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Use of dermoscopy in the evaluation of connective tissue diseases

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ABSTRACT

Recently, dermoscopy has begun to be used for the observation of nailfold capillaries in connective tissue disease (CTD). However, dermoscopic features of other skin lesions and the utility of such information remains unclear. In this review, we summarize the typical dermoscopic findings of nailfold capillaries in CTD and discuss their significance. We compared the findings between dermoscopy and video capillaroscopy, and propose that dermoscopy could serve as a substitute to some extent for video capillaroscopy. The utility of dermoscopy for othe skin lesions of CTD remains unknown. However, dermoscopy findings may help to differentiate discoid lupus erythematosus from other skin disorders in patients with systemic lupus erythematosus. Interestingly, telangiectasia found in the skin other than nailfold resembles the nailfold capillary changes in patients with systemic sclerosis. Gottron's sign accompanied with punctate hemorrhage may reflect the existence of rapidly progressive interstitial pneumonia. We propose that daily use of dermoscopy could improve the clinical care of CTD patients, since it enables the recognition of vascular structures and other subtle features that are less visible to the naked eye. We hope that this review will promote increased use of dermosopy for clinical practice in patients with CTD, and believe that further investigation will yield additional valuable information in the near future.

KEYWORDS: Dermoscopy, Capillaroscopy, Systemic sclerosis, Lupus erythematosus, Dermatomyositis

ABBREVIATIONS: CTD, connective tissue disease; NVC, nailfold video capillaroscopy; SSD, scleroderma spectrum disorder; SSc, systemic sclerosis; DM, dermatomyositis; SLE, systemic lupus erythematosus; DLE, discoid lupus erythematosus; MDA, melanoma differentiation-associated protein.

INTRODUCTION

Connective tissue disease (CTD) causes various skin lesions that are composed of vascular tissue and inflammation. Dermoscopy has been widely used in differentiating malignant skin disorders. However, dermoscopy may be useful for evaluating nonpigmented skin disorders, since it provides an improved view of vascular structures and other subtle features that are usually not visible to the naked eye (1-4).

Much work has been done to show that nailfold video capillaroscopy(NVC) can distinguish the Raynaud's phenomenon associated with scleroderma spectrum disorder (SSD; systemic sclerosis (SSc) and its related diseases) from primary Raynaud's phenomenon (Raynaud's disease) (5-8). Distinct NVC patterns are also be useful in evaluating the severity and stage of SSD microvascular damage. Furthermore, NVC changes are as prevalent and as prominent in dermatomyositis (DM) as in SSD (9, 10). However, such findings are not found in patients with other connective tissue diseases. Routine use of NVC at the bedside has yet to become fully integrated into standard clinical practice, since the equipment is relatively expensive and not easily transported. Recently, it has been suggested that dermoscopy can replace NVC, to some extent, for detection of representative nailfold capillary abnormalities (11-15). However, dermoscopic finding and its significance of nailfold capillaries have not been summarized yet.

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Furthermore, there are few studies regarding the use of dermoscopy for other skin lesions of CTD and an overview of them is missing. In this review, we show some representative dermoscopic findings and pictures of skin lesions in CTD.,

Usage of dermoscopy for nailfold capillaries

NVC observation

Given a patient with Raynaud's phenomenon and no other symptoms, it is first important to determine whether the patient has "Raynaud's disease" or "Secondary Raynaud's phenomenon associated with CTD". Raynaud's phenomenon is most frequently found in patients with SSD, and is usually the first symptom of the disease. Therefore, the existence of SSD or other CTD must be determined. Blood examination for antinuclear antibodies, including CTD-specific autoantibodies, enable the most accurate diagnosis. However, NVC findings are also useful for early diagnosis of SSD, especially in patients negative for CTD-specific autoantibodies. When we use dermoscopy for evaluating CTDs the established findings of capillaroscopy are definitely useful. Therefore, we would like to review capillaroscopic findings of CTD before discussing our findings using dermoscopy.

