Dermoscopy could be useful in differentiating sarcoidosis from necrobiotic granulomas even after treatment with systemic steroids

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ABSTRACT

Background: Diagnosing cutaneous sarcoidosis and necrobiotic granulomas is challenging.

Objective: Assessing the value of dermoscopy in differentiating cutaneous sarcoidosis from necrobiotic granulomas and evaluating whether their dermoscopic features will be altered after treatment.

Methods: Nineteen cutaneous sarcoidosis and 11 necrobiotic granuloma patients (2 necrobiosis lipoidica, 4 granuloma annulare and 5 rheumatoid nodule) were included in this study. The diagnosis was confirmed by skin biopsy. The lesions were examined using non-contact polarized dermoscope (Dermlite 2 HR-Pro; 3Gen, San Juan Capistrano, CA).

Results: Ten out of 19 cutaneous sarcoidosis patients and 7/11 necrobiotic cases group were receiving treatments (topical, intralesional or systemic steroids ± chloroquine) but still have cutaneous lesions. Treatment duration in the sarcoidosis group ranged from 2 months to 10 years (median 3 years) and in the necrobiotic cases group ranged from 3 months to 16 years (median 2 years). Pink homogenous background, translucent orange areas, white scar-like depigmentation and fine white scales were significantly associated with the cutaneous sarcoidosis compared to necrobiotic cases group. On the other hand mixed pink, white and yellowish background was significantly associated with the necrobiotic cases group. No significant difference in the dermoscopic findings was detected between treated and non-treated patients.

Conclusion: Some dermoscopic findings are shared between the cutaneous sarcoidosis group and the necrobiotic cases group, yet dermoscopy could be a useful aid in differentiating them even after treatment.

Introduction

Dermoscopy is gaining popularity in the diagnosis of inflammatory dermatoses. Polarized dermoscopes are widely used due to their better visualization of the deeper epidermis and papillary dermis [1].

A granulomatous disorder is a pathological description of a variety of conditions that have different etiologies but

TABLE 1. Demographic data of the patients [Copyright: ©2016 Ramadan et al.]

	Cutan Cutaneous sarcoidosis (n=19) eous sarcoidosis (n=19)	Necrobiotic cases group (n=11)
Females	16	8
Males	3	3
Age (mean)	25-62 (45±9.8)	18-69 (37.7±17.1)
Fitzpatrick's skin type (number)	IV (18), V (1)	IV (7), V (2), VI (2)
Disease duration range (median)	2 months-10 years (3 years)	3 months- 16 years (2 years)
Total number of examined lesions (range, median)	1-16 (3)	1-14 (2)

share granuloma formation pathologically. A granuloma is an organized collection of epithelioid histiocytes with variable number of multinucleated giant cells [2]. Granulomas include sarcoidal, foreign body granuloma and necrobiotic granuloma [3]. Necrobiotic granulomas include granuloma annulare, necrobiosis lipoidica, rheumatoid nodules, rheumatoid fever nodules and foreign body reactions.

The diagnosis of cutaneous sarcoidosis is challenging due to the variety of clinical presentations of the disease [4]. Moreover, differentiating cutaneous sarcoidosis from necrobiotic granulomas is sometimes difficult [5], and the existence of both conditions in the same patient was already reported [6]. In this work we aimed to assess the value of dermoscopy in differentiating cutaneous sarcoidosis from necrobiotic granulomas.

Patients and methods

This is a cross sectional study that was conducted between January and November 2014 in our department. All patients diagnosed as cutaneous sarcoidosis or necrobiotic granulomas during this period were included in this study. Patients were subjected to history taking, clinical examination, and skin biopsy to confirm the diagnosis and dermoscopic examination using polarized dermoscope (Dermlite 2 HR-Pro). This study was approved by the ethical committee of the Dermatology Department and was conducted according to the declaration of Helsinki principles.

