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Title: Onychoscopy with red-light for vascular pattern identification: a study of 33 patients.

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All authors contribute to: design, data acquirement, study writing, editing.

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Abstract

BACKGROUND: Nail dermoscopy (onychoscopy) during physical examination assists in correct diagnosis. Often further magnifications are necessary for an effective differential diagnosis. With the addition of a red-light to the dermoscope important vascular features can be visualized.

OBJECTIVE: To describe common features observed at onychoscopy with a new device that combines the regular white-light with the red-light illumination, demonstrating it's useful for diagnosis of nail disorders.

METHODS: We enrolled 33 consecutive patients referred to the Nail Diseases Dermatology Unit of the University of Modena and Reggio Emilia and to the Outpatient Consultation for Nail Disease of the Dermatology Unit of the University of Bologna. Patients were assessed with a standard hand-held dermoscope and at the red-light dermoscope. Dermoscopic images were collected.

RESULTS: The new prototype was used during daily clinical practice and allowed a more accurate visualization of some details that classic onychoscopy can miss. In particular, with the help of the red-light it was possible to better visualize nail lesions that were characterized by some kind of color change or vascular alterations.

CONCLUSION: The new device of red-light for vascular pattern onychoscopy can be a new investigation method to observe nail alterations, especially due to vascular pattern, even with low magnification, without the necessity to use higher resolutions.

Introduction

Nail disorder differential diagnosis is often clouded with uncertainty, as most nail disorders are due to infectious origins ($\approx 50\%$) but may also be due to trauma, contactants, inflammatory skin diseases, general medical diseases, drug induced nail abnormalities and tumors.¹ Nail assessment is often performed by means of clinical inspection and dermoscopy, and can be accompanied by diagnostic imaging, microbiological (including mycological) testing, and histopathological examination. The dermoscopy for nail disease assessment (onychoscopy) has the power to magnify clinical features of nail diseases to assist in clinical diagnosis.¹

At ten-fold magnification routine onychoscopy, some signs of nail disorders can be visualized.² Higher magnifications can also be used by means of digital dermoscopy devices. However, during the onychoscopy examination, fine details of nail alterations, which can be very useful for differential diagnosis such as nail apparatus mass, nail surface alterations or the vascular pattern of different nail conditions, can be complicated to detect. In these cases, invasive procedures such as nail biopsy or avulsion, are required to achieve a correct diagnosis.

With the objective to expand the diagnostic potential for onychoscopy, a new device for manual dermoscopy has been developed. This device combines regular white-light onychoscopy, which illuminates the digit from above (as per the regular dermoscopy), with the addition of a red-light led illumination from under the digit. The red-light illumination is intended to enhance the visualization of deep vascular and pigmented structures.

In this study, we describe common features observed at onychoscopy in a series of consecutive patients encountered at 2 dermatology centers over a 4 months period, comparing the image clarity of white-light onychoscopy (10x), magnified white-light onychoscopy (40x) and red-light onychoscopy (10x).

Materials and Methods

Consecutive patients referred to the Nail Diseases Dermatology Unit, University of Modena and Reggio Emilia and University of Bologna, Italy, presenting history of difficult to diagnose nail alterations between March 2018 and June 2018, were examined. Examinations included white-light onychoscopy (white polarized images at 10x and 40x magnifications) and a red-light led enhanced onychoscopy (polarized images at 10x magnification only) with the Nailio[®] dermoscope (3Gen, San Juan Capistrano, CA, USA), Figure 1.

All lesions were initially examined with onychoscopy, the Nailio[®] dermoscope, which combines 3Gen's photo contact dermoscope "Photo X", capable of producing polarized and non-polarized white-light of a spectrum similar to daylight. The patient's digit is placed on a circular resting plate, initially under the white polarized light, radiating from the lens positioned above the digit. A wide range of digital cameras and smartphones may be attached to the "Photo X" dermoscope, either magnetically or via a threaded connection. Initial images for this study were visualized under white-light (10x) with an iPhone 6S (Apple[®]). A

