Nailfold Capillaroscopy Abnormality in Behcet's Disease and Relation to Disease Activity among Egyptian Patients

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ABSTRACT

Background: Behcet's disease is a systemic autoimmune disease. Treatment mainly is immunosuppression. It has no sure diagnostic tests and relies mainly on clinical diagnosis. There are few scores to assess Behcet's disease activity; (Behcet's Disease Current Activity Form) BDCAF score. Nailfold capillaroscopy is a technique to visualize capillaries in nailfold area. It can correlate many diseases with the abnormalities in shape of blood capillaries.

Objectives: The aim of the work was to find out nailfold capillaroscopy abnormality in Behcet's disease and its relation to the disease activity.

Patients and Methods: A cross sectional-case control study which was done on 50 Behcet's patients and 30 healthy controls. We assessed nailfold capillaroscopic changes in Behcet's patients in comparison to controls and the correlation of BDCAF score with nailfold capillary abnormalities.

Results: We found that 70% of Behcet's disease patients had nailfold capillaroscopy abnormalities, a highly statistically significant changes in the capillaries in the form of capillary dilatation (24%), hemorrhage (54%), and tortuosity (64%) in comparison to the control group (P<0.001). However, pattern was not specific as BDCAF Score wasn't related to the capillary changes.

Conclusion: Nailfold capillaroscopy showed nonspecific pattern in 70% Behcet's disease patients. Tortuosity, hemorrhages, dilation were not related to disease activity. Capillaroscopy is a good primary test for Bechet's disease and can reflect the presence and extent of microvascular involvement and thereby might have diagnostic and prognostic value.

Keywords: Behcet's Disease, Nailfold Capillaroscopy Abnormality.

INTRODUCTION

Behçet's disease (BD) is a systemic variable sized vasculitis of uncertain etiology with specific affection of venules. Onset is typically in young adults with recurrent oral and genital ulceration, uveitis, skin manifestations, arthritis, neurological manifestation, and increased risk of thrombosis. International diagnostic criteria have been proposed; however, diagnosis can be difficult, particularly if the typical ulcers are not clear at presentation. Treatment is challenging and must be tailored to the pattern of organ affection for each patient and often requires combination therapies [1].

BD still remains a clinical diagnosis, and for the purposes of international research the diagnostic criteria proposed by the International Study Group in 1990 and revised in 2010 is now widely accepted [2]. Vascular involvement, is one of the serious manifestations of BD, it is considered as a poor prognostic manifestation. Most of the studies about vascular involvement are related to large vessel involvement; however, few studies commented on microvascular damage in BD. Capillaroscopy is a non-invasive diagnostic technique designed to evaluate small vessels of the microcirculation [3].

BD is classified as a variable sized vasculitis, and it is characterized by endothelial dysfunction and chronic inflammation. Vascular involvement, which is reported in 18.2% of the patients, includes arterial and venous involvement. Arterial thrombosis, aneurysms, deep vein thrombosis, large vein thrombosis, and superficial phlebitis are the most common forms of vascular involvement; nevertheless, all sizes of vessels may be involved therefore, the involvement of the capillaries is an expected finding in BD [3].

The aim of the current work was to find out nailfold capillaroscopy abnormality in Behçet's disease and its relation to the disease activity.

PATIENTS AND METHODS

This is a cross sectional-case control study which was done on 50 Behcet's disease patients and 30 healthy controls within the year 2018. The study group was divided into 2 groups: (1) 50 patients with Behcet's disease fulfilling the criteria for the diagnosis by International Team for the Revision of the International Criteria for Bechet's Disease [2], patients with other autoimmune diseases, diabetic, hypertensive were excluded from the study. (2) 30 healthy controls who were medically free.

Ethical approval:

An approval of the study was obtained from Ain Shams University academic and ethical committee. Every patient signed an informed written consent for acceptance of the operation.

Collected data included: Clinical assessment through: Full History taking emphasizing on Behcet's disease clinical data. Thorough clinical examination including general and musculoskeletal system, with special attention to: Recurrent oral, genital ulceration, eye lesions, hemoptysis, CNS manifestations, joint manifestation, laboratory assessment; Complete blood count (CBC), erythrocyte sedimentation rate (ESR) in the first hour, C-reactive protein (CRP), disease activity which was assessed according to BDCAF score (Behcet's Disease Current Activity Form)[4].