Scleroderma NVC pattern

We used a video capillaroscopy system (Kekkan bijin, Kenkou Kagaku Kenkyu-kai, Co., Ltd, Kyoto, Japan). Diagnostic capillaroscopy patterns are grouped as follows: normal pattern, scleroderma pattern, and nonspecific pattern(12). The normal pattern in Figure 1A. shows homogeneous capillary distribution in the nailfold plexus without capillary loss (normal linear density: 30 capillaries per 5 mm) and no morphological alterations. The scleroderma pattern in Figures 1B-D is defined according to Maricq et al. (16, 17), with modifications according to Bergman et al. (13).Two or more of the following abnormalities are observed:①enlarged capillaries (Figures 1B and C);②hemorrhages (more than two punctuate hemorrhages per finger or confluent hemorrhage areas)(Figure 1C);③disorganization of the normal capillary distribution (Figure 1B-D);④moderate or extensive capillary loss (avascular areas)(Figure 1 D), and ⑤tortuous, crossed, and/or ramified capillaries (Figure 1D). The nonspecific pattern lacks the complete scleroderma pattern criteria.

Subclassification of scleroderma NVC pattern

The NVC scleroderma pattern is subdivided further as previously reported (18). The subclasses are as follows: (1) Early NVC pattern (Figure 1B): few enlarged/giant capillaries, few capillary hemorrhages, relatively well-preserved capillary distribution, and no evident loss of capillaries; (2) Active NVC pattern (Figure 1C): frequent giant capillaries, frequent capillary hemorrhages, moderate loss of capillaries with some avascular areas, mild disorganization of the capillary architecture, and absence of ramified capillaries; and (3) Late NVC pattern (Figure 1D): irregular capillary enlargement, few or absent giant capillaries, absence of hemorrhages, severe loss of capillaries with large avascular areas, severe disorganization of the normal capillary array, and frequent ramified/bushy capillaries. We have summarized the typical findings from each scleroderma pattern in Figure 1E (19). This subclassification has been useful for evaluation of activity and severity of vascular injury. In severe SSc cases with anti-topoisomerase I Ab present, the NVC pattern progresses quickly to the characteristic Late pattern, within two years of disease onset. On the other hand, mild SSc patients who have anticentromere Ab, gradually progress to the late pattern, more than 20 years after disease onset (20). NVC findings can be improved after treatment of SSc (21)(22).

NVC pattern in other CTD

NVC patterns are also found at high frequency in patients with DM and are generally similar to the patterns found in SSD patients [9], although the frequency of Raynaud's phenomenon is much lower. NVC patterns are referred to as a "scleroderma-like pattern" if thepattern is found in DM or disorders other than SSD. Although subtle capillary abnormality such as mild disorganization can be detected in patients with systemic lupus erythematosus (SLE), a typical scleroderma-like pattern is rarely found.

Nailfold capillary findings using dermoscopy

Nailfold capillaries may also be observed using dermoscopy. Although we use several types of dermoscopy, the picutres in this review were taken using dermoscopic camera lens with adaptor (Heine Optotechnik, Herrsching, Germany). We usually choose the third or fourth finger for examination. In a healthy person, we can see homogeneously-lined capillary distribution around the nailfold without hemorrhage (Figure 2A). Most specific NVC findings can also be detected by dermoscopy [11-15]. Our dermoscopic observations of nailfold capillariesare as follows:

1) Disorganization of the capillary architecture

Disorganization of capillary loops can be found in patients with CTD including SSD (Figure 2B~2D), DM (Figure 2E~G), and SLE (Figure 2H).

2) Enlarged/giant capillaries

Enlarged capillaries can be found in patients with CTD-associated Raynaud's phenomenon. Extremely enlarged capillaries (giant capillaries) are specific for SSD (Figure 2C) and DM (Figure 2F). The enlarged/giant capillaries are considered to be an abnormal angiogenic response, secondary to peripheral ischemia.

3) Capillary hemorrhages

Dotted or lined microhemorrahges can be found located peripheral to capillaries in patients with SSD and DM. Single hemorrhages may rarely be found in healthy persons, but plural hemorrhages are specific for SSD (Figure 2C) and DM (Figure 2F). The hemorrhages likely reflect capillaryinjury caused by ischemia-reperfusion (Raynaud's phenomenon). Using dermoscopy, we can detect some microhemorrahges that are not visible to naked eye.

