Dermoscopic Features of Actinic Cheilitis and Other Common Inflammatory Cheilitis: A Multicentric Retrospective Observational Study by the International Dermoscopy Society

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Abhijeet Kumar Jha[a] Martyna Sławińska[b] Keshavamurthy Vinay[c] Bengu Nisa Akay[d] Grażyna Kamińska-Winciorek[e] Michał Sobjanek[b] Md Zeeshan[a] Anupama Singh[a] Balachandra S. Ankad[f] Yasmeen Jabeen Bhat[g] Aimilios Lallas[h] Zoe Apalla[h] Iris Zalaudek[i] Enzo Errichetti[j]

[a]Department of Skin & VD, Patna Medical College & Hospital, Patna, India; [b]Department of Dermatology, Venereology and Allergology, Faculty of Medicine, Medical University of Gdańsk, Gdańsk, Poland; [c]Department of Dermatology, Venereology and Leprology, Postgraduate Institute of Medical Education and Research, Chandigarh, India; [d]Department of Dermatology, Faculty of Medicine, Ankara University, Ankara, Turkey; [e]The Department of Bone Marrow Transplantation and Onco-Hematology, Maria Sklodowska- Curie National Research Institute of Oncology (MSCNRIO), Gliwice Branch, Gliwice, Poland; [f]Department of Dermatology, S. Nijalingappa Medical College, Navanagar, Bagalkot, India; [g]Department of Dermatology, Government Medical College, Srinagar, India; [h]First Department of Dermatology, Aristotle University, Thessaloniki, Greece; [i]Department of Dermatology, University of Trieste, Trieste, Italy; [j]Institute of Dermatology, Santa Maria della Misericordia University Hospital, Udine, Italy

Keywords
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Abstract
Background: Clinical differentiation between different cheilitis variants may be difficult. Application of mucoscopy, in addition to clinical background, could provide additional diagnostic clues facilitating initial patient management. ***Objectives:*** To determine mucoscopic clues differentiating actinic cheilitis from the main forms of inflammatory cheilitis, including eczematous cheilitis, discoid lupus erythematosus, and lichen planus of the lips. ***Methods:*** This was a retrospective, multicenter study being a part of an ongoing project "Mucoscopy – an upcoming tool for oral mucosal disorders" under the aegis of the International Dermoscopy Society. Cases included in the current study were collected via an online call published on the IDS website (www.dermoscopy-ids.org) between January 2019 and December 2020. ***Results:*** Whitish-red background was found in actinic cheilitis as well as in cheilitis due to discoid lupus erythematous and lichen planus. Polymorphous vessels were more likely to be seen in actinic cheilitis compared to other causes of cheilitis. White scales, ulceration, and blood spots predominated in actinic cheilitis and lichen planus, whereas yellowish scales typified eczematous and discoid lupus erythematous cheilitis. Radiating white lines although most common in lichen planus patients were also seen in actinic cheilitis. ***Conclusion:*** Despite differences in the frequency of mucoscopic structures, we have not found pathognomonic features allowing for differentiation between analyzed variants of cheilitis.

Abhijeet Kumar Jha and Martyna Sławińska contributed equally to this work.

Introduction

Actinic cheilitis (AC) is a cheilitis caused by chronic exposure to ultraviolet radiation mainly involving the lower lip. Similarly to actinic keratosis, it is considered a premalignant disorder, yet the risk of progression to squamous cell carcinoma (SCC) in AC seems to be higher [1]. Thus, careful assessment of the lips should be an integral part of dermatological assessment, especially in individuals with signs of chronic skin photodamage [2]. AC may manifest in wide clinical presentations, from subtle dryness and scaling to indefinite demarcation of the vermilion border, erythematous or whitish areas, hyperkeratotic plaques, or ulceration with a crust. Such cases need to be differentiated primarily with invasive SCC, but also with several inflammatory diseases affecting the lips.

Dermoscope has recently become an accessory tool in diagnostics of neoplastic and inflammatory conditions of the skin; however, mucoscopy is still in its early stages of development [3]. More precise knowledge on dermoscopic patterns observed in this special anatomical region could improve patient management. Previous studies concerning mucoscopy of AC include case reports and case series, while no analysis comparing mucoscopic findings of AC and inflammatory cheilitis has been published so far [4–6]. The aim of the study was to determine mucoscopic clues differentiating AC from the main forms of inflammatory cheilitis, including eczematous cheilitis, discoid lupus erythematosus (DLE), and lichen planus (LP) of the lips.

