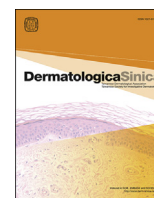


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ORIGINAL ARTICLE

The nailfold videocapillaroscopy findings of Behçet's syndrome

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ABSTRACT

Background: Nailfold videocapillaroscopy (NVC) is a diagnostic method for evaluating the microvasculature. Behçet's disease (BD) can affect vessels of all types and sizes.**Methods:** We performed NVC in 82 randomly selected patients with BD. NVC was performed for eight fingers (excluding the thumbs) with a 200× magnification.**Results:** Of the 82 patients with BD, 75 had at least one capillaroscopic change, including tortuosity in 75 (91.5%), bizarre capillaries in eight (9.8%), microhemorrhages in four (4.9%) and mega capillary in two (2.4%). The mean number of capillaries/mm length of nailfold in the group with BD was 10.17 ± 1.23 and was 11.45 ± 0.99 in the healthy controls ($p < 0.001$).**Conclusion:** In this study, the BD group had significantly more capillaroscopic pathological findings than did the healthy control group. However, the detected capillaroscopic pathology rate in BD patients was significantly lower than that of three previously published studies. Further studies are needed to clarify the diagnostic and prognostic value of capillaroscopy in BD.

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Introduction

Nailfold videocapillaroscopy (NVC) is a diagnostic method for evaluating the microvasculature. NVC is used to assess microcirculatory disturbances of skin capillaries in patients with autoimmune connective tissue diseases.^{1,2}

NVC has been reported to be useful in the noninvasive diagnosis and follow-up of several autoimmune systemic diseases, particularly systemic sclerosis.³ In addition, NVC has been successfully used in systemic lupus erythematosus (SLE), dermatomyositis, Sjögren's syndrome, antiphospholipid syndrome, and familial Mediterranean fever.^{4,5} NVC is safe, simple, noninvasive, and inexpensive.^{6,7}

Behçet's disease (BD), which is classified as a vasculitide, is a systemic disease that is characterized by multiorgan involvement.⁸

Conflicts of interest: The authors declare that they have no financial or non-financial conflicts of interest related to the subject matter or materials discussed in this article.

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BD can affect vessels of all types and sizes. There is large arterial and venous vessel involvement in nearly 25% of patients with BD.⁹ Vascular involvement patterns are classified as systemic arterial vasculitis, pulmonary arterial vasculitis, or venous system involvement.¹⁰ Major vessel involvement may be an important cause of morbidity and mortality in this disease; it is considered to be a poor prognostic sign.¹¹ Thus, nailfold capillaroscopy may be useful in determining the diagnosis and prognosis of BD. To our knowledge, there are only a few studies regarding microvascular involvement in BD.^{12,13}

In this study, we investigated the association between the pathologic capillaroscopy findings and other clinical characteristics of BD. In addition, we evaluated the features of nailfold capillaries in a large series of patients with BD, and to our knowledge, our current study is the first to examine nailfold capillaries with 200× magnification.

Methods

In the current prospective study, we performed nailfold capillaroscopy in 82 selected patients with BD who were referred to the BD

outpatient clinic of the Rheumatology Department in Pamukkale University Hospital, Denizli, Turkey between January 2015 and March 2015. All 82 patients fulfilled the International Study Group criteria for BD.¹⁴ The age, gender, disease onset, disease duration, and clinical features of the disease for each patient were recorded. Eighty-two gender and age matched healthy controls (relatives of the patients and our hospital staff) were also enrolled in this study. This study was approved by the local ethics committee, and informed consent was obtained from all participants prior to enrollment. Capillaroscopy was performed jointly by two observers in eight fingers (excluding the thumbs) with 200× magnification (Videocap; DS MediGroup, Milan, Italy) simultaneously. To better visualize the capillaries, immersion oil was used on the nailfolds of the fingers. The physician performing the procedure was unaware of the patient's condition. Patients were informed to protect their hands from trauma for 3 months prior to the capillaroscopy examination. The room temperature of the examination room was kept at ~24°C, and all patients rested in the room for at least 20 minutes prior to the procedure. All patients were asked about their history of Raynaud's phenomenon, smoking habits, ischemic ulcers, and history of high blood pressure. Patients were excluded from this study if they had a history of smoking, Raynaud's phenomenon, connective tissue disorders, hypertension, if they were a professional who may be exposed to hand trauma (e.g., gardener, farmer, etc.), and if they had a history of other systemic disorders. The length/number of capillaries (in millimeters) on all fingers were counted and averaged for each patient. The nailfold capillary system was evaluated in terms of capillary distribution, capillary density, and capillary morphology according to Maricq's criteria modified by Bergman et al.¹⁵ Literature reports indicate that nailfold capillaroscopy in healthy controls reveals regularly arranged, hairpin or U-shaped capillary loops, but in patients with rheumatic disease accompanied by Raynaud's phenomenon, characteristic findings include enlarged capillaries or giant capillaries, architectural disarrangement of the nailfold microvascular network, angiogenesis, loss of capillaries, and/or avascular areas.¹⁶