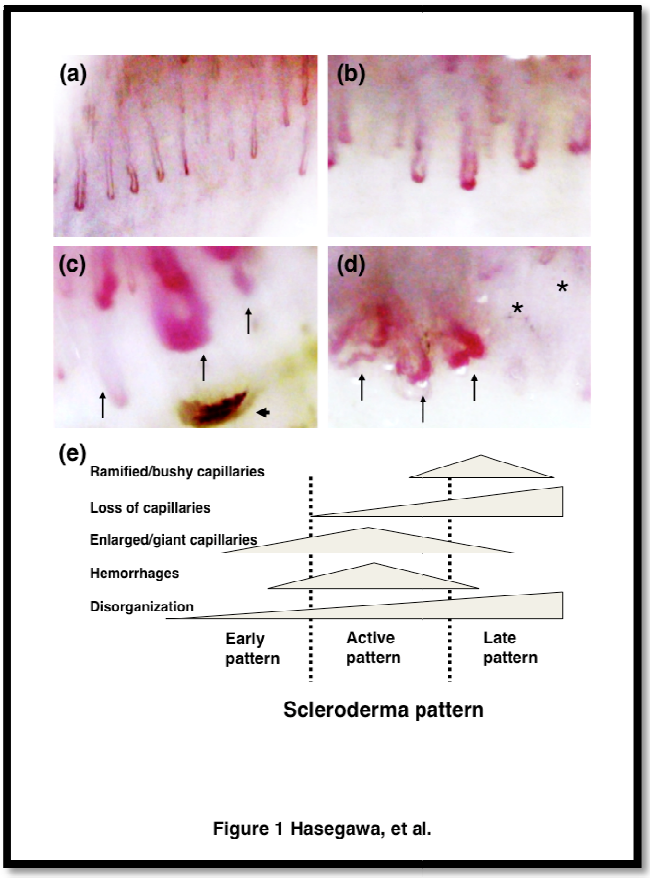

Figure 1. Nailfold video capillary findings

a) Normal pattern (normal capillaries in healthy persons): lower side represents the peripheral direction (nail plate). Note homogeneous capillary distribution in the nailfold plexus without capillary loss and no morphological alterations.
b) Early scleroderma pattern: modestly enlarged capillaries and slight disorganization of capillaries.
c) Active scleroderma pattern: frequent giant capillaries (fine long arrows), frequent capillary hemorrhages (heavy short arrows), and moderate loss of capillaries.
d) Late scleroderma pattern: severe loss of capillaries with large avascular areas (asterisks), severe disorganization of the normal capillary array, and frequent ramified/bushy capillaries (fine long arrows).
e) The relationship between each NVC finding and scleroderma pattern.

4) Capillary loss or avascular areas

The existence of moderate to severe loss of capillaries (avascular areas) is characteristic for SSD (Figure 2D) or DM (Figure 2G). The severity reflects the peripheral circulatory disturbance of SSD or DM. SSD patients with severe capillary loss frequently develop intractable digital