2.1 Statistical analysis

Data were statistically described in terms of mean ± standard deviation (± SD), median and range, or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was done using Mann-Whitney U test for independent samples. For comparing categorical data, Chi square (χ^2) test was performed. Exact test was used instead when the expected frequency was less than 5. Correlation between various variables was done using Spearman's rank correlation equation. Accuracy

was represented using the terms sensitivity, specificity, +ve predictive value, -ve predictive value, and overall accuracy. P values less than 0.05 was considered statistically significant. All statistical calculations were done using computer program SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) release 15 for Microsoft Windows (2006).

2.2 Accuracy calculations

Sensitivity = T(+)ve ÷ [T(+)ve + F(-)ve]
Specificity = T(-)ve ÷ [T(-)ve + F(+)ve]
Positive predictive value = T(+)ve ÷ [T(+)ve + F(+)ve]
Negative predictive value = T(-)ve ÷ [T(-)ve + F(-)ve]
Overall accuracy = [T(+)ve + T(-)ve] ÷ All sample

Results

The demographic data of the patients are summarized in Table 1. Nineteen cutaneous sarcoidosis cases and 11 necrobiotic cases groups (2 necrobiosis lipoidica, 4 granuloma annulare and 5 rheumatoid nodule) were included in this study. The number of examined lesions in the cutaneous sarcoidosis group ranged from 1 to 16 lesions (median=3). The number of examined lesions in the necrobiotic cases group (necrobiosis lipoidica, granuloma annulare and rheumatoid nodule) ranged from 1 to 14 lesions (median=2).

Ten out of 19 cutaneous sarcoidosis cases and 7/11 of the necrobiotic cases group were receiving treatments but still had cutaneous lesions. The cutaneous sarcoidosis patients received systemic steroids and chloroquine. One patient received adjuvant intralesional steroids. Three patients from the necrobiotic cases group received topical steroids, 1 patient received systemic steroids, 2 patients received systemic steroids and methotrexate and 1 patient received systemic steroids, methotrexate and chloroquine.

The dermoscopic findings are summarized in Table 2.

The results showed that pink homogenous background, translucent orange areas, white scar-like depigmentation and fine white scales (Figure 1) were significantly associated with cutaneous sarcoidosis compared to the necrobiotic

TABLE 2. Summary of the dermoscopic findings [Copyright: ©2016 Ramadan et al.]

|	Cutaneous sarcoidosis (n=19)	Necrobiotic cases group			P value
		Granuloma annulare (n=4)	Necrobiosis lipoidica (n=2)	Rheumatoid nodule (n=5)	
Background color					
Pink homogenous background	14	0	0	3	*0.018
Mixed pink and white homogenous background	0	1	0	1	0.298
Mixed pink, white and yellowish background	0	2	2	0	*0.012
Mixed pink and orange background	5	0	0	0	0.082
Translucent orange globules and areas					
Translucent orange globules	4	0	0	0	0.141
Translucent orange areas	12	0	0	0	*0.001
Blood vessels					
Arborizing vessels	5	0	2	1	0.637
Short linear blood vessels	9	0	2	1	0.245
Pigmentation					
Hypopigmented areas	0	2	0	0	0.367
Scar like depigmentation	7	0	0	0	*0.025
Reticulate pigmentation	1	1	2	1	*0.047
Scales					
Fine white scales	9	0	0	0	*0.006