Materials and Methods

This was a retrospective, multicenter study being a part of an ongoing project "Mucoscopy – an upcoming tool for oral mucosal disorders" under the aegis of the *International Dermoscopy Society* (IDS). Cases included in the current study were collected via an online call published on the IDS website (www.dermoscopy-ids.org) between January 2019 and December 2020. Initial observations of benign cheilitis (including LP, lichen sclerosus, plasma cell cheilitis, irritative cheilitis, allergic cheilitis, fixed drug eruption, cheilitis in the course of lupus erythematosus) were previously published along with a literature review [3]. Only histopathologically confirmed AC cases with high-quality clinical and dermoscopic/videodermoscopic pictures were included. Clinical and dermoscopic findings in the study group of AC cases were analyzed and compared with dermoscopic findings of patients diagnosed with inflammatory cheilitis (eczematous cheilitis, DLE, and LP of the lips) by the diagnostic gold standard (histology for DLE and LP and clinical features/course for eczematous cheilitis; histological examination was performed in case of doubts also for the latter). Dermoscopic images were taken either with a DermLite DL4 manual hand-held dermoscope (3Gen, LLC) coupled with an iPhone 11 pro or Fotofinder platform-based dermoscopy system GmbH, Germany (camera Medicam 800HD). Images with DermLite DL4 were obtained using polarized non-contact dermoscopy at a default optical magnification of ×10, whereas FotoFinder-based images were obtained using non-polarized contact dermoscopy (NPCD) at ×20 magnification. In cases where NPCD was applied, an ultrasound gel was used to facilitate vessel visualization.

Clinical and dermoscopic pictures were evaluated by consensus of two experienced investigators (A.K.J. and K.V.) using dermoscopy in their daily practice, according to the predefined criteria. The investigators were not blinded to the final diagnosis. In case of discrepancy, the final score for a particular case and structure was obtained based on the decision of a third experienced evaluator. Dermoscopic features that were assessed included background color, morphology, and distribution of vessels and scales and any special structures according to previous studies [3–7]. The consensus statement of *International Dermoscopy Society* on dermoscopic terminologies was adopted for assessment and description of the dermoscopic features [7].

Data analysis was carried out using SPSS version 26.0 statistical software package (IBM Corp). Informed consent form of every patient was required, and approval from the Patna Medical College & Hospital local ethics committee was obtained.

Results

One hundred and thirty-four cases provided by 12 centers from 5 countries (India, Italy, Greece, Poland, and Turkey) were included in the final analysis. The study group consisted of 45 patients with AC, and the control group of 89 patients with inflammatory cheilitis (eczematous cheilitis, $n = 52$; cheilitis in the course of DLE, $n = 23$; and LP of the lips, $n = 14$). Table 1 and Figure 1 show details on dermoscopic analysis of AC cases and controls.

Background Color

The background colors assessed were a combination of white (representing keratinization) and red (representing vascularity). In addition, among patients with darker skin phototypes, bluish-grey color was observed. A background color of whitish-red was positively associated with AC (34/45; 75.5%) compared to eczematous cheilitis, which predominantly showed a whitish-yellow background color. However, whitish-red background was also prevalent among cheilitis due to DLE and LP (Table 1).

Vessel Morphology and Distribution

Polymorphous vessels were more likely to be seen in AC (38/45; 84.4%) compared to other causes of cheilitis, with linear-irregular vessels (32/45; 71.1%) being the

