

ORIGINAL ARTICLE

VASCULAR COMPLICATIONS OF BEHÇET'S DISEASE

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Background- This study was conducted to identify the frequency of vascular complications in patients with Behçet's disease (BD) and to determine the average time period between disease onset and development of complications.

Methods- Vascular findings of 343 patients with BD referred to the Behçet's Disease Research Clinic of Namazee Hospital in Shiraz, South West Iran were assessed over a 6-year period. Data was extracted from the medical records of each consecutive patient. Doppler sonography, computed tomography, digital subtraction angiography and/or conventional angiography were done in cases of positive clinical findings.

Results- The records of 343 patients (mean age, 34.4 ± 7.1 years, 235 females, 108 males) with BD were analyzed, and 113 vascular events in 48 (14%) patients (mean age, 31.5 ± 7.5 years, 16 females, 32 males) were assessed. The interval between the onset of BD and the appearance of vascular complications was 5.9 ± 5.1 years. Venous and arterial complications were found in 8.2% and 5.7% of patients, respectively. Combined arterial and venous complications were detected in 16 (4.6%) patients. Erythema nodosum-like skin lesions were seen in 69% of the patients with vascular involvement compared to 13.6% of patients without vascular involvement. The presence of one vascular complication increased the chance of developing another major vessel complication in the same patient ($p < 0.001$) with relative risks of 114 for arterial and 18 for venous sites.

Conclusion- Vascular complications of BD are common and might occur on average 5-6 years after the onset of the disease. Both arteries and veins are involved and multiple vascular complications are common.

Keywords • Behçet's disease • erythema nodosum • vascular complications

Introduction

Behçet's disease (BD) is a multisystem inflammatory disorder characterized by mucocutaneous, genital, acne-like and erythema nodosum-like skin lesions. Uveitis, CNS involvement and vascular complications are also evident. The vasculopathy of BD is distinctive among the vasculitides in that it involves both arteries and veins of all sizes. Vascular lesions include superficial thrombophlebitis, complete occlusion of the superior and inferior vena cava and arterial aneurysm formation.¹

In the present study, we report a variety of

vascular complications in patients with BD from Shiraz, Southwest of Iran.

Patients and Methods

The records of patients with BD from 1992 to 1998 at the Behçet's Disease Research Clinic of Namazee Hospital in Shiraz, Iran, were reviewed. Patients who were hyperlipidemic, diabetic or heavy smokers were excluded from the study.

Data were extracted from the medical records of each consecutive patient with BD. The patient's history and the notes on the physical examination were reviewed with special attention to the vascular system signs, in the first as well as in subsequent follow-up visits (like thrombophlebitis, skin manifestations and pulmonary vasculitis). Data were recorded according to our protocol and

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later analyzed. In patients with abnormal vascular findings, radiologic evaluations were performed using Doppler sonography, computed tomography (CT) and digital subtraction, and conventional angiography of suspected sites.

The analysis of data was performed by using Fisher's exact test and student's *t*-test.

Results

A total of 343 patients with BD (235 females, 108 males, mean age, 34.4 ± 7.1 years) among whom 48 (14%) patients (16 females, 32 males, mean age, 31.56 ± 7.55 years) had vascular complications (Tables 1 and 2).

Males had twice the chance for developing vascular manifestations in comparison to females. Among the 48 patients with vascular involvement, the duration of vascular complications at the time of study ranged from less than 1 year to 16 years, without any mortality. No significant correlation existed between duration of BD and the interval needed for development of vascular complications.

Of the 113 vascular complications, 96 were venous and 17 were arterial events. Venous events included superficial thrombophlebitis (Tables 3 and 4) and deep venous thrombosis (DVT) of the lower extremities or other deep veins (Table 4). Arterial complications were mostly aneurysmal and thrombotic in type (10 and 7 cases, respectively) and involved many arteries, mostly the pulmonary arteries. Femoral, brain and coronary arteries were also involved in our patients (Figure).

Venous thrombosis was more common than arterial thrombosis, and arterial aneurysms were more common than arterial occlusion. Combinations of multiple arterial and venous lesions occurred in 16 (4.6%) patients with vascular involvement. Another interesting observation was that 71% of the patients with superficial thrombophlebitis also had DVT at another site and 6.3% of them had no other vascular lesions. In contrast, in only 1.5% of patients with DVT, superficial thrombophlebitis was not seen ($p < 0.001$).

Superficial thrombophlebitis increased the risk

Table 1. Age distribution and duration of disease in and duration of disease in patients with Behçet's disease at various periods

	Female (n = 235)	Male (n = 108)
Mean age at onset (year)	32	31
Minimum and maximum age at time of vascular complication (years of range)	19–50	17–45
Mean time interval between onsets of BD and vascular complications (years of range)	5.3 (0.6–17.2)	6.2 (0–17)
Mean duration of disease at time of study (years of range)	9.6 (3–20)	10.2 (0.66–22)

of DVT in other sites in the same patient by 11 times. Furthermore, 24% of patients with DVT of the lower extremities had concomitant thoracic venous or arterial lesions, and 50% had concomitant intra-abdominal DVT.

