Dermatoscopic and mucoscopic features of lesions in patients with Behcet's disease

Ghodsi SZ[1], Bahrololoumi Bafruee N[1], Chams Davatchi C[1], Rosendahl C[2], Akay BN[3], Davatchi F[4], Chams H[4], Shahram F[4], Nadji A[4], Akhlaghi M[4], Faezi T[4], Kavosi H[4]

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ABSTRACT

Objective: Behcet's disease (BD), as a vasculitis, can affect small and large vessels. As dermatoscopy has been shown to improve the accuracy in diagnosis of various skin lesions especially vascular patterns, we set this study to find if there is any characteristic pattern in the dermatoscopy of Behcet's mucocutaneous lesions.

Methods: This prospective cross-sectional observational study designed to evaluate dermatoscopic features of Behcet's mucocutaneous lesions. Fifty six consecutive patients presenting at the outpatient clinic of the BD Research Unit were included. If present, for each patient one oral, one skin and one genital lesion were evaluated by dermatoscopy. When indicated, pathergy test was performed according to a standard protocol and the results were evaluated by dermatoscopy.

Results: A total of 40 oral, 8 genital, 14 skin lesions and 14 pathergy tests were evaluated by dermatoscopy. While vascular component was the most prominent feature in oral aphthae, this component was less prominent in genital lesions. Dot vessels were the most common form of vessels in both oral and skin lesions. All the oral lesions were characterized by a central white structureless area. Skin lesions were characterized by a red structureless background. In pathergy tests, negative pricks showed absence of specific features while positive pricks were characterized by a structureless background in pink, purple or red. No obvious vascular component was detected in any of the pricks.

Conclusion: It seems that these findings have no specific clues for the diagnosis of BD, but our study is the first study in this field and the findings may give way to further investigations.

Keywords: Behcet's disease; Dermatoscopy.

1. Department of Dermatology, Razi Hospital, Tehran University of Medical Sciences, Tehran, Iran
2. Faculty of Medicine, The University of Queensland, Brisbane, Australia
3. Department of Dermatology, Ankara University, Medicine Faculty - Ankara, Turkey
4. Rheumatology Research Center, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran

INTRODUCTION

Behcet's disease (BD) is a multisystem vasculitis, with a relapsing remitting nature, most commonly presenting with mucocutaneous lesions such as oral and genital aphthous ulcers, erythema nodosum-like features, papulopustular lesions and pseudo-folliculitis as well as a variety of possible non-cutaneous features including uveitis, arthritis, vascular manifestations, epididymitis and neural and gastrointestinal disorders[1-4]. This rare disease was originally endemic in geographic areas along the ancient silk road, including Iran; however due to migration it is now encountered worldwide[5,6].

All of the clinical presentations of BD are nonspecific. There are more than 16 sets of diagnostic/classification criteria for the disease, all of them based on clinical features of the disease[7]. However, there is no specific laboratory test, the only available test being cutaneous pathergy, a test which must be read by an expert after 24-48hours[8].

Recently dermatoscopy, a novel non-invasive diagnostic technique, has been employed for the evaluation of pigmented and non-pigmented skin, nail apparatus and mucocutaneous lesions, including tumors as well as some inflammatory and infectious diseases. It enables recognition of vascular structures and other subtle features that usually are not visible to the naked eye[9]. It is not known if dermatoscopy improves the diagnostic accuracy of BD in comparison with examination with the unaided eye. We designed this study to determine whether if there is any characteristic dermatoscopic pattern in BD which might assist in the diagnosis.

PATIENTS AND METHODS

Between January and September 2016, 56 consecutive patients presenting at the outpatient clinic of the BD Research Unit (Rheumatology Research Center, Shariati Hospital affiliated to Tehran University of Medical Sciences, Tehran, Iran) were recruited. They all fulfilled BD criteria as defined by the original International Criteria for Behcet's Disease (ICBD) and each of them had at least one mucocutaneous lesion at the time of their initial visit[10-11]. Patients using topical treatment less than one month prior to recruitment were excluded.