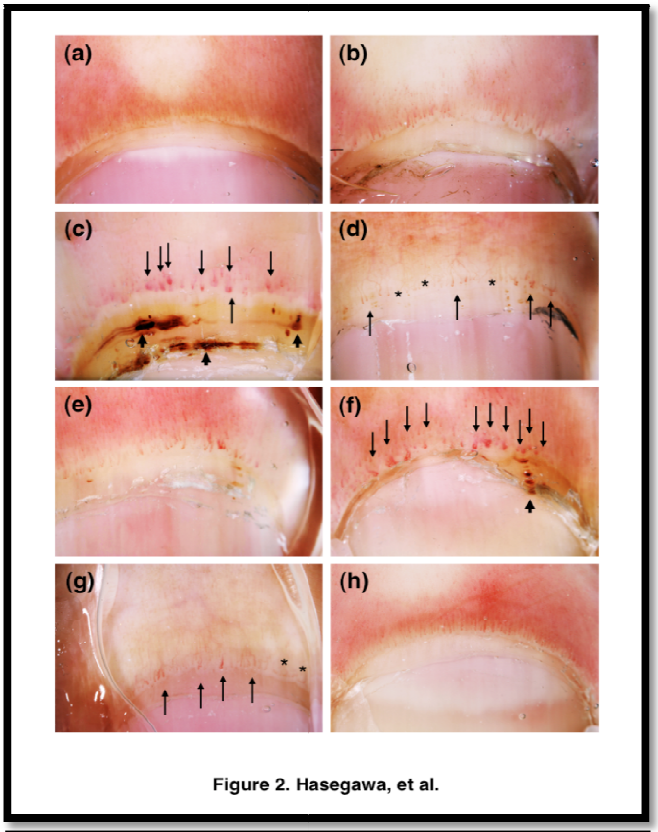

Figure 2. Dermoscopy findings in healthy persons and systemic sclerosis and its related disease (SSD).

a) Normal capillaries in healthy persons.
b) Early pattern in patients with SSD: mild disorganization of the capillary architecture and modestly enlarged capillaries.
c) Active pattern in patients with SSD: enlarged/giant capillaries (fine long arrows) and hemorrhages (heavy short arrows).
d) Late pattern in patients with SSD: loss of capillaries with large avascular areas (astrisks) and ramified/bushy capillaries (fine long arrows).
e) Early pattern in patients with dermatomyositis: mild disorganization of the capillary architecture and modestly enlarged capillaries.
f) Active pattern in patients with dermatomyositis: enlarged/giant capillaries (fine long arrows) and hemorrhages (heavy short arrows).
g) Late pattern in patients with dermatomyositis: loss of capillaries with large avascular areas (astrisks) and ramified/bushy capillaries (fine long arrows).
h) Modestly enlarged capillaries in patients with SLE. This does not fit the criteria of scleroderma pattern, since other abnormalities are not detected.

5) Ramified/bushy capillaries

Ramified or bushy capillaries can be found in the hypovascular area of patients with SSc (Figure 2D) and DM (Figure 2G). This advanced vascular damage is an abnormal angiogenic response to the hypoxic state.

Usage of Dermoscopy for Skin Lesions of CTD

Dermoscopic findings in inflammatory skin diseases

Dermoscopic evaluation for inflammatory skin diseases should include the following: I. vascular morphology (dot, globule, linear, glomerulus-like); II. vascular arrangement (regular, clustered, patchy, peripheral, in rings); III. background color (dull-red, light red, yellowish); IV. scale colour (white, yellow); V. scale distribution (patchy, peripheral, diffuse, central); VI. presence of white crossing streaks (Wickham-striae) [1,23].

Systemic lupus erythematosus

Malar rash and discoid lupus erythematosus (DLE) are specific skin lesions of SLE. However, DLE is sometimes clinically difficult to distinguish from other skin diseases such as lichen planus, psoriasis vulgaris, nummular eczema, and cutaneous sarcoidosis.

The dermoscopic findings of DLE are not necessarily specific to the disease (Figure 3). The background colour is usually light red or orange, and often accompanies partial/whitish homogeneous lesions and/or white scales. Variously arranged dilated capillaries with varied morphology are highly visible. It has been reported that follicular keratin plugs, which correlate histologically with prominent hyperkeratosis in follicular openings, are detected only in active lesions (Figure 3B), not in scars or healed skin of DLE (Figure 3C) [24]. The finding of keratin plugs may therefore be useful as an estimate of disease activity or response to treatment in patients with DLE.

Regarding differential diagnosis of DLE, representative dermoscopic findings of psoriasis vulgaris are regularly distributed, dotted, globular, glomerular, or twisted loop-like vessels over a light red background and white scales (Figure 4A) [3,23,25]. The tortuous and dilated blood vessels within the elongated dermal papillae in psoriasis are present as regularty distributed red dots, red globules, glomerule-like vessels, and twisted red loops [2]. Dermoscopy of lichen planus shows diagnostic white crossing lines (Wickham striae) and red dotted or globular vessels at the periphery (Figure 4B) [25,26]. In eczematous lesions including nummular eczema, serum exudates can be seen dermoscopically as shiny yellow clods (Figure 4C) [27]. Cutaneous sarcoidosis as well as other cutaneous granuloma show dermoscopically translucent yellow to orange, globular-like or structureless areas associated with linear vessels (Figure 4D) [28].

