BEHÇET HASTALIĞINDA TROMBOFİLİK FAKTÖRLER VE KLİNİK BULGULARLA BİRLİKTELİĞİ

THROMBOPHILIC FACTORS IN BEHÇET'S DISEASE AND ASSOCIATION WITH CLINIC MANIFESTATIONS

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Özet

Amaç: Behçet hastalığı çeşitli sistemleri etkileyebilen multisistemik bir vaskülittir. Venöz tromboz bu hastalığın temel karakteristik bir özelliğidir. Bu çalışmada BH'da tromboz gelişiminde trombofilik faktörlerin rolü incelendi.

Metod: Bu çalışmaya 23'ü erkek 40 Behçet hastası ve 12'si erkek 20 sağlıklı kontrol vakası alındı. Ayrıca hastalar hastalık aktivitesine göre aktif (n=26), inaktif (n=14) ve vasküler tutulumu olanlar (n=14) ve olmayanlar (n=26) olarak gruplara ayrıldı. Bütün hastalarda ve kontrol grubunda protein C ve S, vWF, AT-III, aktive protein C rezistansı, CRP veESH parametreleri ölçüldü.

Sonuçlar: Hastalar ve kontrol grubu arasında protein C ve S, vWF, AT-III düzeylerinde anlamlı fark tespit edilmedi. Fakat Behçet hastalarında kontrol grubuna göre vWF, aktive protein C rezistansı düzeyleri anlamlı olarak yüksek bulundu ($p<0.0001$). Bu anlamlı fark BH'da bazı hemstatik anormalliklerin varlığını göstermektedir. Bununla beraber bu faktörler vasküler tutlumu olanlarda olmayanlara göre anlamlı bir fark bulunmadı ($p>0.05$). Üstelikyukarıda belirtilen trombofilik faktörler aktif ve inaktif Behçet hastaları arasında da anlamlı fark tespit edilemedi ($p>0.05$). Bütün Behçet hastaları ve kontrol grubu karşılaştırıldığında CRP ve ESH değerleri hasta grubunda anlamlı olarak daha yüksekti.

Sonuç: Behçet hastalığında görülen vasküler trombozun etyolojisini açıklayabilen spesifik bir trombofilik faktör tespit edilememiştir. Hemostazın moleküler marker'larındaki değişiklikler BH'na bağlı gelişen spesifik anormalliklerden çok sistemik bir inflamasyona bağlanabilir.

Anahtar kelimeler: *Behçet hastalığı, Trombozis, Trombofilik faktörler, Fibrinolizis, Hemostaz*

Summary

Objective: Behçet's disease (BD) is a multisystemic vasculitis disorders that may attack several systems. Vascular involvement with thrombosis is one of the basic characteristics of this disease. In this study, the role of thrombophilic factors in the formation of vascular thrombosis was evaluated in BD.

Methods: Fourty patients with Behçet's disease (23 males; mean age: 33,9 ± 8,8, range:18-54 years) and 20 healthy adults (12 males; mean age: 30,9 ± 7,5, range: 20-45 years) were included in this study. Additionally, the patients were grouped and evaluated with respect to the presence vasculary involvement (n:14) or not (n:26) and active (n:26) or inactive disease (n:14) according to the activity of the disease. In all patient and control subjects, protein C, protein S, von Willebrand Factor (vWF), antithrombin-III (AT-III), activated protein C resistance (aPC-R), C-reactive protein (CRP) and erythrocyte sedimentation rates (ESR) were measured.

Results: There was no significant difference between the patients and control cases regarding protein C, protein S and AT-III levels ($p>0,05$). However, vWF, aPC-R, values were significantly higher in the Behçet patients than in the control cases ($p<0,001$). These significant differences indicate the presence of some hemostatic abnormalities seen in BD. Nevertheless, any significant difference was not determined between BD with and without vascular involvement in terms of any thrombophilic factor mentioned above ($p>0,05$). Moreover, there was not any significant difference between active and inactive BD patients for thrombophilic factors ($p>0,05$). In the evaluation of the total patients with BD and control cases, CRP and ESR values were significantly higher in patients group than in the control group ($p<0,001$).

Conclusions: Any specific pathology was not detected in thrombophilic factors which may explain the etiology of vascular thrombosis seen in BD. Alterations in the molecular markers of the hemostasis could be attributed to systemic inflammation rather than being a spesific abnormality of BD.