All patients were examined in a multidisciplinary clinic by physicians who were experts in the diagnosis and management of BD, including rheumatologists, ophthalmologists, and dermatologists.

For each patient one oral, one skin, and one genital lesion were evaluated dermatoscopically if present. If there was more than one lesion of each type, the most recently developed lesion was evaluated. If pathergy testing was indicated it was performed according to the following protocol: three intradermal pricks were performed on the forearm with a needle, the first prick being done with a 21-gauge needle, the second with a 25-gauge needle, and the third with a 25 gauge needle with the injection of one to two drops of normal saline. The test was read 24 hours later by an expert dermatologist. A positive pathergy test was defined by an erythematous papule > 2 mm in diameter surrounded by a large area of erythema or a pustule forming at the site of the needle prick [12-14]. The pathergy test reactions were also evaluated by dermatoscopy after they had first been determined as either positive or negative.

Capture of dermatoscopic images was performed using a DermLite DL3N (San Juan Capistrano, CA, USA) in polarizing mode. All dermatoscopy images were obtained by a single physician (N.B.B).

In order to check the reproducibility of the findings, all of the dermatoscopy images were evaluated by two experts (B.N.A and C.R) and one of the experts (C.R) rechecked all of the images three months later.

For all continuous variables, mean and standard deviation were calculated but for categorical variables, frequencies were reported.

The study protocol was reviewed and approved by the Dermatologic Review Board Committee and the Ethics Review Committee of Tehran University of Medical Sciences. All patients provided written informed consent.

RESULTS

Fifty-six patients that fulfilled the original ICBD criteria (mean score of 5.31 ± 1.06) and had at least one mucocutaneous lesion were included. The mean age of the patients was 36.8 ±10.9 years and the majority were male (62.5%). Ocular involvement and arthritis were detected in 30 (53.6%) and six (10.7%) patients, respectively. A total of 40 oral, 8 genital, 14 skin lesions, and 14 pathergy tests were dermatoscopically evaluated. Some of the dermatoscopic patterns observed are shown in Figures 1-6. The baseline characteristics of the patients according to the site of the lesions are provided in Table I.

ORAL APHTHOUS ULCERS:

All of the 40 oral lesions were characterized by a central white structureless area. Apart from the white structureless area the vascular component was the most prominent feature. The vessels were mostly distributed at the periphery (75%) being mainly in dot form (67.5%) (Figures 1-4). In nine cases (22.5%) no obvious vascular component was detected (Table II).

GENITAL APHTHOUS ULCERS:

All the eight genital ulcers were characterized by a central white structureless area. The vascular component was a less prominent feature compared to oral lesions and vessels were distributed at periphery in 50% of the cases. Dot and curved were the most common vessels structure in the genital lesions there being 50% in each category (Table II). In three cases (37.5%) no obvious vascular pattern was detected. The fiber sign (Figure 5), a dermatoscopic sign associated with ulceration was prevalent in these lesions (62.5%).

SKIN LESIONS:

Overall, skin lesions (n=14, including erythema nodosum n=5, pseudo-folliculitis n=7, thrombophlebitis n=1, and erythematous edematous plaque n=1) were characterized by a red structureless area with a vascular pattern only seen in four cases (28.6%). These lesions showed an absence of any specific features (Table II, Figure 6).

PATHERGY TESTS:

For 14 patients pathergy testing was performed with three prick tests as described. In all of these patients at least one of the prick tests was positive (in five cases all three were positive, in five cases two were positive,

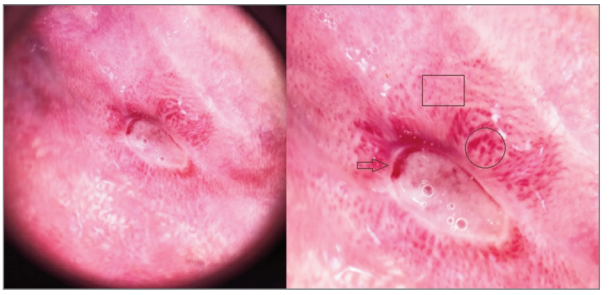

FIGURE 1. Oral aphthous ulcer: a central white structureless area surrounded by a white collarette (arrow) as well as coiled (circle) and dotted (rectangle) vessels

