may include hypercoagulability, hypofibrinolysis and endothelial injury. We sought to evaluate the frequency of erythema nodosum-like lesions (ENLL) due to the presence of vasculitis in ENLL observed in BD in male patients with BD with and without deep vein thrombosis. To our knowledge this is the first study to investigate the association of ENLL between the groups with or without thrombosis in only male patients with BD.

PATIENTS AND METHODS: The study included 92 patients, 41 of whom had deep vein thrombosis (DVT) and 51 had no thrombosis that met the international diagnosis criteria for BD. Vascular involvement was diagnosed based on clinical signs; radiological findings from Doppler, ultrasonography and/or angiography computed tomographic or magnetic resonance. ENLL were diagnosed by means of biopsy in suspected cases.

RESULTS: Since both groups were age-matched, there were no statistically significant differences in regard to age ($p > 0.05$). Twenty-four patients (66%) of the DVT group, had ENLL, while18 patients (35%) of the group without DVT had ENLL. In male patients with vascular involvement, the frequency of ENLL was significantly higher than that of male patients without vascular involvement ($p < 0.05$).

CONCLUSIONS: The male Behçet's patients with ENLL compose high-risk patient group in terms of complications, such as DVT. We therefore recommend that male patients with ENLL be monitored more carefully for DVT.

Key Words:
Behçet's disease, Deep vein thrombosis, Erythema nodosum.

Introduction

Behçet's Disease (BD) is a multisystemic vasculitis of unknown etiology characterized by involvement of both arteries and veins and vessels of all sizes. Vascular lesions appear in 10-30% of patients. The most common vascular lesions include superficial thrombophlebitis and involvement of the deep veins of the lower extremities[1]. The pathogenesis of thrombosis in BD is unknown, however, the condition may be induced by multiple factors. The most likely cause is assumed to be endothelial cell injury and/or pathological activation resulting from vasculitis[2,3]. On the other hand, thrombophilic defects may play a role in the pathogenesis of thrombotic events in BD[4-7].

Cutaneous and mucosal symptoms are the most important findings of BD. Of the cutaneous symptoms, particularly erythema nodosum like lesions (ENLL) can be detected as initial symptom and cutaneous and mucosal symptoms appear prior to serious organ involvement in most of the patients. ENLL is observed less frequently particularly in male patients with BD. Observing in males, we assumed that an association might exist between this inflammatory process and serious complications, including deep vein thrombosis (DVT); furthermore, we sought to find out the role of ENLL in the prognosis. Given that vasculitis is identified in ENLLs in BD, the study examined the frequency of erythema nodosum in male patients with BD with and without deep vein thrombosis. The literature contains little data on the association between DVT and ENLL in BD. To our knowledge, this study is the first

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study investigating the relationship between deep vein thrombosis and ENLL in male patients with Behçet's disease.

Patients and Methods

The study included 92 male patients with BD. They were divided into two groups; the first group comprised 41 male patients with DVT (mean age 32.9 years, age range 19-52 years) and the second group was composed of 51 male patients without DVT (mean age 32 years; age range 19-54 years), who were referred to the Department of Behçet's Out-patient Clinic between 2008-2010. Since all the patients in the DVT group were males, the group without DVT were also composed of only males. Behçet's disease was diagnosed in accordance with the criteria of three or more International Study Groups[9]. The Department of Cardiovascular surgery referred the majority of the patients with DVT to Dermatology Department. The patients without DVT were included among Behçet's patients without a history of thrombosis for at least 5 years. Vascular involvement was diagnosed depending on clinical signs, as well as on radiological findings. DVT was diagnosed by color Doppler ultrasonography and consulting a cardiovascular surgeon specialized on BD. A number of biopsies confirmed the diagnosis of ENLL in clinical and suspected cases. The detailed clinical characteristics of each patient were recorded. The Ethics Committee of our hospital gave the approval for the study.

Statistical Analysis

For statistical analysis, the Student-*t* and Chi square tests were used. $p < 0.05$ value was accepted statistically significant.