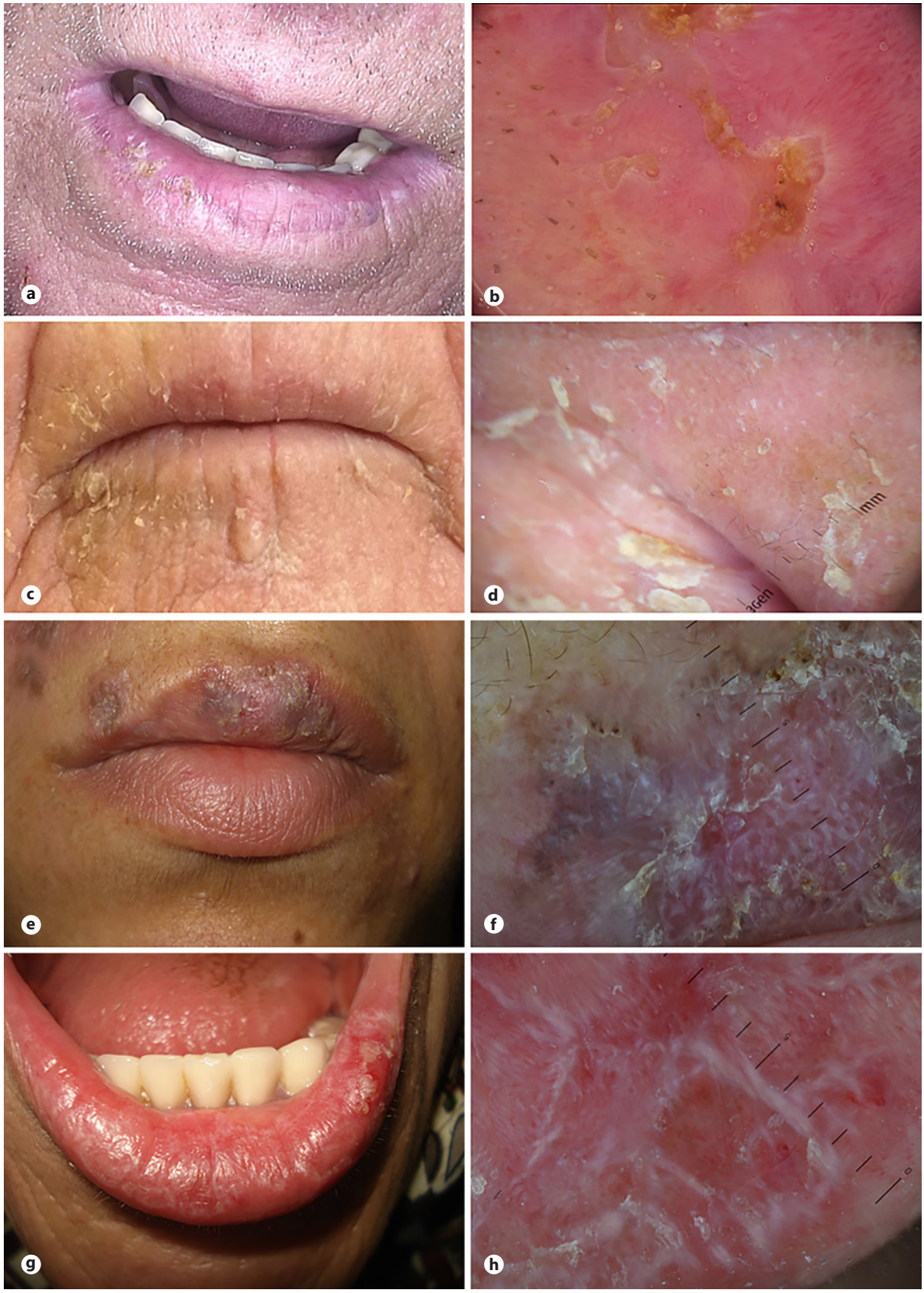
Table 1. Observed dermoscopic findings and statistical differences in actinic cheilitis and control groups (eczematous cheilitis, lip discoid lupus erythematosus, and lichen planus of the lips)