Key words: *Behçet's disease, Thrombosis, Thrombophilic factors, Fibrinolysis, Hameostasis*

Introductıon

Behçet's disease (BD) is a multisystemic inflammatory disease that can involve more than one system characterizing oral and genital ulcers and uveitis, and developing recurrently and in remission. The etiology of BD is not adequately known at present. Vascular involvement and the thrombosis in this system are among the basic characteristics of this disease (1,2). Venous and arterial involvement occurs in almost 25% (10-37) of patients with BD (1). Thrombosis in venous system occurs more frequently than arterial system. Thrombosis increases in patients with BD. For this reason, the disease is regarded as a hypercoagulable prothrombotic condition (3,4).

The reason of thrombotic tendency in BD is not clear; may studies have been carried out on it. Today endotel cells are known to play vital roles on vascular hemeostatic mechanisms. Endothel cells are effective on procoagulant, anticoagulant, fibrinolyitic, vasomotor tonusand vascular permeability. However, it is thought that endothel cell injury or vasculitis alone is not the reasonfor thrombosis in these patients. It is not totally clear why only thrombosis among vasculitis is common the vasculopathy of BD and why thrombosis is seen in some of BD (5).

Coagulation and fibrinolytic systems, among the compenents of hemostatic systems, are normally in a dynamic balance. Natural anticoagulants (protein C, protein S, antitrombin III) are indispensable to provide the balance between coagulation and anticoagulation. Eliminating the formed fibrin thrombus by fibrinolysis, the structure and function of the tissue is maintained. In healthy person, congenital or acquired lack of any of these anticoagulants cause an increased thrombosis risk. Besides, fibrinolytic activity disorder is thought to develop in vasculitis (3,4,5).

In order to make clear thrombosis, one of the important clinical findings of BD, the relation between anticoagulants, fibrinolytic system, endothel cell injury or disfunction and other thrombophilic factors has not been satisfactorily determined. This study is intended to search the relation among natural anticoagulants, parameters affecting the fibrinolytic system, some trombophilic factors and vasculitis. For this reason, plasma protein C (P-C), protein S (P-S), antithrombin III (AT-III), von Willebrand factor (vWF), active protein C resistance (aPC-R) in BD patient group and the control group of healthy persons was studied.

Material and Methods

This study included 40 patients with BD who were diagnosed to have the disease for the first time or who were under control in departments of internal, dermatology, Eye, and cardiac surgery in faculty of medicine. The patients were aged between 18-54 (33.9±8.8). Of these patients, 17 were female and 23 were male. The duration of the illness of the patients changed between 1-22 years. The BD diagnosis was made according to the diagnosis criteria proposed by international study group for BD (ISG) (6).

20 healthy individuals were included in the study as the control group. This group had important systemic illness previously, had no health problem at the time of study, and showed no patological findings in systemic investigation and physical examination. Thier ages were between 20-45 (30.9±7.5). 8 of them were female and 12 were male.

All the patients included in the study were divided into two groups according to the activiting of the disease. Those patients having at least two of oral aphthous ulser,genital ulcer, eye involvement, skin findings, arthritis, or vascular lesions in the last month prior to the study were accepted to have active BD, and those without any two symptoms in the last month prior to the study were accepted to have inactive BD.

Tablo 1. *Clinical Characteristics of the Patients with Vascular BD*

number of patients	clinical characteristics
7	DVT in lower extremity
1	DVT and surface thrombophlebitis in lower and upper extremity
1	artery aneurysm in upper extremity
1	artery aneurysm and thrombosis in lower extremity
1	cerebral vein thrombosis
1	optical vein thrombosis and surface thrombophlebitis in lower extremity
2	surface thrombophlebitis and DVT in lower extremity

DVT: Deep vein thrombosis

Tablo 2. *Symptoms of Active BD*

symptom	number of patient	%
oral aphtous ulcer	25	96
skin lesion	22	84,6
genital aphtous ulser	15	57,7
eye involvement	11	42,3
patergy test positivity	13	50
Arthritis / arthralgia	12	46
vascular involvement	11	42,3
CNS involvement	1	3.8

CNS: Central Nervous System

This meant that 26 of the patients had active BD, and 14 inactive BD. 10 of the patients with active BD were female, and 16 male. 7 of the patients with inactive BD were female, and 7 were male. With respect of vascular involvement, the patients were divided into two groups: those having vascular involvement and those without vascular involvement.