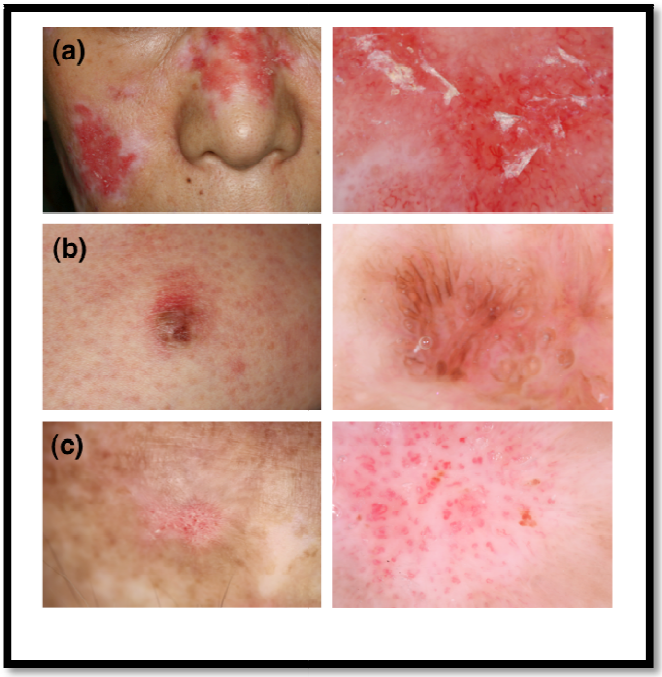

Figure 3. Dermoscopic findings in discoid lupus erythematosus (DLE). Clinical pictures and their dermoscopic counterparts are shown.

a) Active DLE at the cheek. Background is light red and mild pigmentation and depigmentation are mixed. Irregularly arranged enlaged ramified vessels are highly visible.

b) Active and prolonged (hypertrophic) DLE at the chest. Light red and white lesions are mixed in the background. Follicular keratin plugs and peripheral linear irregular vessels are found.

c) Healing stage of DLE at the forehead. Background is light red and mild partial depigmentation and white scales are found. Many dotted or hairpin-like vessels are highly visible.

Thus, although the dermoscopic findings of DLE are not entirely specific, dermoscopy can add important clues that help distinguish DLE from other skin disorders.

Systemic sclerosis

Telangiecatases are frequently detected on face, hand, mucous membranes, and other sites in patients with SSc. They are vascular lesions composed of vasodilated post-capillary venules without evidence of neovascularization or inflammation [29,30]. The mechanism by which telangiectases develop in SSc patients remains unknown. However, it may be the result of an aberrant attempt to increase blood perfusion to hypoxic tissues as a consequence of impaired circulation [31]. A recent study reported that

increased numbers of telangiectases strongly associated with the presence of pulmonary arterial hypertension in patients with SSc [31]. However, there are almost no studies that have investigated the findings in detail using dermoscopy. Morphologically, there are at least two kinds of telangiectases in SSc.