Assessment of any activity regarding the eyes using fundus examination, which was done at Ain Shams University Ophthalmology Clinic, focusing on any sign of uveitis, flare cells, retinitis and any other abnormality that could be detected. Assessment of the capillary circulation for patients and control using the nailfold capillaroscopy, which was done using (Optilia Digital Capillaroscopy, Basic kit). The following parameters were considered; Comment on the shape of the capillaries (normal hairpin, or abnormal shapes e.g. Branching capillaries or tortuous), the diameter of the capillaries (dilated loops if the diameter is >20 μm and mega capillaries if≥ 50 μm), the capillary length (normal or elongated ≥300μm), capillary hemorrhage (two or more in at least two finger [5].

Statistical analysis

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for the Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Wilk test. Qualitative data were represented as frequencies and relative percentages. Chi square test (χ^2) or Fisher's exact test was used to calculate difference between two or more groups of qualitative variables. Quantitative data were expressed as mean ± SD (Standard deviation) and range. Independent samples t-test was used to compare between two independent groups of normally distributed variables (parametric data). P value < 0.05 was considered significant.

RESULTS

Our BD patients: 62% (31) were males and 38% (19) were females, their age ranged between 19-57 years with a mean (32.48± 8.57) years, Control subjects: 50% (15) were males and 50% (15) were females, their age ranged between 19-56 years with a mean (30.367±10.972) years. Regarding BDCAF score findings among patients headache was the most common one with 54% of patients was affected, , Patients BDCAF score ranged from 0-11 with a mean of 4.9 (Figure 1).
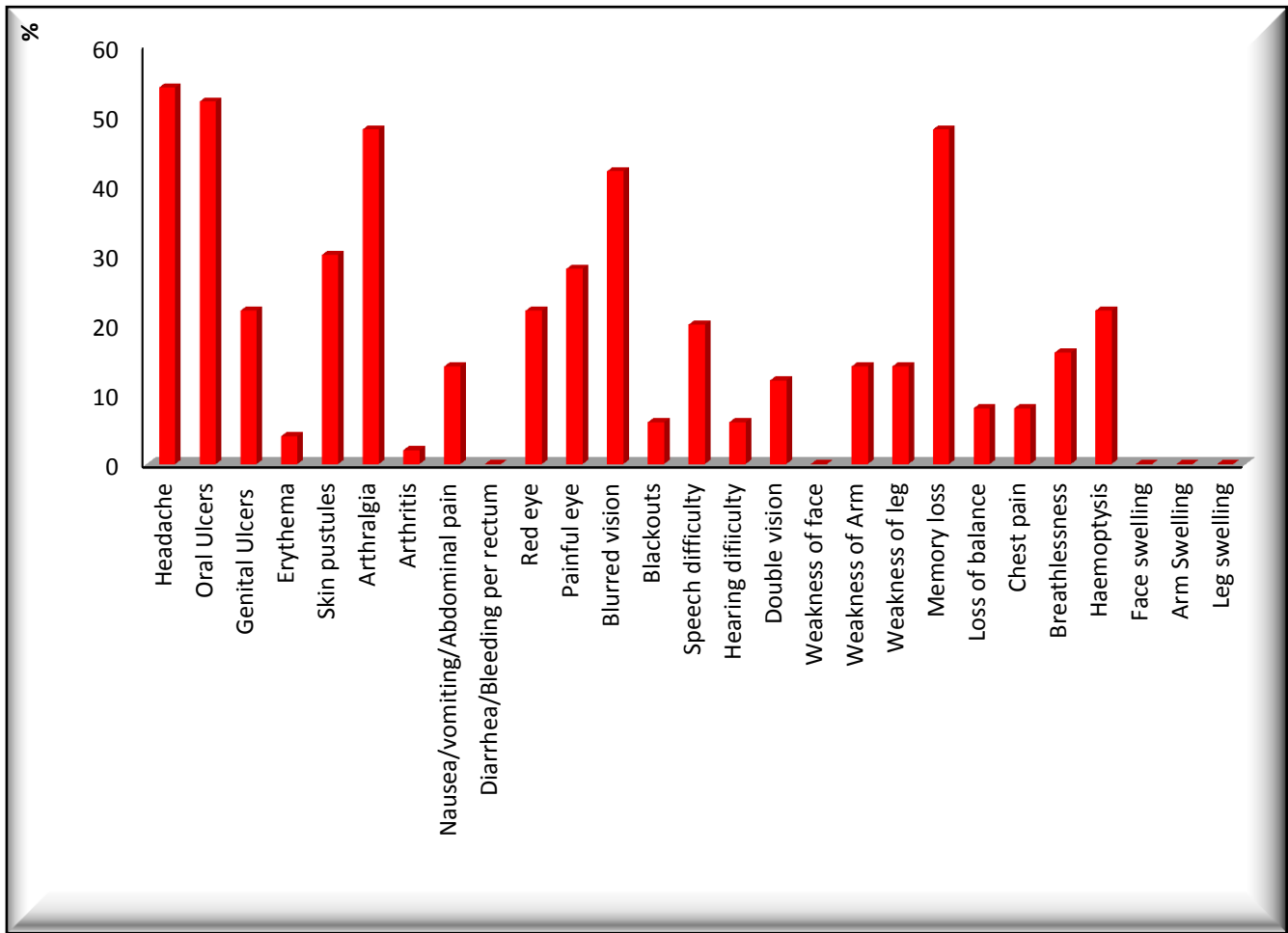
Fig. (1): Distribution of the most common symptoms according to BDCAF score