The following findings were considered abnormal. (1) Avascular area: Loss of at least two consecutive capillaries or ≤ six capillaries over each 1 mm length. (2) Microhemorrhage: Two or more punctate bleeds around a single capillary in at least two fingers. (3) Tortuosity: Two or more cross capillaries over each 1 mm length. (4) Megacapillary: Capillary wall diameter > 0.05 μm. (5) Bizarre (strange) capillary: Capillaries outside normal view. (6) Ectatic capillaries (regular or irregular): Capillary wall diameter between 0.02 and 0.05 micrometers.

Statistical analyses were performed using SPSS software (version 20.00; SPSS Inc., Chicago, IL, USA). Continuous data were presented as mean ± standard deviation. The Kolmogorov-Smirnov test was used to determine if the data were normally distributed. Differences in continuous variables between groups that were not normally distributed (i.e., age, number of capillaries) were determined by the Mann–Whitney *U* test. Categorical variables are presented as percentages and were compared with the χ^2 test. The level of statistical significance was defined as $p < 0.05$.

Results

Of the 82 patients with BD, 75 had at least one capillaroscopic change. These changes included: tortuosity in 75 (91.5%) patients, bizarre capillaries in eight (9.8%) patients, microhemorrhages in four (4.9%) patients, and megacapillary in two (2.4%) patients (Figure 1). The mean number of capillaries/mm length of nailfold in the BD group was 10.17 ± 1.23 and was 11.45 ± 0.99 in the healthy control group ($p < 0.001$). None of the patients had neo-vascularization, avascular areas, or microaneurysm. There was a




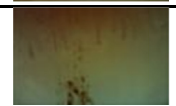

| | | |
|-------------------|-----------|---|
| Normal | 7 (8.5) |  |
| Tortuosity | 75 (91.5) |  |
| Bizarre capillary | 8 (9.8) |  |
| Microhemorrhage | 4 (4.9) |  |
| Megacapillary | 2 (2.4) |  |

Figure 1 Images of capillaroscopic findings of nailfolds of patients with Behçet's disease.

significant difference between the patient and healthy control groups with respect to tortuosity and bizarre capillaries ($p < 0.001$ and $p = 0.017$, respectively), but there was no difference in avascular areas, capillary density, or capillary distribution ($p > 0.05$) (Table 1). Results of evaluating the nailfold capillaries in the patients and healthy controls are shown in Table 1. The clinical features of the patients with BD are shown in Table 2. The disease duration was significantly longer in patients who had tortuosity or any capillary pathology than in patients who had no tortuosity or capillary pathology ($p = 0.010$). Other capillaroscopic changes were not associated with sex or clinical characteristics.

Discussion

NVC has been used for the analysis of microvascular abnormalities, which are present in several rheumatic disorders and extra-rheumatic diseases.^{1,17} Nailfold capillaries in the healthy individual usually show a regular structure, and uniform figure, distribution, and diameter, and most of them show a bodkin or U shaped aspect (Figure 1)

BD is a vasculitis that can affect vessels of all types and sizes. In the current study, we used NVC to assess capillary dilatations and microhemorrhages in patients with BD and in healthy controls. Our

Table 1 Demographic and capillaroscopic findings of patients with Behçet's syndrome and healthy controls.

| | Patients <i>n</i> = 82 | Controls <i>n</i> = 82 | <i>p</i> |
|-----------------------------|---------------------------|---------------------------|----------|
| Age (y) | 36.95 ± 11.80 | 36.56 ± 7.67 | 0.849 |
| Male gender | 48 (58.5) | 45 (54.9) | 0.636 |
| Family history (+) | 7 (8.5) | — | — |
| Age at onset of disease (y) | 29.89 ± 9.72 | — | — |
| Duration of disease | 7.04 ± 8.33 | — | — |
| No. of capillaries | 10.17 ± 1.23 | 11.45 ± 0.99 | <0.000 |
| Bizarre capillary | 8 (9.8) | 1 (1.2) | 0.017 |
| Tortuous capillary | 75 (91.5) | 4 (4.9) | <0.000 |
| Microhemorrhage | 4 (4.9) | 0 (0) | 0.060 |
| Megacapillary | 2 (2.4) | 0 (0) | 0.248 |
| Capillary density | 0 (0) | 0 (0) | — |
| Avascular areas | 0 (0) | 0 (0) | — |

Data are presented as *n* (%) or mean ± standard deviation.