Dermoscopic finding	Actinic cheilitis (n = 45) n (%)	Controls (n = 89)			
		eczematous cheilitis (n = 52) n (%)	lip discoid lupus erythematosus (n = 23) n (%)	lichen planus of lips (n = 14) n (%)	p value*
Background color					
White	4 (8.8)	10 (19.2)	3 (13.0)	1 (7.1)	<0.0001
White-yellow	3 (6.6)	36 (69.2)	0 (0.0)	1 (7.1)	<0.0001
White-red	34 (75.5)	4 (7.6)	16 (69.5)	12 (85.7)	<0.0001
Red	2 (4.4)	2 (3.8)	4 (17.3)	0 (0.0)	0.006
Blue-grey	2 (4.4)	0 (0.0)	0 (0.0)	0 (0.0)	
Vessels					
Vessels' morphology					
Linear-irregular	32 (71.1)	18 (34.6)	20 (86.9)	5 (35.7)	<0.0001
Dotted	9 (20.0)	4 (7.6)	1 (4.3)	3 (21.4)	<0.0001
Hairpin	18 (40.0)	4 (7.6)	11 (47.8)	6 (42.8)	0.001
Vessels' monomorphism/polymorphism					
Monomorphous	7 (15.5)	22 (42.3)	12 (52.1)	8 (57.1)	0.004
Polymorphous	38 (84.4)	4 (7.6)	11 (47.8)	6 (42.8)	<0.0001
Vessels' distribution pattern					
Diffuse	40 (88.8)	22 (42.3)	14 (60.8)	2 (14.2)	<0.0001
Central	2 (4.4)	2 (3.8)	2 (8.6)	0 (0.0)	0.5
Peripheral	3 (6.6)	2 (3.8)	7 (30.4)	10 (71.4)	0.003
Clustered	0 (0.0)	0 (0.0)	0 (0.0)	2 (14.2)	
Scales					
Scales' color					
White	20 (44.4)	8 (15.3)	5 (21.7)	13 (92.8)	<0.0001
Yellow	8 (17.7)	38 (73.0)	14 (60.8)	1 (7.1)	<0.0001
Scales' distribution pattern					
Central	2 (4.4)	10 (19.2)	5 (21.7)	0 (0.0)	0.001
Peripheral	1 (2.2)	7 (13.4)	4 (17.3)	0 (0.0)	0.001
Patchy	20 (44.4)	5 (9.6)	0 (0.0)	14 (100.0)	<0.0001
Diffuse	5 (11.1)	24 (46.1)	10 (43.4)	0 (0.0)	<0.001
White structures					
Radiating lines	14 (31.1)	0 (0.0)	0 (0.0)	11 (78.5)	0.005
Circles	4 (8.8)	0 (0.0)	0 (0.0)	3 (21.4)	0.052
Dots/globules	11 (24.4)	19 (36.5)	0 (0.0)	0 (0.0)	0.001
Structureless areas	27 (60.0)	0 (0.0)	12 (23.0)	0 (0.0)	<0.0001
Other structures					
Blood spots	5 (11.1)	0 (0.0)	0 (0.0)	1 (7.1)	0.005
Ulceration	14 (31.1)	0 (0.0)	0 (0.0)	3 (21.4)	0.001
Pigment dots/globules	9 (20.0)	7 (13.4)	0 (0.0)	3 (21.4)	0.002

* χ^2 test, t test and ANOVA test were used.

Fig. 1. Clinical and dermoscopic (mucoscopic) pictures of the main variants of cheilitis analyzed in the study. **a**, **b** Actinic cheilitis in a patient with skin phototype II. Mucoscopy shows yellow scale surrounded with polymorphous vessels (linear irregular, dotted, hairpin) over red background. **c**, **d** Eczematous cheilitis in a patient with skin phototype II. Mucoscopy shows yellow and white scale and diffuse dotted vessels over white-red background. **e**, **f** Lip involvement the course of DLE in a patient with skin phototype IV. Mucoscopy shows white and yellow scale, white structureless areas, red background, brown globules, and brown structureless areas. **g**, **h** Lichen planus of the lips in a patient with skin phototype III. Mucoscopy shows white scale, white radial lines in perpendicular distribution over white-red background and diffuse dotted and linear irregular vessels.

(For figure see next page.)



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commonest, followed by hairpin (18/45; 40%) and dotted vessels; this polymorphous morphology was diffuse in distribution. In contrast, monomorphous vessels were more likely to be seen in benign pathology with peripheral hairpin and linear irregular vessels seen in LP.

Scale Morphology and Distribution

White scales were predominantly seen in both AC (20/45; 44.4%) and LP (13/14; 92.8%), whereas eczematous (38/52; 73%) and DLE (14/23; 60.8%) cheilitis were typified by yellowish scales. The scales showed patchy distribution in LP and AC, while they were diffusely distributed in eczematous cheilitis and DLE.

White Structures

Radiating white lines (11/14; 78.5%) were more likely a feature of LP, whereas white structureless areas were seen commonly in AC (27/45; 60%).

Other Structures

Ulceration and blood spots were more often seen in AC and LP compared to eczematous cheilitis and DLE (shown in Fig. 1).

Discussion

Previous studies concerning mucoscopy of AC included case reports/case series and identified main patterns observed in AC, namely white structures (white structureless areas, white halos, shiny white streaks, white circles, and scales), pink to red structureless areas and radially arranged blood vessels surrounding ulcerations [4–6].

In our study, the most prevalent AC dermoscopic variables were white-red structureless background, polymorphous vessels, linear irregular vessels, and white structureless areas. Ulceration, shown in previous studies as highly prevalent feature in lip SCC, was present only in 31.1% cases of AC in our analysis. Notably, it was seen also in 21.4% cases of lip LP and not observed in eczematous cheilitis and DLE [3, 6].