According to (NFC) abnormalities among patients; capillary hemorrhage, ramified, tortuous capillaries were present in (64%) of the patients, elongated capillaries in (60%), and dilated capillaries in (24%) (Table 1).

Table (1): Nailfold capillaroscopy findings in BD patients

(NFC) findings	Patients N=50	
	No.	%
Capillary dilatation	12	24%
Capillary hemorrhage	32	64%
Ramified, tortuous capillaries	32	64%
Elongated capillaries	30	60%
Sub-papillary venous plexus	0	0%
Avascular area	0	0%

Dilated, tortuous capillaries and presence of capillary hemorrhage were significantly more frequent among patients (Table 2) and mean capillary length and width were significantly higher among patients (Table 3).

Table (2): Comparison between patients and control group regarding nailfold capillary changes

Capillaries Changes		Groups						Chi-Square	
		Patients (N=50)		Control N=30		Total		X^2	P-value
		N	%	N	%	N	%		
Capillary dilation	Positive	12	24	0	0	12	15	8.471	0.004*
	Negative	38	76	30	100	68	85		
Capillary microhemorrhage	Positive	27	54	0	0	27	33.75	24.453	<0.001*
	Negative	23	46	30	100	53	66.25		
Ramified , tortuous capillary	Positive	32	64	0	0	32	40	32.000	<0.001*
	Negative	18	36	30	100	48	60		

Table (3): Comparison between patients and control regarding capillary length and width

	Groups		P-value
	Patients N=50	Control N=30	
Capillary length: Range Mean ±SD	100 - 250 167.100 ± 35.370	110 - 200 123.333 ± 31.598	<0.001*
Capillary width: Range Mean ±SD	20 - 50 31.340 ± 8.319	20 - 25 22.200 ± 7.208	0.053*

Behçet's patients whose capillaroscopy showed presence of dilated capillaries, presence of ramified or tortuous capillaries had significantly higher mean values of ESR compared to those patients whose capillaroscopy didn't show these finding. However mean CRP titer was not significantly different (Table 4).

Table (4): Association of NFC abnormalities and ESR and CRP

Capillary changes		ESR				P-value
		N	Mean	±	SD	
Capillary dilation	Positive	12	29.750	±	22.145	0.053*
	Negative	38	15.684	±	10.086	
Capillary microhemorrhage	Positive	27	23.963	±	11.012	0.558
	Negative	23	21.565	±	17.430	
Capillary ramified , tortuous	Positive	32	26.469	±	16.278	0.015*
	Negative	18	16.444	±	5.617	
		CRP				
Capillary dilation	Positive	12	5.667	±	1.155	0.156
	Negative	38	7.105	±	3.376	
Capillary microhemorrhage	Positive	27	6.296	±	1.815	0.248
	Negative	23	7.304	±	4.028	
Capillary ramified , tortuous	Positive	32	6.063	±	1.294	0.062
	Negative	18	7.711	±	4.602	

Regarding different Behçet's disease clinical manifestations and nailfold capillaroscopic abnormalities; patients with posterior chamber affection had significantly more frequent presence of ramified and tortuous capillaries compared to those without affection (Table 5) and those with anterior chamber affection had significantly higher mean capillary length (Table 6).