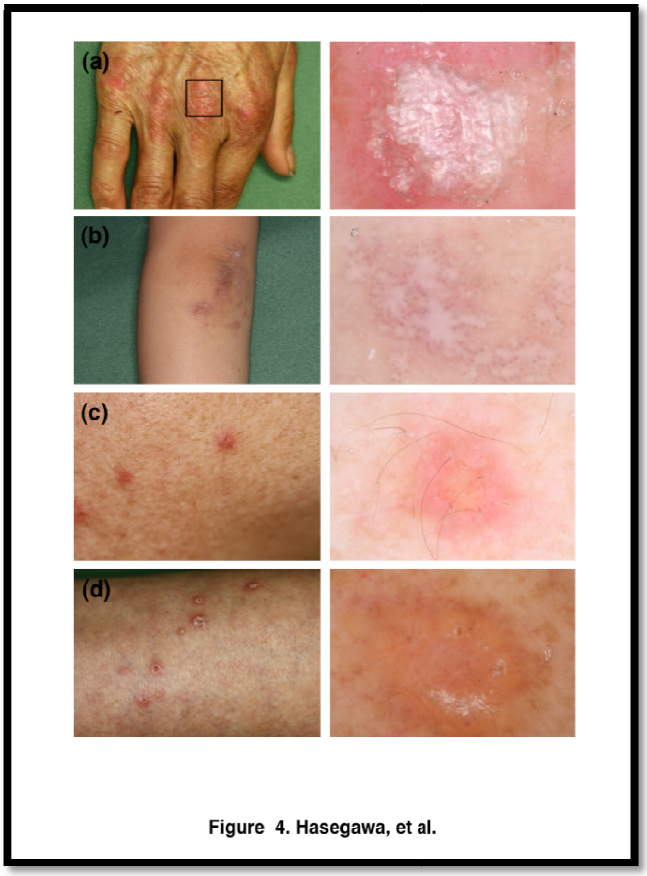

Figure 4. Dermoscopic findings in skin disorders that should be differentiated from discoid lupus erythematosus (DLE). Clinical pictures and their dermoscopic counterparts are shown.

a) Psoriasis vulgaris at dorsal surface of the hand. Background is light red covered with white large scale. Dotted vessels are found outside of the scale.
b) Lichen planus on the arm. Diagnostic white crossing lines (Wickham striae) are detected.
c) Nummular eczema on the arm. Serum exudates can be seen dermoscopically, as shiny yellow clods.
d) Cutaneous sarcoidosis on the arm. Yellow to orange structureless areas associated with linear vessels

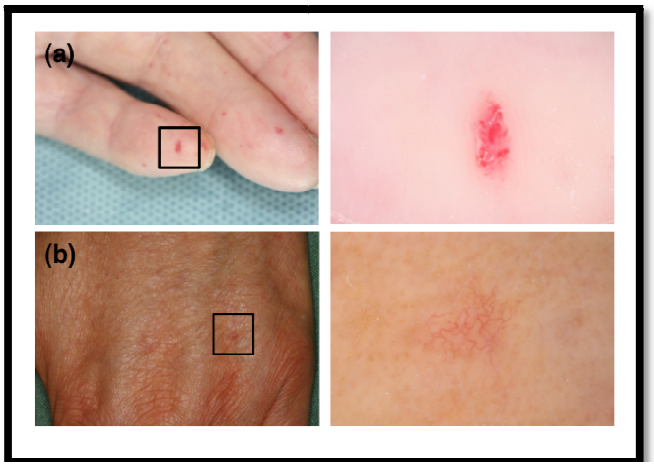

Figure 5. Dermoscopic findings in systemic sclerosis. Clinical pictures and their dermoscopic counterparts are shown.

a) Well-circumscribed dense telangiectases referred to as "matted" lesions.
b) Poorly-marginated light telangiectases referred to as "stellate" lesions.

The first are well-circumscribed dense telangiectases referred to "matted" lesions [31]. This type is frequently detected in patients with anticentromere Ab and the telangiectases are composed of enlarged capillaries (Figure 5A). The second are poorly-marginated light telangiectases referred to as "stellate" lesions [31]. This type is often found in patients with anti-topoisomerase I Ab. Here the telangiectases are composed of fine linear, tortuous, and/or ramified capillaries that are typically arranged in stellatepatterns (Figure 5B). Interestingly, the dermoscopic findings of enlarged capillaries are similar to giant capillaries/enlarged capillaries detected as the scleroderma active-pattern in the nailfold. On the other hand, the dermoscopic findings of fine capillaries are similar to that of tortuous, crossed, and/or ramified capillaries found as scleroderma late-pattern in the nailfold. However, the pathological and clinical significance of telangiectases remains unestablished, in contrast to nailfold capillary findings.