In the largest previously published study by Benati et al. [6], which compared lip SCC with AC cases (n = 16), white halos and white structureless areas were present in 56% and 75% of cases, respectively, while only two AC cases (13%) revealed white circles. The study did not mention the frequency of other structures, including vessel morphology. In our study, white circles occurred in 8.8% of AC cases, but also in 21.4% (3/14) of cases diagnosed with LP of the lips.

Most commonly reported vessel morphology was linear irregular vessels, being present in 71.1% (32/45) of the analyzed AC cases, in line with previous observations [5]. In our study, linear vessels were found to be non-specific, and highly prevalent also in inflammatory dermatoses, yet in AC they occurred more commonly in association with other vessel types in the spectrum of polymorphous pattern.

To our knowledge, previous studies did not report pigment dots/globules in AC. In our study, they were found in 20.0% of AC and 21.4% of LP cases, mostly in patients with darker skin phototypes.

Current knowledge on dermoscopic presentation of LP of the lips is based on single case reports/case series, which described the presence of Wickham striae (linear and circular), violaceous to pink background and scaling [8, 9]. Recently published case series by Neema et al. [10] (n = 12) described additionally leaf venation-like Wickham striae, hairpin vascular pattern, and rosettes. Wickham striae, in our study descriptively defined as radiating white lines, was present in 78.5% (11/14). Moreover, the structures resembling Wickham striae were seen in patients suffering from LP-like chronic GvHD [11].

In a case series (n = 7) of lip DLE described by Salah et al. [12] most common dermoscopic features were hairpin vessels (5/7), brown pigment spots (6/7), and scales (6/7). In contrast, in our study, DLE cases presented mostly with white-red background, linear irregular vessels, and yellow scale.

Eczematous cheilitis, besides of our initial report [3], was not previously a subject of dermoscopic analysis. Dotted vessels highly prevalent in eczematous skin lesions were detected in only 7.6% of the analyzed cases. Such differences in vessel morphology could be associated with a convex structure of the lips.

The main limitation of this study is its retrospective design as well as the fact that dermoscopic pictures were made with different models of dermoscopes/cameras. Other limitations are lack of SCC in situ in the control group and other less common variants of inflammatory cheilitis, which have to be considered among differential diagnoses. The proportion of patients with different skin phototypes in this study differed depending on the diagnosis. Finally, some clinically obvious eczematous cheilitis responding well to anti-inflammatory topical therapy were not confirmed with histopathological examination.

In conclusion, though we found certain mucoscopic features, namely reddish-white background color, pres-

ence of diffusely distributed polymorphic vessels, ulceration, and blood spots to be suggestive of AC, there was a considerable overlap of these mucoscopic features with other benign causes of cheilitis. Our study did not find any pathognomonic mucoscopic features allowing for differentiation between analyzed variants of cheilitis.

Key Message

Clinical differentiation between different cheilitis variants may be difficult. Despite differences in the frequency of mucoscopic structures, we have not found pathognomonic features allowing for differentiation between analyzed variants of cheilitis.

Statement of Ethics

The study was approved by Institutional Ethics committee Patna Medical College, Patna (project MF/192). Institutional permission for participation in the study and signed informed consent form of every patient was essential; approval from the local ethics committee was obtained.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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None.

Author Contributions

A.K.J. planned the study design, sample cohort, supervised the study, analyzed the images, co-authored the manuscript and revised the final manuscript version. M.Sł. gathered the subjects' data, prepared manuscript draft and figures, and revised the final manuscript version. K.V. gathered the subject's data, analyzed the images, and co-authored manuscript. B.N.A. gathered the subjects' data. G.K.W. gathered the subjects' data, revised the initial manuscript draft and revised the final manuscript version, is a corresponding author. M.So. gathered the subjects' data and revised the final manuscript version. M.Z. gathered the subjects' data, prepared statistics and revised the final manuscript version. A.S. gathered the subjects'data and revised the final manuscript version. B.S.A. gathered the subjects'data and revised the final manuscript version. Y.J.B. gathered the subjects'data and revised the final manuscript version. A.L. gathered the subjects'data and revised the final manuscript version. Z.A. gathered the subjects'data and revised the final manuscript version. I.Z. gathered the subjects'data and revised the final manuscript version. E.E. gathered the subjects'data and revised the final manuscript version.

Data Availability Statement

Data available on written request.

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