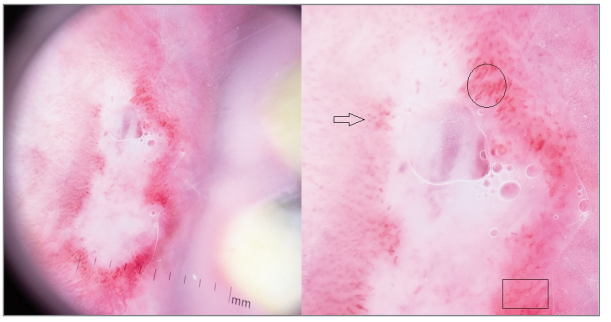

FIGURE 2. Oral aphthous ulcer: a central white structureless area surrounded by polymorphic vessels including dotted (arrows), looped (circle) and curved (rectangle) vessels

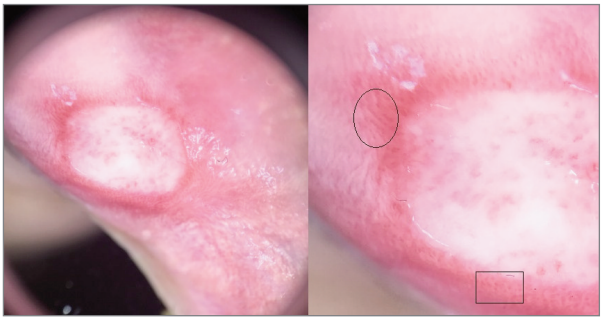

FIGURE 3. Oral aphthous ulcer: a central white structureless area surrounded by dotted (rectangle) and linear (circle) vessels

and in four cases one was positive). All of the 42 prick tests were evaluated dermatoscopically after reading. No obvious vascular pattern was detected at any of these sites.

All positive prick test sites were characterized by a structureless pink, purple or red area, and a central yellow clod was seen in nine (31%). Negative prick tests did not display any specific features showing only a central red dot surrounded by a very small structureless pink area (Table III, Figure 7).

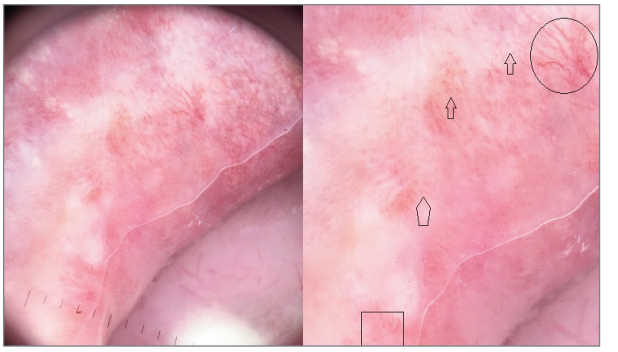

FIGURE 4. Oral aphthous ulcer: a white structureless area surrounded by serpentine (circle), curved (arrows), dotted (pentagon) and looped (rectangle) vessels

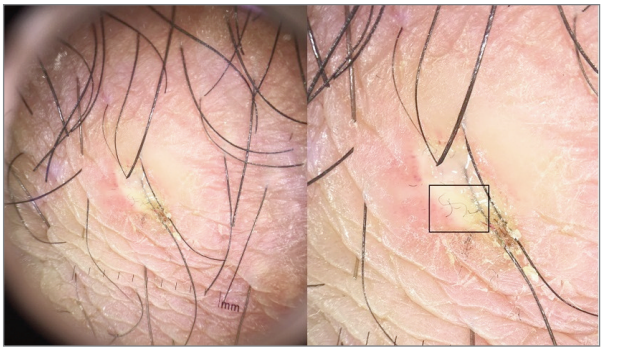

FIGURE 5. Genital ulcer: a yellow structureless area with fiber sign (rectangle) as a clue to ulceration. The minimal peripheral structureless pink area is not associated with any vascular pattern presumably the stratum corneum of genital skin obscures vessel structures and thus vascular patterns.