Group 1: Patients with vascular involvement (n: 14, 2 female, 12 male)

Group 2: Patients with no vascular involvement (n: 26, 15 female, 11 male)

Three of the patients with vascular involvement had inactive BD, and the rest had active BD. When vascular involvement is considered, those patients with previous determined vascular involvement and having vascular involvement determined during the study were included in the analysis. Vascular involvement were determined with doppler ultrasonography, computarized tomography and angiography. A s a result of the findings obtained in this way, 14 patients with vascular involvement and 26 without vascular involvement included in the study. None of the patients included in the study used corticosteroid or immunosupressive drugs when their blood samples were taken.

The total blood count and erythrocyte sedimantation rate of the patient group and the control group were made with standart methods. Besides, their serum C-reactive protein values were studied nephelometrically. After the completion of all these laboratory investigations, blood samples of the patients were taken in the morning before eating anything, from brachial vein. 2 ml venous blood was taken to polistren tubes including 1 ml 0.10 gM trisodium sitrat, and 4 ml to two seperate vacuum tubes with no mixture. The tubes were centrifuged for 10 minutes in 3000 G, were divided as serum and plasma and were stored in deep freze in -80^0 C till the date of the study.

P-C, P-S, AT-III, aPC-R and vWF were detected in the reseach laboratory. All these parameters was automatically studied with STA Compact coagulation System (Diagnostica Stago, France). STA staclot Protein C kit (Diagnostica Stago) was used fpr P-C. Normal plasma limitsfor P-S are 60-140%. STA Liatest vWF kit (Diagnostica Stago) was used vWF. Normal levels of vWF in plasma are 50-160%. STA-staclot aPC-R kit (Diagnostica Stago) was used for aPC-R. Normal limits for aPC-R in plasma are 120-300.STA-stachrom AT-III kit (Diagnostica Stago) was used for AT-III. Normal plasma limits for AT-III are 80-120. Thrombin time was measured automatically simultanously in the same apparatus. Normal value of thrombin time is 70-100% and INR (International Normalized Ratio) is 0.9-1.1.

Data were given as mean ± standart deviation. For statistical evaluation, student's test, Mann-Whitney U test, and Pearson correlation coefficient were used. P values <0.05 were accepted as statistically significant. SPSS Windows version 8.0 software was used for statistical analyses.

Results

43% (17/40) of BD patients were female and 52% (23/40) were male. 40% (8/20) of the control group were female and 60% (12/20) were male.Male/female ratio was 1.2. The duration of the illness of the patients included in the study changed between 1-22 years. The average period was 8±5 years. 14 (35%) of the patients had vascular involvement, 2 (14%) of the patients had vascular involvement were female and 12 (86%) were male. 14% of the patients had arterial, and 86% of them had venous involvement. Clinical characteristics of the patients with vascular involvement are shown in table 1.

Symptoms belonging to patients with active BD are summarized in table 2. Minor oral aphtous ulcer recurring from time to time in inactive patient group wes determined in 9 patients.

Tablo 3. *Mean Values Etween all BD Patients and Control Group*

parameter	BD	control	p
P-C	117,6±28,4	124,9±17,9	p>0,05
P-S	82,6±28,9	90,8±20,5	p>0,05
vWF	133,1±54,5	65,0±35,5	P<0,001*
aPC-R	141,7±28,4	181,4±41,5	P<0,001*
AT-III	117,6±11,1	110,9±12,7	p>0,05
CRP	1,5±0,7	0,4±0,2	P<0,001*
ESR	35,9±27,9	20,7±9,1	P<0,001*

**Results found to be statistically significant*

Tablo 4. *Comparison of Thrombophilic Factors Between Active and Inactive Patient Groups*

thrombophilic parameters	active BD (n:26)	inactive BD (n:14)	p
P-C	114,8±33,1	122,9±16,4	p>0,05
P-S	79,9±27,6	87,7±31,5	p>0,05
vWF	140,9±53,4	118,7 ±55,4	p>0,05
aPC-R	138,9±34,0	147,0 ±12,0	p>0,05
AT-III	119,5±9,6	114,0±13,0	p>0,05

For each group study, the mean of P-C, P-S, AT-III, aPC-R, C-reactive protein (CRP) and erythrocyte sedimantation rate values was assessed statistically.