transparent ultrasound gel was then applied to the nail plate and to the proximal and lateral periungual tissue to improve visualization of nail color alterations at magnifications >10x. Images were again acquired with an iPhone 6S placed on the lens with the white polarized light. The white polarized images were then uploaded to a video dermoscopy Fotofinder Medicam 800[®] (Teachscreen Software, Bad Birnbach, Germany) for the visualization of the acquired images at higher magnification (40x). The circular resting plate contains a single led producing red-light (625 nm), which trans-illuminates the digit from below. In order to achieve the desired visualization of superficial vs. deeper structures, the dermoscope has four brightness settings, allowing adjustment of the white-light vs. red-light ratio. For photographing the nail at oblique angles, or to capture the distal nail, the dermoscope head can be tilted in relation to the resting nail plate within a range of 0° to 90°. Images were again acquired with the iPhone 6S placed above the lens at a standard 90° angle. In the case of alterations affecting multiple nails of the same patient, images from the nail with the most significant clinical alterations were acquired. Experienced nail doctors made the diagnoses and collected the images in a dedicated file for retrospective analysis. All nail tumors were confirmed by excisional biopsy and histologic examination. For clarity of image analysis, images were randomly displayed to 4 dermatologists in training with at least 2 years of experience in nail disorders, who were asked to evaluate white-light (10x), magnified white-light (40x) and red-light (10x) images for the presence of common features associated with specific diagnoses according to their absence and their presence with a level of clarity, ranging from 0 to 3 (3 representing the clearest visualization of the feature).

Statistical analysis

Statistical analysis was done using STATA[®] software version 14 (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP.). Qualitative data were expressed as frequency and percentage. Chi-square test (Fisher's exact test) was used to examine the relation between qualitative variables. A p-value <0.05 was considered significant.

Results

A total of 33 consecutive patients were recruited into the study, with mean age 44.3 (range 13-78 years), including 16 (48%) female patients. Diagnoses included traumatic onycholysis (3), subungual hematoma (3), frictional pyogenic granuloma (3), glomus tumor (3),

onychopapilloma (3), onychomatricoma (3), digital mucoid cyst (3), fibrokeratoma (3), nail alterations in alopecia areata (3), nail psoriasis (3) and pustular nail psoriasis (3). All features assessed for each nail disorder are outlined in Table 1.

In our population, nail alterations due to traumatic disorders were verified in both fingernails and toenails of 6 patients. Of the features observed for traumatic onycholysis, the whitish to yellow subungual space was found to be significantly more visible at white-light and red-light compared to magnified white-light. Other features associated with the traumatic disorders were visualized similarly among the three methodologies of image acquisition (Figure 1).

In frictional pyogenic granuloma, the use of the red-light was evaluated as offering an enhanced visibility of the red discoloration, with a milky red veil and a regular vessel pattern of the vessels (Figure 2).

Nail tumors were the most commonly observed nail disorder in the study population (n=9). For glomus tumors, a significant difference was observed for the clarity of visualization of a deep red-purple subungual mass with blurred borders at red-light ($p=0.012$) (Figure 3). Additionally, the red-light assisted in revealing a discrete linear vascular structure on the nail plate that helped to localize the precise site of the tumor (data not shown).

Onychopapilloma usually shows in onychoscopy a longitudinal band, often associated with splinter hemorrhages. The red-light function revealed an improved clarity of the onycholysis ($p=0.005$), starting from the lunula and reaching to the distal margin (Figure 4a). The fissure of the distal nail plate and subungual filiform hyperkeratotic mass was best observed at magnified white-light and red-light, compared to white-light alone, ($p=0.002$).

In onychomatricoma, the splinter hemorrhages or vascular alterations resulted statistically more clearly visible with the red-light function, as compared to the white-light images ($p=0.012$). The yellowish discoloration and the longitudinal striae were equally visible with the white-light and red-light functionalities compared to magnified white-light ($p=0.018$) (Figure 4b).

Digital mucoid cysts periungual mass was exclusively visible (at partial and full clarity) with the red-light functionality ($p=0.017$). Similarly, the longitudinal furrow was classified as visible and fully clear at red-light, partially clear at white-light, and not visible at magnified white-light ($p<0.001$). Additionally, the red-light assisted in identifying the precise location of the lesion (Figure 5).