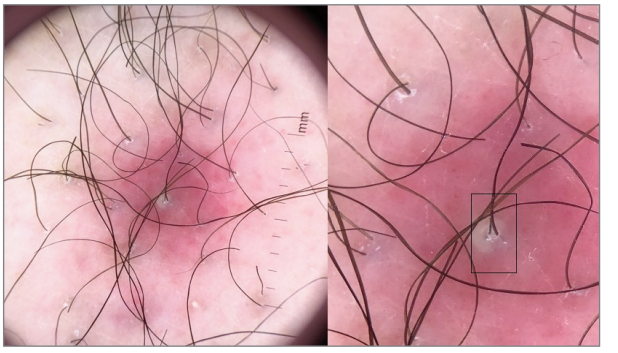

FIGURE 6. Papulopustular lesion: a central yellow clod (rectangle) centered on a pink structureless area without any visible vessel pattern

DISCUSSION

Behcet's disease is a vasculitis which can affect vessels of all types and sizes. Micro- and macro-vascular in-

TABLE I. PATIENTS' DEMOGRAPHIC CHARACTERISTICS ACCORDING TO THE SITE OF THE LESIONS

		Site of the lesions			
	Total	Genital (n=8)	Oral (n=40)	Skin (n=14)	Pathergy (n=14)
Sex (male)	35 (62.5%)	6 (85%)	23 (57.5%)	11 (78.6%)	8 (57.1%)
Age	36.8±10.9	34.1±6.3	36.8±10.0	40.6±13.5	34.9±10.2
		n=7	n=31	n=5	n=10
HLA					
HLA-B27	3 (7.9%)	2 (40%)	3 (9.7%)	1 (14.3%)	0 (0%)
HLA-B5	25 (65.8%)	3 (60%)	20 (65.4%)	6 (85.7%)	6 (42.9%)
HLA-B51	20 (52.6%)	1 (20%)	16 (51.6%)	5 (71.4%)	6 (42.9%)
Ocular involvement	30 (53.6%)	4 (50%)	18 (45%)	8 (57.1%)	8 (57.1%)
Arthritis	6 (10.7%)	2 (25%)	2 (5%)	3 (21.4%)	1 (7.1%)

TABLE II. FREQUENCY OF DERMATOSCOPIC CRITERIA IN ORAL, SKIN, GENITAL LESIONS AND PATHERGY TEST

	Total (n=104)	Oral lesions (n=40)	Skin lesions (n=14)	Genital lesions (n=8)	Pathergy test (n=42)	
					Negative	Positive
Vessel						
Distribution						
peripheral	36 (34.6%)	30 (75%)	2 (14.3%)	4 (50%)	0 (0%)	0 (0%)
central	9 (8.7%)	6 (15%)	2 (14.3%)	1 (12.5%)	0 (0%)	0 (0%)
Shape						
dot	34 (32.7%)	27 (67.5%)	3 (21.4%)	4 (50%)	0 (0%)	0 (0%)
linear	17 (16.3%)	15 (37.5%)	0 (0%)	2 (25%)	0 (0%)	0 (0%)
serpentine	6% (5.8)	4 (10%)	1 (7.1%)	1 (12.5%)	0 (0%)	0 (0%)
coiled	4 (3.8)	3 (7.5%)	0 (0%)	1 (12.5%)	0 (0%)	0 (0%)
looped	1 (1%)	1 (2.5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
curved	11 (10.6)	7 (17.5)	0 (0%)	4 (50%)	0 (0%)	0 (0%)
Central white structureless	48 (46.1%)	40 (100%)	0 (0%)	8 (100%)	0 (0%)	0 (0%)
Collarette scale	4 (3.8%)	1 (2.5%)	1 (7.1%)	2 (25%)	0 (0%)	0 (0%)
Structureless collarette	1 (1%)	0 (0%)	0 (0%)	1 (12.5%)	0 (0%)	0 (0%)
Fiber sign	7 (6.7%)	2 (5%)	0 (0%)	5 (62.5%)	0 (0%)	0 (0%)
Red structureless halo	21 (20.2%)	18 (45%)	1 (7.1%)	2 (25%)	0 (0%)	0 (0%)
Crust	3 (2.9%)	0 (0%)	2 (14.3%)	1 (12.5%)	0 (0%)	0 (0%)
Red structureless area	50 (48.1%)	0 (0%)	13 (92.9 %)	1 (12.5%)	7 (53.8%)	29 (100%)
Central yellow clod	9 (8.6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	9 (31%)
Central red dot	32 (30.8%)	0 (0%)	0 (0%)	0 (0%)	13 (100%)	19 (65.5%)
Brown dot	1 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (3.4%)