When all BD patients and control group were evaluated, while P-C activity was found to be between 45-180% (117.6±284) in BD patients, it was 88-150% (124.9±17.9) in control group. While P-S activity was 36-140% (82.6±28.9) in BD patients, it was 60-123% (90.8±20.5) in control group. While vWF activity was 51-276% (133.1±54.5) in BD patients, it was 18-122 (65.0±35.5) in control group. While aPC-R level was 73.8-246.3 (141.7±28.4) in BD patients, it was 92-276 (181.4±41.5) in control group. While AT-III activity was 87-135% (117.6-11.1) in BD patients, it was 77-126% (110±12.7) in control group. CRP level was 0.05-6.2 (1.5±0.7) in BD patients and 0.01-1.4 (0.4±0.2) in control group. ESR level was found to be 8-89 mm/h (35.9±22.5) in BD patients, and 5-35mm/h (20.7±9.1) in control group.

2 of the BD patients had P-C activity and 8 of BD patients had P-S activity below normal. Both patients with lower P-C activity had thrombosis history. 4 of the 8 patients with lower P-S activity had thrombosis history. None of the control group had P-C and P-S levels below normal. While all BD patients had lower P-C and P-S levels compared with control group, this difference was not statistically significant (p>0.05). AT-III levels were at normal levels in BD patients. In control group, 1 person had AT-III level slightly below normal, which was not clinically important. There was no statistically significant difference for AT-III activity between BD patients and control group.

vWF activity was significantly higher ib BD patients than control group (p<0.001). aPC-R was detected in 7 of the BD patients and 1 of the control group (18% vs 5%). 4 of the 7 (57%) patients with aPC-R had thrombosis history. aPC-R was found to be significantly lower in BD patients than control group (p<0.001). CRP and ESR levels in BD group was found to be higher than those in control group, and this difference was statistically significant. Mean values and comparison of the parameters for all BD patients and control group are shown in Table 3.

We could not find any significant difference between thrombophylic factors between group 1 and group 2 (p>0.05). The comparison of active group and inactive group is shown in Table 4.

In the active patient group ESR changed between 10-89 mm/h (Mean:45.7±21.8), and CRP value was between 0.05-6.20 (mean2.2±0.9) In the inactive patients group, ESR changed between 8-38 mm/h (mean 17.7±8.1), CRP level was between 0.24-0.80 (mean 0.4±0.1). ESR and CRP values were statistically different in the active and inactive patient groups and it was significantly higher in the active patient group (p<0.001) (Table 5).

We could not find any significant difference between thrombophylic factors between group 1 and group 2 (p>0.05). The comparison of group 1 and group 2 is shown in Table 6.

While mean ESR value in group 1 BD patients was 48.0±24.6, it was 29.4±18.7 in group 2, and this difference was found to be statistically signifcant (p<0.001). Besides, CRP values between group 1 and group 2 was statistically signifcant (p<0.001).

Mean CRP value was found to be 2.6±1.2 in group one, and 0.9±0.5 in group 2. The comparison of ESR and CRP is given in Table 7. BD patients with vascular involvement were 11 as regards active patients clinically in group 1.

There was no statistically significant difference between parameters in BD patients and the control group (p>0.05). There was positive corelation between P-C and P-S (r=0.469, p<0.01), and between ESR and CPR (r=0.704, p<0.001) when the relation between the parameters were analyzed.

Table 5. *Comparison of ESR and CRP in Active and Inactive Patient Group*

patient group	ESR	CRP	p
active BD	45,7±21,8	2,2±1,9	p<0,001*
inactive BD	17,7±8,1	0,4±0,1	p<0,001*

** Results found to be statistically significant*

Tablo 6. *Comparison of Thrombophylic Parameters Between Group 1 and Group 2*

parameters	group-1	group-2	p
P-C	112,0±38,6	120,6±21,4	p>0,05
P-S	82,7±34,8	82,6±25,9	p>0,05
vWF	154,9±59,4	121,4±48,8	p>0,05
aPC-R	134,9±22,4	145,4±30,9	p>0,05
AT-III	118,2±9,3	117,3±12,1	p>0,05

Discussion

Vascular ivolvement is an important characteristics of BD and can occur in all kinds and sizes of veins. Clinically, thrombosis in veins and arteries, and arterial aneurysm are the most noteworthy forms (7). The most common form is venous thrombosis (1,6,7,9). The prevalance of vascular involvement changes between 7.7-40 %. Vascular involvement is more common in men then in women (1,7,10). In our study, vascular involvement was observed in 35% (14/40) of the patients with BD. Venous thrombosis was diagnosed in most of the patients with BD. However, in studies in Japan (11) and North America (12) more arterial complications than venous lesions were reported in BD. Of those with vascular involvement in our study, 12 (86%) were male and 2 (14%) were female. Male/female ratio for patients with vascular involvement was 6 in our study. Vascular involvement is mostly detected in the lower extremity (1,2). In our study, too, it was mostly in the lower extremity (Table 4).