In addition patients with CNS manifestation more frequently showed ramified and tortuous, dilated capillaries and patients with hemoptysis more frequently showed capillary hemorrhage and ramified, tortuous capillaries (Table 5).

Table (5): Association between NFC abnormalities and clinical manifestations

Clinical manifestation			Nailfold capillary changes						Chi-square test (p-value)		
			Capillary dilation		Capillary microhemorrhage		Capillary ramified, tortuous				
			Positive (n=12)	Negative (n=38)	Positive (n=27)	Negative (n=23)	Positive (n=32)	Negative (n=18)	P1	P2	P3
Anterior Chamber Affection	Positive (n=12)	No.	4	8	7	5	8	4	0.385	0.73	0.825
		%	33.3%	66.7%	58.3%	41.7%	66.7%	33.3%			
	Negative (n=38)	No.	8	30	20	18	24	14			
		%	21.1%	78.9%	52.6%	47.4%	63.2%	36.8%			
Posterior Chamber Affection	Positive (n=18)	No.	3	15	9	9	16	2	0.362	0.67	0.015*
		%	16.7%	83.3%	50.0%	50.0%	88.9%	11.1%			
	Negative (n=32)	No.	9	23	18	14	16	16			
		%	28.1%	71.9%	56.3%	43.8%	50.0%	50.0%			
Genital ulcer	Positive (n=11)	No.	2	9	6	5	8	3	0.741	0.763	0.744
		%	18.2%	81.8%	54.5%	45.5%	72.7%	27.3%			
	Negative (n=39)	No.	10	29	21	18	24	15			
		%	25.6%	74.4%	53.8%	46.2%	61.5%	38.5%			
Oral ulcer	Positive (n=25)	No.	8	17	16	9	18	7	0.321	0.256	0.377
		%	32.0%	68.0%	64.0%	36.0%	72.0%	28.0%			
	Negative (n=25)	No.	4	21	11	14	14	11			
		%	16.0%	84.0%	44.0%	56.0%	56.0%	44.0%			
CNS manifestations (weakness upper-lowerlimb)	Positive (n=14)	No.	8	6	12	2	13	1	0.002*	0.013*	0.020*
		%	57.1%	42.9%	85.7%	14.3%	92.9%	7.1%			
	Negative (n=36)	No.	4	32	15	21	19	17			
		%	11.1%	88.9%	41.7%	58.3%	52.8%	47.2%			
Hemoptysis	Positive (n=11)	No.	6	5	10	1	11	0	0.321	<0.006*	<0.004*
		%	54.5%	45.5%	90.9%	9.1%	100.0%	0.0%			
	Negative (n=39)	No.	6	33	17	22	21	18			
		%	15.4%	84.6%	43.6%	56.4%	53.8%	46.2%			
Arthritis	Positive (n=24)	No.	5	19	10	14	18	6	0.863	0.162	0.207
		%	20.8%	79.2%	41.7%	58.3%	75.0%	25.0%			
	Negative (n=26)	No.	7	19	17	9	14	12			
		%	26.9%	73.1%	65.4%	34.6%	53.8%	46.2%			

P1: Comparison between Capillary dilation with clinical manifestation

P2: Comparison between Capillary microhaemorrhage with clinical manifestation

P3: Comparison between Capillary ramified, tortuous with clinical manifestation

Table (6): Comparison between patients with and without (anterior-posterior) chamber affection regarding nailfold capillary length and width

Capillary changes	Anterior chamber affection						P-value
	Positive (N=12)			Negative (N=38)			
	Mean	±	SD	Mean	±	SD	
Capillary length	197.750	±	31.560	157.421	±	30.980	<0.001*
Capillary width	30.167	±	5.734	31.711	±	9.016	0.580
	Posterior chamber affection						
Capillary length	164.556	±	32.819	168.531	±	37.160	0.707
Capillary width	30.778	±	8.454	31.656	±	8.361	0.724

Other clinical manifestation didn't show significant difference. On comparing patients with nailfold capillary abnormalities and those without regarding mean BDCAF score, there was no significant statistical difference (Table 7).