volvement is always seen and correlates with the clinical presentations[15]. The inflammatory vessel lesions are the histologic and pathogenic substrate of the disease and are responsible for the clinical patterns that are the main clues in the diagnostic clinical criteria of BD[15].

For in vivo evaluation of microcirculation in BD, nailfold capillaroscopy (NFC) was used in previous studies[16-18]. These studies have shown NFC abnormalities with different frequencies and different patterns in patients with BD. These differences between published studies may be due to different magnification (3.2× to 200×) employed for capillaroscopy, different exclusion

TABLE III. FREQUENCY OF DERMATOSCOPIC FINDINGS IN PATHERGY TESTS (42 PRICKS)

	Total (n=42)	Negative Pathergy (n=13)	Positive pathergy (n=29)
Vessels	0 (0%)	0 (0%)	0 (0%)
Central yellow clod	9 (21.4%)	0 (0%)	9 (31%)
Central hemorrhagic crust	32 (76.2%)	13 (100%)	19 (65.5%)
Brown dot	1 (2.4%)	0 (0%)	1 (3.4%)
Pink structureless	22 (52.4%)	5 (38.5%)	17 (58.6%)
Purple structureless	7 (16.4%)	2 (15.4%)	5 (17.2%)
Red structureless	7 (16.4%)	0 (0%)	7 (24.1%)
Structureless in total	36 (85.7%)	7 (46.1%)	29 (100%)

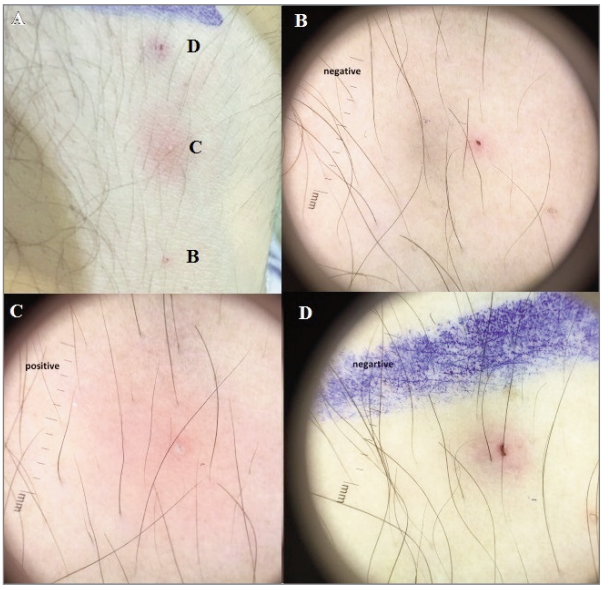

FIGURE 7. Pathergy Test: A: Close-up image of pathergy test with 3 pricks applied as described in the text, with the prick sites variously labelled B, C and D. B: Dermatoscopic view of the prick test B shown in the first image with a negative result manifested by a central red dot and minimal surrounding erythema. C: Dermoscopic view of the prick test C shown in the first image with a positive result manifested by a central yellow clod and a wide area of surrounding erythema. D: Dermoscopic view of prick test D shown in the first image with a negative result manifested by a red dot and minimal surrounding erythema as in image "B".

criteria, and varying definitions of abnormality or because of the ethnic variations between patients.