There have been many studies to explain the hypercoagulable prothrombotic condition of BD. Basicly, three systems are suggested to explain the thrombosis in BD: vein endothel, coagulation system, fibrinolytic system. In which system, most patology causes thrombosis is still unknown (4,5,13,14). Vascular endothel cells play an important role to protect cells from thrombosis. Vascular endothel cells has procoagulable, anticoagulable, and fibrinolytic features. Although the antibody was detected primarily in BD, it couldn't be regarded as the evidence of cytotoxisity (15). In use of ELISA test, antiendothel cell antibody prevalence was found to be higher in BD and the existence of these antibodies was in correlation with clinical activity. Endothel cell injury or pathological activity was evaluated as a characteristic features of BD (16,17). vWF is synthesized from endothel and has a function in the aggregation of thrombosis and stabilization of factor-VIII. The increase in vWF level provides the protection of Factor-VIII from degradation and increases its function (18). Almost all studies reported increaseed vWF level in BD (3,19,20). Studies suggest that high vWF level is due to endothel injury (21). In our study, vWF level was found to be significantly higher in BD than the control group ($p<0.001$).

A lot of studies have reported that vWF and tPA levels sysnthesized from endothel cells increase in BD than control group. Demirer et al. reported that tPA and vWF level was significantly higher in 127 BD patients than the control group of 24. They also found tPA and vWF levels in BD patients with thrombosis higher than other BD patients (19). It has also been reported that thrombomodulin concentration, an endothel injury marker, increases in BD (22). Researchers have reported that the increase of vWF and tPA levels in BD results from endothel cell injury (319,22). Our findings also support this proposition. The lack of P-C, P-S and AT-III, which are natural anticoagulant, is an important risk factor for thrombosis. Studies on P-C and P-S in BD heve revealed different results. Bayraktar et al. reported a BD case with intestinal infarcts and lack of P-C (23). O. Chafa et al. reported the case of a BD patient with P-S deficiency. They suggested that first hemostatic investigation should be made to find out additional causes of thrombosis when thrombotic occurences are seen in BD (24). Guermazi et al. found in a BD group of 30 patients, while P-C lavels were normal, P-S level was significantly lower compared with the control group. In the same study, antibody resistant the P-S was detected in half of the patients with decreased P-S activity, and authors proposed that autoimmune P-S deficiency might occur in thrombosis pathogenesis in BD. Fusegawa et al. found that P-C and P-S levels increased in a BD group of 20 (25). Contrary to this report, Hampton et al. found P-C level to be lower in 18 BD patients with active thrombosis (3). Lenk et al. found P-C and P-S levels to be normal in 18 BD patients without active thrombosis and not receving anticoagulant treatment (26). Mader et al. found P-C and P-S levels to be normal in 25 patients with active BD. 8 of those patients had thrombosis history (15). Nalcacı and Pekcelen found P-C, P-S, and AT-III levels to be normal in 35 BD patients (27). Houman et al., in their study including 113 BD patients, reported 43% vascular involvement and found P-C, P-S, and AT-III levels to be normal in all patients (10).

Table 7. *Comparison of ESR and CRP Between Group 1 and Group 2*

	ESR	CRP	p
group-1	48,0±24,6	2,6±1,2	P<0,001*
group-2	29,4±18,7	0,9±0,5	P<0,001*

** Results found to be statistically significant*

In the study carried out by Fusegawa et al, all BD patients had active thrombosis and increased D-dimer and increased thrombin-antithrombin complex were measured. Increased P-C activity could be expected in such patients and secondary changes more than primary hemostatic abnormalities must be considered. Hampton et al. found lower P-C levels in BD patients than the control group but none of the values below normal rate. They concluded that this difference does not have any functional importance (3). Nalcacı and Pekcelen found AT-III level lower in 40%, P-C level in 17%, and free P-S level 42.8% in their study with 35 BD patients and control group of 10. However, they could not find any statistical difference between BD group and control group (29). Other studies have reported that no change has occured between P-C and P-S levels (15,28).

In our study P-C level was below normal in 2 and P-S levelwas below normal in 8 BD patients. But this difference was not statistically significant (p>0.05). No statistically significant difference could be found in any study between P-C and P-S levels between those with and without vascular involvement (p>0.05).