Dermatomyositis

Dermoscopic findings of Gottron's sign are not specific. Irregular arrangement of venules and scales are found on a light red background (Figure 6A and 6B). However and interestingly, the Gottron's sign observed by dermoscopy was impressive in one of our cases where anti- melanoma differentiation-associated protein 5 (MDA-5) Ab was present [32]. Anti-MDA-5 Ab is highly associated with the

development of rapidly progressive interstitial pneumonia [32]. Gottron's sign of her elbows were usual as determined by the naked eye (Figure 6C). However, dermoscope findings showed punctuate hemorrhage in addition to the usual Gottron's sign findings. In fact, she developed rapidly progressive interstitial pneumonia. The punctuate hemorrhage thoroughly disappeared after intensive immunosuppressive treatment and stabilization of interstitial pneumonia. Since it is known that DM patients with anti-MDA-5 Ab exhibit skin ulcer more frequently than patients without the Ab [33], we suspect the hemorrhage detected on Gottron's sign may be reflecting vascular injury associated with rapidly progressive interstitial pneumonia.

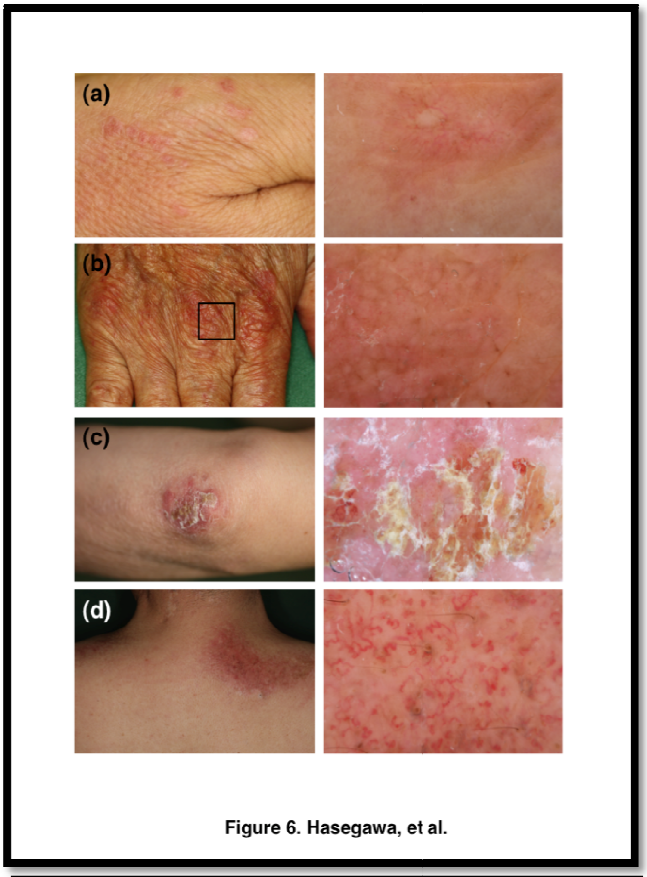

Figure 6. Dermoscopic findings in dermatomyositis. Clinical pictures and their dermoscopic counterparts are shown.

a, b)Gottron's sign of the dorsal face of the hand. Background is light redaccompanied by white lesions. Linear irregular vessels are found.

c) Gottron's sign at the elbow. Dermoscopy findings showed punctuate hemorrhage in addition to usual Gottron's sign's findings. The patient developed rapidly progresive interestitial pneumonia.

d) Poikiloderma on the back. Enlarged, linear, irregular vessels are highly visible and pigmentation and depigmentation are mixed.

Another interesting finding was made by dermoscopy of poikilodermaskin lesions in patients with DM. Enlarged linear irregular vessels are visible and pigmentation and depigmentation are mixed (Figure 6D). Although poikiloderma is often detected in pateints with DM, but it is not specific for DM and usually detected by naked eyes. However, the confirmation using dermoscopy may be useful to distinguish poikiloderma from other skin lesions.

CONCLUSION

Our findings are preliminary and are not based on systematic studies of large numbers of patients. Nonetheless, we propose that dermoscopic observations are helpful for diagnosing and evaluating disease activity in some clinical situations. Improved visualization of vessels and color variations, that are difficult to recognize with the naked eye, can be observed using dermoscopy. A more detailed determination of specific dermoscopic features of skin lesions of CTD may be a valuable resource for clinical assessment. Furthermore, these findings may provide clues that improve our understanding of the pathogenesis of skin lesions and of CTD itself. We hope that dermoscopy becomes widely used for the evaluation of CTD and believe that further investigation will soon yield information valuable to the clinical practitioner.

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CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

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