*P value <0.05 is significant
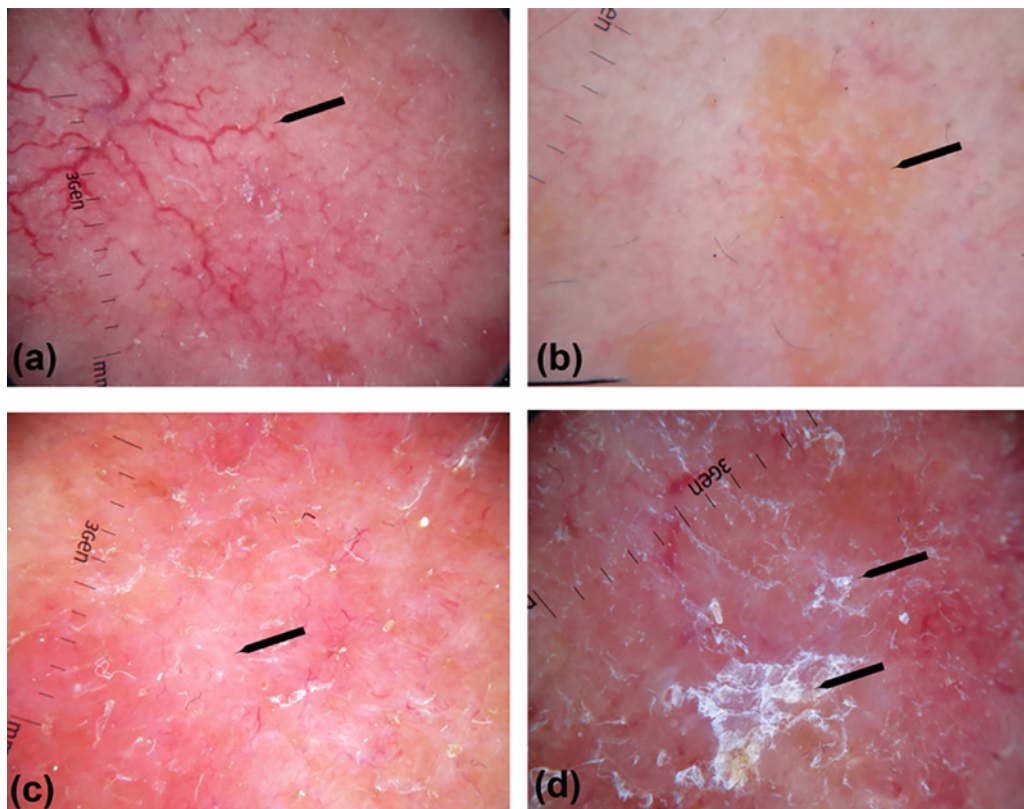
Figure 1. Dermoscopic picture of cutaneous sarcoidosis cases showing (a) arborizing blood vessels (black arrow) (no treatment); (b) translucent orange areas (black arrow) (treatment for 3 years); (c) scar-like depigmentation (black arrow) (no treatment); (d) white scales (black arrow) (no treatment). [Copyright: ©2016 Ramadan et al.]
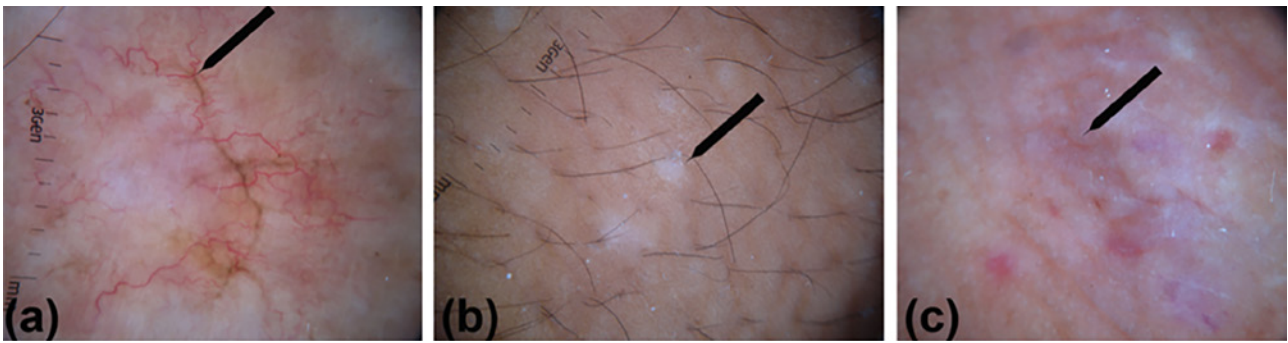
Figure 2. Dermoscopic picture of necrobiotic cases group (a) necrobiotic granuloma showing mixed pink, white and yellowish background and arborizing blood vessels (black arrow) (no treatment); (b) granuloma annulare showing hypopigmented areas (black arrow) (no treatment); (c) rheumatoid nodule showing mixed pink and white background and short linear vessels (black arrow) (treatment for 2 years). [Copyright: ©2016 Ramadan et al.]