Table (7): Comparison between patients with nailfold capillary abnormalities and those without regarding mean BDCAF score

Variants		BDCAF score				P-value
		N	Mean ± SD			
Elongated capillaries	Positive	12	6.250	±	3.671	0.134
	Negative	38	4.500	±	3.407	
Capillary dilation	Positive	12	6.000	±	3.717	0.226
	Negative	38	4.579	±	3.430	
Capillary microhemorrhage	Positive	27	4.778	±	3.566	0.760
	Negative	23	5.087	±	3.528	
Capillary ramified, tortuous	Positive	32	4.875	±	3.892	0.905
	Negative	18	5.000	±	2.828	

DISCUSSION

Behcet's disease is a systemic vasculitis, that has an autoimmune etiology but with uncertain mechanisms it may complicates with multiple vascular complication [6]. Nailfold video-capillaroscopy (NVC) has been used for the analysis of microvascular abnormalities, which are present in several rheumatic disorders including systemic sclerosis, systemic lupus erythematosus [7].

In the current study the most frequent NFC abnormalities in BD patients were microhemorrhage in (64%), ramified, tortuous capillaries in (64%) and elongated capillaries in (60%) of patients; coming in agreement with **Movasat et al.** [8] who demonstrated that 70% of his Behcet patients had abnormal capillary pattern; most prevalent change was tortuosity 64%, microhemorrhages 54%, and capillary dilation 12% respectively, also **Aytekin et al.** [9] concluded that 75% of their studied patients showed abnormal nailfold capillary findings in the form of dilated capillaries and presence of capillary hemorrhage, also **Alan et al.**[10] reported that tortuous capillaries was present in 91% of his studied patients.

On comparing our patients and healthy control regarding nailfold capillaroscopic findings, abnormal findings like dilated, ramified, tortuous capillaries and capillary hemorrhage were more frequently observed among patients compared to control. Moreover mean capillary length and width were significantly higher among patients. Our data were nearly similar to **Tabanlioglu-Onan et al.** [3] who concluded that capillary morphologic alterations were encountered significantly more in BD group, however **Wechsler et al.**[11] slightly undermined the role of capillaroscopy in Behcet's disease which probably was related to the time of the study.

We observed that BD patients who showed dilated, ramified or tortuous capillaries had significantly high ESR mean values, which was in harmony to **Tabanlioglu-Onan et al.**[3] who documented the presence of the relation of acute phase reactant (ESR-CRP) and morphological abnormalities of nailfold capillaroscopy in BD patients.

Several studies suggested that NVC might be useful in the determination of the systemic extension of vascular damage, systemic manifestations and the degree of vessel wall alteration in BD [3].

In our work regarding study the association of different BD clinical manifestations and nailfold-capillaroscopic abnormalities, we observed that patients with posterior chamber affection showed more frequent presence of ramified and tortuous capillaries and also those with anterior chamber affection had significantly higher mean capillary length compared to patients without affection. Moreover patients with CNS manifestations showed higher frequency of the presence of capillary hemorrhage, tortuous, ramified and dilated capillaries and patients with hemoptysis more frequently showed capillary hemorrhage and ramified, tortuous capillaries. However BDCAF score was not related to capillaroscopic abnormalities. These were in agreement with **Movasat et al.**[8] study who concluded that the presence of capillary hemorrhages tended to be associated with articular symptoms. Also **Vaiopoulos et al.** [12] reported a significant association between capillaroscopic abnormalities and skin manifestations, arthritis/arthralgia, and pathergy test in their patients. However, **Aytekin et al.** [9] reported that capillaroscopic changes were not associated with clinical characteristics. Also **Alan et al.**[10] did not find any association between abnormal capillary changes and different manifestations of BD.

In conclusion nailfold capillary abnormalities were more frequently present in patients with BD compared to healthy control, some clinical manifestations were associated with some (NFC) abnormalities, however (NFC) abnormalities weren't related to disease activity. Further studies are needed to identify the diagnostic and prognostic value of capillaroscopy in BD.

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