Since vasculitis is a basic pathological condition in BD, anticoagulation factor abnormalities rather than primary abnormalities are probable to result from less production or more consumption caused by defective inhibitor of activated coagulation factors. AT-III deficiency affects primarily venous system and has 50% venous thrombosis (20). Fusegawa et al. and Özoran et al found AT-III level to be lower in active BD (20,24). Şengül et al. found AT-III level to be higher (28). Demirer et al. found prothrombin fragment 1+2 and AT-III level to be normal (19). Other studies reveal no significant changes in BD (3,14,27). We could not find changes below or above normal level as regards AT-III levels in the patient group. There was no statistical difference a AT-III level between BD group and control group, between BD group divided according to vascular involvement, and between active-inactive patient groups (p>0.05). These results are in line with most studies.

aPC-R is often a hereditary defect and is related with idiopathic venous thrombosis (18). In most of the cases point mutation in aPC-R Factor V is the phenotypical apperance of these cases (5). Mutant Factor V inhibits aPC more and decreases thrombin inhibition. When thrombin inhibition decreases it turns into fibrinogen to fibrin. This genetic coagulation defect may be as high as 37.5% of BD patients with deep venous thrombosis history (29). Or may be lower to an extent not to be detected in any patient (30). Similarly, while Factor V Leiden mutation was significantly higher in BD patients, there was no significant difference between patinets with and without vascular involvement (31).

aPC-R was detected in 7 of the 40 BD patients in our study (17.5%). It was detected in 1 person in control group (5%). 4 of the patients with aPC-R had thrombosis history. This difference between control group and BD group was found to be statisticlly significant (p<0.001). However, there was no statistically significant difference between those with and without vascular involvement.

Koşar et al. found aPC-R in 17 patients (29.3%) in BD group of 38. In healthy control group, this ratio was only 5%. 6 of the patients with aPC-R had thrombosis history (32). Öner et al. detected aPC-R in 22.7% of BD patients and 7.1% of the control group in their study on 44 BD patients (33). Altınbaş et al. reported this rate to be 22.5 in 43 BD patients (34).

Gül et al. found Factor V Leiden mutation in 32 BD patients (without thrombosis), 32 BD patients (with thrombosis), and control group of 107 to be 9.4%, 37.5%, and 10.3%, respectively (29). Contrary to these results, Germazer et al. found aPC-R frequency in 65 BD patients, a control group of75 and 70 patients with isolated thrombosis to be 9.5%, 10.6%, and 30%, respectively (35).

aPC-R is more common in European population and seldom in American, African and Japanese population due to Factor V mutation (18). Studies in Turkey have always revealed that aPC-R increases and Factor V Leiden prevalance is high. However, studies in Israel and Tunusia have reported no increase (14,35).It may be possible to attrribute various prevalances to genetic variations of study groups with different ethnic origin.

Yet, heterozigot polimorphism Factor V Leiden is common in our general population and thus aPC-R frequency may be just a coincidence. Besides, vacsular occlusion is not common BD with Factor V mutant, and this may be in concordance with the above view. aPC-R was found to be high like other findings coming from other parts of Turkey. This difference was found to be statistically significant between BD group and control group (p<0.001). But,

we could not find any difference between the cases and without thrombosis.

As a result, this study reveals that there are some hemeostatic abnormalities in BD. Changes in coagulation and fibrinolytic system shows that there is a hypercogulable prothrombotic condition in BD. That P-C, P-S, and AT-III deficiencies were found to be high levels in BD compared with the control group,but vWF and aPC-R at higher levels, makes us think that they may cause a hypercoagulable condition affecting other. The basic patological feature of the disease is vasculitis. The higher rate of vWF supports the occurence of vascular inflammation. Vascular inflammation may be the reason that starts or increases hemeostatic process.

The thrombotic vasculopathy of BD may occur as aresult of the co-existence of many risk factors. No spesific patological laboratory findings have not been defined for BD. In our study, there were no spesific patological abnormalities to explain the etiology of the thrombosis seen in BD.

Changes in hemeostatic parameters may be thought to result from systemic inflammation rather than the spesific abnormalities of BD. However, the existence of coagulopathy at the top of a vasculitis process may be worsening factors that contributate occlusive happening with the sinergic affect the thrombolytic factors. None of the abnormalities detected had correlation with clinical findings.

It will be understood, considering the complexity of the subject, that many more studies are to be carried out in order to explain the factors playing role on the formation of venous thrombosis in BD.

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