TABLE 3. Comparison between dermoscopic findings in treated and untreated cases
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	Cutaneous sarcoidosis (n=19)			Necrobiotic cases group (n=11)		
	Untreated cases (9)	Treated cases (10)	P value	Untreated cases (4)	Treated cases (7)	P value
Background color						
Pink homogenous background	5	9	0.119	0	3	0.212
Mixed pink and white homogenous background	0	0		0	2	0.382
Mixed pink, white and yellowish background	0	0		3	1	0.088
Mixed pink and orange background	4	1	0.119	0	0	
Translucent orange globules and areas						
Translucent orange globules	1	3	0.333	0	0	
Translucent orange areas	7	5	0.22	0	0	
Blood vessels						
Arborizing vessels	4	1	0.119	1	2	0.721
Short linear blood vessels	4	5	0.586	1	2	0.721
Pigmentation						
Hypopigmented areas	0	0		2	0	1
Scar like depigmentation	2	5	0.22	0	0	
Reticulate pigmentation	0	1	0.526	2	2	0.47
Scales						
Fine white scales	5	4	0.414	0	0	

cases group. P values were 0.018, 0.001, 0.025 and 0.006 respectively.

On the other hand, mixed pink, white and yellowish background was significantly associated with the necrobiotic cases group; p value was 0.012 (Figure 2).

We tried to evaluate whether receiving treatment affected the dermoscopic findings. We compared the dermoscopic findings of the patients who were receiving treatment with those who had not started any treatment. However, the results were not significant in all the dermoscopic findings (Table 3) (Figure 3).

Discussion

The spectrum of inflammatory diseases that can be diagnosed using a dermoscope has markedly increased. Granulomatous skin diseases are a group of inflammatory dermatoses that are characterized pathologically by granuloma formation. Few studies evaluated the use of dermoscopy in diagnosing cutaneous sarcoidosis; the largest of which was using 7 cases [7]. In this work we aimed to assess the value of the dermoscope in diagnosing cutaneous sarcoidosis using a larger number of patients. Moreover, we tried to evaluate whether receiving
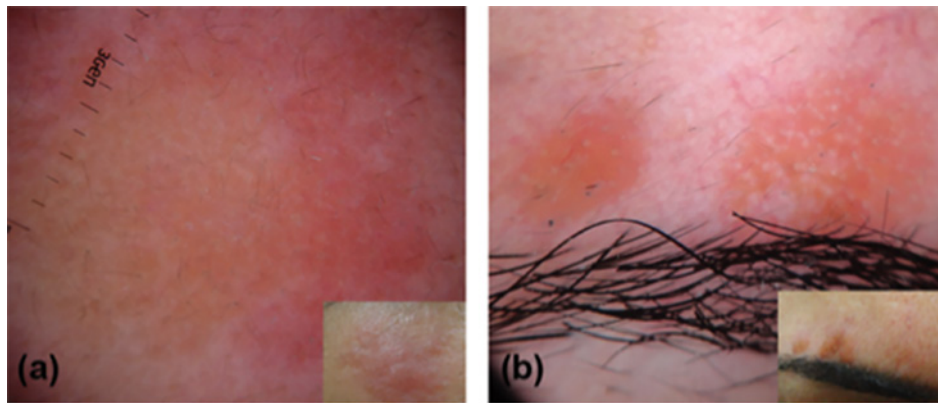
Figure 3. Treatment did not affect the dermoscopic findings of cutaneous sarcoidosis. Translucent orange areas in the forehead of a non-treated male (a) and a treated female for 3 years with systemic steroids (b). [Copyright: ©2016 Ramadan et al.]

treatment affected the dermoscopic findings of cutaneous sarcoidosis and necrobiotic granulomas.