Results

Since the study group was age-matched, no statistically significant differences were detected between two groups with respect to age ($p = 4.98$, $p > 0.05$). The site of lesions of DVT was lower extremity and all patients were young males. In addition, of the patients with DVT, four had superficial thrombophlebitis, two had sigmoid and transverse sinus thrombosis and one also had abdominal aortic aneurysm. 24 patients (58.5%) in the group with DVT had ENLL, while 18 patients (35.3%) in the group without DVT had ENLL. The patients with vascular involvement had significantly higher frequency of erythema nodosum as compared with the patients without vascular involvement ($p = 0.01$, $p < 0.05$). No statistical significance was detected in patients with and without thrombosis in terms of oral aphtae, genital ulcers, positive pathergy test and joint involvement, whereas presence of ocular involvement in the patient with DVT was statistically significantly higher than that of the group without DVT ($p = 0.002$, $p < 0.05$). Table I shows skin manifestations, positive pathergy test and joint involvement in the patients with and without thrombosis.

Table I. Clinical characteristics of groups with and without thrombosis.

	Group with deep vein thrombosis (N = 41)	Group without deep vein thrombosis (N = 51)	*p*
Male	41	51	2.951
Age (years)	32.9	32.0	4.981
Oral aphthae	41 (100%)	51 (100%)	3.407
Genital ulcer	26 (72.2%)	36 (70.6%)	1.872
ENLL	24 (58.5%)	18 (35.3%)	0.01*
Papulopustular skin lesions	24 (66.6%)	37 (72.5%)	0.763
Positive pathergy test	20 (80%)	29 (56.8%)	2.752
Ocular involvement	21 (41.2%)	5 (13.9%)	0.002*
Joint involvement	6 (16.6%)	13 (25.5%)	0.515

ENLL: Erythema nodosum like lesion.

Discussion

Cutaneous and mucosal findings are the symptoms that are most frequently detected at the onset or in any stage of Behçet's disease and are also extremely important for the diagnosis of the disease. The most frequent initial symptom has been reported to be oral ulcers almost all around the world. The most frequently observed cutaneous symptoms represent erythema nodosum like lesions (15-78%) and papulopustular lesions (50-96%)[10,11]. What is conspicuous is that while patients are being investigated for erythema nodosum, 38.4% of cases are diagnosed with BD, since these patients have other BD findings for almost 4.8 years on average, ENLL is the finding that prime physicians to diagnose BD[12].

The condition is noted most frequently in women on lower extremities as painful nonulcerated erithematous lesions, resolving within 10-20 days without scar formation, but with pigmentation in some cases. It clinically resembles erythema nodosum observed in other diseases. An intense inflammation with prominent lymphocytes is dermatopathologically noted in some cases rich in neutrophils in the subcutaneous tissue. Neutrophilic or lymphocytic vasculitis involving by 50% of venules and arteries is determined in the lesions. Erythema nodosum-like lesions observed in Behcet's disease are different from erythema nodosum in other diseases due to the presence of vasculitis[13-15]. In the light of these data, this study aims to demonstrate the ways for evaluating the frequency of ENLL in male Behçet's patients with and without deep vein thrombosis. Consequently, we detected a statistically significant relationship between ENLL and DVT in our study.

In a recent study from Turkey, Duzgun et al[16] detected the frequency of erythema nodosum at a higher rate in patients with BD with DVT, in compliance with our study. In the same study, a statistically significant relationship was also pointed out between erythema nodosum and ocular involvement. In addition, another studies have also reported an increased incidence of ENLL in patients with venous thrombosis in Turkish population[1-17]. Another study by Silingardi et al[18] showed that no significant differences were found with regard to demographic and clinical characteristics of the patients with and without DVT in a series of Italian patients. The results of that study may be different from ours due to the geographical and gender differences. A variety of other studies demonstrated a statistically significantly higher frequency of pathergy positivity[19], eye involvement[1,19] as well as ENLL in patients with vascular lesions[1]. We were not able to detect a statistically significant relationship between DVT and pathergy test, papulopustular skin reactions and joint involvement. However, our study demonstrated a statistically significantly higher frequency of ENLL and eye involvement in patients with DVT.

Finally, the presence of ENLL in young male patients could be considered to be a factor that could negatively affect the prognosis of the disease in terms of severe complications such as DVT, ocular involvement.

Conclusions

We recommend male patients with ENLL be monitored more meticulously for DVT development; therefore, it is of paramount importance to recognize ENLL.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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