The presence of one vascular complication increased the probability of developing another major vessel complication. The relative risk for arterial site is 114 and for venous site lesion is 18. Recent major vessel involvement in these patients was treated with 1 mg/kg of oral prednisolone pulse, with 1 to 2 mg/kg of oral cyclophosphamide per day for the first 1 to 2 months, after which appropriate maintenance therapy was given for the next 1 to 2 years. Anticoagulants with warfarin were included for patients with thrombosed vessels, in the absence of aneurysmal arteries.

Surgical management included two successful femoral aneurysmectomies and a Teflon graft insertion for an aortic aneurysm in one patient² and a pulmonary lobectomy for a patient with hemoptysis due to an arterial aneurysm fistula into the bronchus.

Skin manifestations, in form of erythema nodosum-like skin lesions were seen in 69% of the patients with vascular complications compared to 13.6% of erythema nodosum in patients without vascular involvement.

Males had twice the rate of vascular manifestations as females ($p < 0.0001$). Other clinical manifestations such as positive pathergy

Table 2. Vascular complications in 48/343 patients with Behçet's disease (BD).

Sex	No. of patients with vascular complications (%)	Total BD-cases	Vascular complications as % of total cases
Female	16 (33%)	235 (68.5%)	6.8% (16/235)
Male	32 (67%)	108 (31.5%)	29.6% (32/108)
Total	48 (100%)	343 (100%)	14.0% (48/343)

Vascular Complications of Behçet's Disease

Table 3. Superficial thrombophlebitis in 48 patients with vascular manifestations of Behçet's disease.

Sex	No. of patients	Frequency of patients with vascular manifestations	Frequency in all BD patients (n = 343)
Female	7	14.5%	3%
Male	17	35.5%	16%
Total	24	50%	19%

tests, uveitis and skin lesions were also observed. Positive pathergy tests with disposable 21 G needle were observed in 83.3% of patients with vascular involvement and 69% of all 343 patients. Uveitis had no statistically significant relation with vascular complications in the patients with vascular involvement ($p = 0.6$).

Discussion

Vascular involvement of BD affects both arteries and veins of all sizes. A wide range of vascular involvement (7%–29%) has been reported in the literature and accounts for most of the deaths due to BD. Among the arterial lesions, which are estimated to be up to 3.6% of all vascular lesions, about 2/3 are aneurysms, often multiple, and 1/3 are thrombotic.^{1,3} Davatchi et al found 308 (8.9% ± 1%) patients with vascular manifestations of Behçet's disease among 3,443 Iranian patients with BD.⁴ The vascular manifestations included phlebitis (6.3%, 217/3443), large vein thrombosis (1%, 34/3443), arterial thrombosis (2 patients) and aneurysms (9 patients).⁴ In another study, Koc et al, studied the prevalence of large vessel arterial and venous lesions in 137 Turkish patients and showed that 49 patients had arterial lesions, 181 had venous lesions and 498 had combined arterial and venous lesions. They also showed that DVT of the extremities or trunk and intracranial venous sinus thrombosis, often accompanied superficial thrombophlebitis in 30% to 40% of patients.⁵

Our findings reconfirm previous reports that the duration of BD has no significant relation to vascular complications.^{6,7} Nonetheless, we found a



Figure. Multiple pulmonary artery aneurysm and pulmonary artery thrombosis.

significant correlation between the presence of superficial thrombophlebitis and development of DVT in other sites ($p < 0.001$). These findings are similar to those reported by Koc et al.⁵ Despite the poor prognosis of patients with BD and the presence of aortic or pulmonary artery aneurysms in BD patients,⁵⁻⁷ no mortalities occurred in our study.

Most other clinical manifestations, such as uveitis, had no statistically significant relationship with the presence of vascular complications. The only exception was a skin manifestation in the form of erythema nodosum-like lesions, which occurred in 69% of patients with vascular complications of BD compared to only 13.6% of patients without vascular manifestations of BD.

It can be concluded that vascular complications in BD are common, fatal and often involves multiple vessels. The frequency and the pattern of vascular complications in this study were not found to be significantly different from other countries. Although there is no association

Table 4. Sites of deep vein thrombosis among 48 patients with vascular complications of Behçet's disease.

	Pop	Tibia	Femo	Iliac	IVC	SVC	Sub	Axilla	Jug	Inom	Cerebral venous sinus
Female	11	-	1	2	2	2	-	-	1	-	1
Male	25	1	7	1	4	6	3	2	-	1	2
Total	36	1	8	3	6	7	3	2	1	1	3

Pop = Popliteal; Femo = femoral; IVC = inferior vena cava; SVC = superior vena cava; Sub = subclavian; Jug = jugular; Inom = inominate.

between the duration of the disease and the onset of vascular manifestations, an average interval of 5-6 years is found between the onset of disease and vascular involvement. Rheumatologists should be aware of such complications and study all the vascular system in case of one vascular finding in BD patients.

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