Pellicano et al. [7] reported that scar-like depigmentation and translucent orange globules were suggestive of cutaneous sarcoidosis. They detected scar-like depigmentation in 5 cases and translucent orange globules in 7 cases of cutaneous sarcoidosis. The translucent orange globules were thought to be equivalent to the apple jelly color in diascopy [8]. Our results showed that scar-like depigmentation was detected in 7/19 (36.8%) cutaneous sarcoidosis cases, which was statistically significant in differentiating cutaneous sarcoidosis from necrobiotic granuloma; p value was 0.025. In our results, translucent orange globules were found in 4/19 (21.1%) cutaneous sarcoidosis cases. Although they were not detected in any necrobiotic granuloma, they were not significant in differentiating cutaneous sarcoidosis from the necrobiotic cases group.

On the other hand, our results added that translucent orange areas were significant in differentiating cutaneous sarcoidosis from the necrobiotic cases group; p value was 0.001. Translucent orange areas were 100% specific and 63.16% sensitive in differentiating cutaneous sarcoidosis from necrobiotic granulomas. However, in spite of their significance, they might not be specific for sarcoidosis. Translucent orange areas were reported before in lupus vulgaris [9]. Interestingly, differentiating sarcoidosis from lupus vulgaris clinically and pathologically is challenging. Therefore it is not surprising that they have the similar dermoscopic features.

Vazquez-Lopez et al. [10] reported the presence of vascular globules in 2 cutaneous sarcoidosis cases. Vascular globules were not detected in this work. Moreover, Pellicano et al. and Vazquez-Lopez et al. reported that linear vessels were associated with sarcoidosis. In this work we detected short linear vessels in 9 (47%) cutaneous sarcoidosis cases and in 3 (27%) of the necrobiotic group. However, the results were not significant. Arborizing blood vessels were the main clue to differentiate necrobiosis lipoidica from sarcoidosis according to Pellicano et al. [11] and Lallas et al. [8]. Those authors stated that arborizing blood vessels were detected in necrobiosis lipoidica while linear vessels were detected in sarcoidosis. Nonetheless, we detected arborizing blood vessels in 5 (26.3%) cases of cutaneous sarcoidosis. Those arborizing blood vessels might be shorter with fewer branches in sarcoidosis than necrobiosis lipoidica.

Necrobiosis lipoidica is a rare disease. Bakos et al. [12], Pellicano et al. [11] and Lallas et al. [13] all reported the presence of arborizing vessels on yellowish background in necrobiosis lipoidica, and our results confirm their findings. Hairpin like structures were detected by Bakos et al. in necrobiosis lipoidica; although we did not detect any hair pin like structures, we noticed that short linear blood vessels can be seen in necrobiosis lipoidica patients.

Lallas et al [13] reported the dermoscopic findings of granuloma annulare in 47 lesions of 24 patients. They found that the dermoscopic findings in granuloma annulare are heterogeneous. The background color is a combination of red and white in 42.6%, dotted vessels in 40.4%, short linear vessels in 21% and arborizing vessels in 14.9% of the lesions. In this work we found mixed pink and white background in 1 patient. Interestingly we found hypopigmented areas in 2/4 granuloma annulare patients and mixed pink white and yellow background in 1 patient.

Some dermoscopic features of inflammatory lesions are lost after treatment with steroids, which makes their diagnosis difficult [14]. Regarding lichen planus, Wickham's striae and peripheral homogenous vascular pattern disappeared after 4 weeks of treatment with topical steroids [14]. Interestingly, our results showed that the dermoscopic findings of cutaneous sarcoidosis and necrobiotic cases group remained even after several years of treatment. Some possible explanations are that topical and systemic steroids may not be effective in treating all patients [15] or that more time may be needed for these lesions to disappear. In addition to that, different drugs with different mechanisms of action may be responsible for different dermoscopic modifications after treatment.

Some limitations of this work should be highlighted: dermoscopic features before and after treatment have not been compared; the limited number of patients, especially in the necrobiotic cases group; and most of the patients were Fitzpatrick's skin type IV skin phototype.

In conclusion, some dermoscopic findings are shared between the cutaneous sarcoidosis and necrobiotic cases group. However, translucent orange areas, white scar-like depigmentation and white scales may be more suggestive of cutaneous sarcoidosis, while mixed pink, white and yellowish background may be more suggestive of necrobiotic granuloma. The dermoscopic features of cutaneous sarcoidosis might remain even after receiving treatment.

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