Pastorelli *et al.*,[18] used videocapillaroscopy at 200 times magnification to evaluate microcirculation, not only in hand and foot nail folds but also in gingival margins, labial mucosa, and conjunctiva. They found videocapillaroscopy to be useful in diagnosis, follow-up, and response to treatment of BD by showing the systemic extension of the vascular inflammatory process and the alteration of vessel structure, especially in peripheral and conjunctival areas.

A number of different devices with different designs and magnifying power have been used for capillaroscopy. A total magnification of 12× to 14× was suggested to provide optimal conditions for evaluating the overall pattern of the capillary bed[19]. On the other hand, it was reported that capillaroscopy findings obtained with a dermatoscope are comparable with those described for other instruments[19, 20]. Dermatoscopy enables the assessment of many lesions in a short time and is accessible in many clinics with the magnification power typically of 10 times. As dermatoscopy has been shown to improve diagnostic accuracy for various skin lesions, we anticipated that it might improve the diagnostic accuracy for BD lesions.

Scherrer *et al.*,[21] assessed dermatoscopic and histologic characteristics of pathergy tests in 23 patients. Dermatoscopy showed needle marks and mild erythema in the negative tests (two patients) and erythematous papule/pustule surrounded by a larger erythematous and/or edematous area in the positive cases. In this study they concluded that dermatoscopy was a useful tool specially to examine the inflammatory aspects of the small lesions (less than 2mm) resulting from pathergy testing[21]. In our study, 14 patients underwent pathergy testing which was performed with three separate prick tests on each patient. In all the patients at least one of the prick tests was positive. All the 42 prick tests were evaluated dermatoscopically after being read. No obvious vascular pattern was detected in any of the prick tests. All positive prick tests were characterized by a structureless pink area as well as a central yellow clod in nine cases (31%). Negative prick tests showed

an absence of specific features except a central red dot surrounded by a very small structureless pink area. This finding was similar to that that made by Scherrer *et al*. The pink structureless area surrounding the prick site would reasonably correlate with the reactive hyperemia which is the basis of pathergy testing, the larger area covered by this hyperemia defining a positive result. It is possible that further studies comparing novices to experienced readers of pathergy tests may show that dermatoscopy may help physicians with less experience, to diagnose a positive pathergy test with more confidence.

Currently dermatoscopy is widely used for the examination of skin lesions but its utility for evaluating mucous membranes has only had limited investigation in a few studies on mucosal melanomas. Dermatoscopic features of lesions located on the mucous membranes are expected to differ compared to skin lesions[22]. Our study showed that a central white structureless area with a peripheral vascular pattern was the most prominent feature in oral lesions, the vascular pattern being less prominent in genital lesions. Dot form was the most common vessel in both lesions. The dermatoscopic central white structureless area seen with mucosal lesions demonstrate the clinically evident ulceration and the surrounding vascular pattern would reasonably demonstrate dilated dermal papillary vessels consistent with reactive hyperemia in response to the ulceration. It is likely that the stratum corneum of genital skin obscures vessel structures and thus vascular patterns.

The main limitation of our study was the absence of any control group. A small number of patients and limitations to skin and genital lesions is another reason for our results to be interpreted with caution. Finally, we did not take into account the duration of the disease in our cases, this being something which may affect the pattern of lesions due to factors of disease progression or medical therapy.

In conclusion, while a central structureless white area and a peripheral vascular pattern were the most prominent features in oral lesions, this vascular pattern was less prominent in genital lesions. Dotted vessels were the most common form in both oral and skin lesions. Skin lesions were characterized by a red structureless area. In pathergy tests, positive prick tests were characterized by a large structureless pink area with no vascular component detected. We discovered no specific clues for the diagnosis of BD but our study is the first study in this field and further investigation may be warranted.

CORRESPONDENCE TO
Negar Bahrololoumi Bafruee
Razi Hospital, Vahdat Islami Sq, 1199663911 Tehran, Iran.
E-mail: negar.bb63@yahoo.com

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