Table 2 Clinical findings of patients with Behçet's syndrome.

| | n = 82 | % |
|-------------------------------|--------|------|
| Oral ulcer | 82 | 100 |
| Genital ulcer | 61 | 74.4 |
| Uveitis | 55 | 67.1 |
| Erythema nodosum | 43 | 52.4 |
| Subcutaneous thrombophlebitis | 11 | 13.4 |
| Pathergy (+) | 36 | 43.9 |
| Arthralgia/arthritis | 73 | 89 |
| Colitis | 1 | 1.2 |
| Vasculitis | 4 | 4.9 |
| Cranial nerve involvement | 2 | 2.4 |
| Epididymitis | 7 | 8.5 |
| Hemoptysis | 6 | 7.3 |
| Fibrosis | 1 | 1.2 |
| Family history (+) | 7 | 8.5 |

results indicated that tortuosity was present in 75 (91.5%) patients, bizarre capillaries were present in eight (9.8%) patients, micro-hemorrhages were present in four (4.9%) patients, and megacapillary was present in two (2.4%) patients with BD. However, these rates are significantly lower than those reported in previous studies.^{18,19} The differences in our results versus those previously published may be because we used a different magnification (200×) for capillaroscopy, the exclusion criteria from the studies were different, and because of the ethnic variations in the patients. Movasat et al¹² reported that enlarged capillaries (in 26%) and hemorrhages (in 16%) were the main features of patients with BD, while capillary loss was detected only in one patient with BD. Previous studies have shown that nailfold capillary changes are useful for detecting transitional patients who later developed a definite connective tissue disease.^{20,21} Microangiopathy, which is an essential feature of systemic scleroderma (SSc), is characterized by a series of events occurring in the microvessels. The characteristic finding of the scleroderma pattern is the presence of megacapillaries and decreased capillary density.⁴ Also, the microvascular changes found in other rheumatic diseases such as SLE, anti-phospholipid syndrome, and Sjögren's Syndrome. The microvascular changes found in SLE include morphological alterations in capillary loops, venular visibility and sludging of blood with variability of capillary loop length.⁴

NVC patterns have also been found to correlate with the severity and stage of SSc. Patients affected by limited SSc were reported to be more likely to have shorter disease duration and "early" or "active" NVC patterns, while patients affected by diffuse SSc were more likely to have longer disease duration and "active" or "late" NVC patterns.²² Similarly, we did not find any association between abnormal capillary changes and different manifestations of BD, with the exception of disease duration and presence of capillary abnormalities. Disease durations of patients with capillary pathology were significantly longer than those who did not have capillary pathology. Wechsler et al¹⁸ found no correlation between capillaroscopic abnormalities and age, sex, duration of disease, or ethnic background. By contrast, Vaiopoulos et al²³ reported a significant association between capillaroscopic abnormalities and skin manifestations, arthritis/arthralgia, and pathergy test in their patients.

Our current study is significantly different from other studies using nailfold videocapillaroscopy. These significant differences include the following: (1) our study utilized videocapillaroscopy for capillaroscopic examination, which enabled detailed evaluation of measurements with 200× magnification and the ability to record the display; (2) the patients in our study protected their hands from trauma before capillaroscopy; (3) patients were excluded from the study if they had a history of smoking, worked in a profession with a suspicion of exposure to microtraumas, and if they had a history

of hypertension and/or Raynaud's phenomenon; (4) capillaroscopic evaluation was performed by two different doctors; and (5) patients were kept at room temperature for 20–30 minutes prior to the procedure.

In the current study, capillaroscopic pathological findings were detected in patients with BD, but there was no relationship found between these and the clinical findings. The detected capillaroscopic pathology rate in our current study was significantly lower than that of the previous three studies. These differences may be because the previous studies did not exclude patients with factors that may confuse the data (e.g., smoking, hypertension, Raynaud's phenomenon), or because the previous studies used different equipment and had an ethnically different population than did our current study.

In conclusion, nailfold capillaroscopic abnormalities, mainly tortuosity and lower capillary density, are frequent in Turkish patients with BD. The frequency of nailfold capillaroscopic abnormalities in our study was less than that of previous studies. Our results indicate that these abnormalities are not associated with any specific clinical symptom of the disease. Also, these abnormalities may be an early sign of vascular involvement of BD. Further studies are needed to clarify the diagnostic and prognostic value of capillaroscopy in BD.

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