A longitudinal furrow was also observed in 3 further patients, but the absence of an associated vascular mass assisted in the differential diagnosis of fibrokeratoma (Figure 6). The red-light was the only modality classified as able to clearly visualize the furrow, with either partial or full clarity ($p=0.017$).

The inflammatory diseases comprised 9 patients; 3 cases of nail alterations in alopecia areata, and 6 cases of psoriasis (3 pustular and 3 vulgar type). In alopecia areata, red-light enhanced the resolution of the regular and homogeneously distributed pits, due to the increasing contrast with the healthy nail plate ($p=0.045$). The irregular pitting was classified as fully clear associated with the red-light images of nail psoriasis compared to the white-light functionalities ($p=0.002$) and assisted in differential diagnosis with alopecia areata (Figure 7). Further, the diffuse subungual hyperkeratosis was significantly clearer with the white-light or the red-light, compared to the magnified white-light ($p=0.018$) but there were no significant differences of the clarity of the image for the onycholytic area.

Finally, pustular nail psoriasis was consistently classified with a fully clear image of 3 associated features of small papules (often not seen with the naked eye), tortuous and elongated capillaries of the hyponychium and onycholysis ($p=0.008$, 0.002 , and 0.017 , respectively), whereas no difference was evident for the nail plate surface alteration. The capillaries of the hyponychium, irregularly distributed, dilated, tortuous and elongated (Figure 8), were not at all visible with white-light, regular dermoscopy.

Discussion

Onychoscopy requires a good knowledge of nail anatomy, physiology and pathogenesis of nail diseases: we have to know which part of the nail we have to look at!³ In daily practice, except for some nail diseases in which it really add a lot to clinical examination, in most of cases, onychoscopy only permits a better visualization of symptoms already evident to the naked eye.⁴

The principal problem of manual dermoscope is the inability to use magnifications superior to 10x, without having to employ a secondary technology, which can also be important for differential diagnosis. In the current study, periungual mass associated with digital mucoid cyst diagnosis was classified as absent by all 4 observers at white-light and magnified white-light, partially or fully clear at red-light. Further, the tortuous and elongated capillaries of the hyponychium was classified as absent by all 4 observed at white-light, and was fully clear at magnified white-light and red-light. Generally, lesions with vascular pattern are never seen with small magnifications like those of manual dermoscopy. Instead, without using higher resolutions that are not always available, these alterations are quite visible with the new device.

The main difficulty encountered by the dermatologist is the distinction between blood and melanin.⁵ The new device, with the help of the red-light, is very useful for the diagnosis nail color change. With classic manual dermoscopy it is possible to distinguish the round shape of hematoma and its homogeneous color, without the typical longitudinal band of melanonychia, with globular pattern and peripheral fading.⁶ The use of red-light has helped to highlight these features, making color alterations resulting from the trauma even clearer.

The red-light resulted even more helpful in case of frictional pyogenic granuloma, which is characterized by onycholysis, pain and subungual oozing and it is related to a history of frequent or prolonged walking. Using the red-light it was possible to better see the white discoloration in the center of the lesion and a red color at the periphery, associated with irregular vessels, peripheral necrotic material and blood clots.

The new prototype was also tested during the examination of some of the best-known nail tumors. Glomus tumor is an uncommon and very painful (especially with cold temperatures) benign tumor that typically develops in the subungual site. The symptoms can be more impressive than the clinical findings and the dermatologic examination may not be sufficient to identify the tumor, particularly when it is small or lacking visible deformity.⁷ Onychoscopy shows a band of erythronychia or a red subungual nodule, while the use of the red-light of the new device identify with greater precision the erythematous spot suggestive of a vascular abnormality.

Onychopapilloma usually affects the thumb and appears as a longitudinal band, associated or composed entirely of splinter hemorrhage. However, its aspect may vary a lot and the band can be in red, white or brown color.⁸ The new prototype reveals a well-defined longitudinal red band with splinter hemorrhages, usually more present in the distal part of the band, and more visible switching on the red-light of the device. Large onychopapilloma can induce onycholysis and may be difficult to distinguish from onychomatricoma due to its evident subungual mass.⁹ Nevertheless, the new device is able to recognize the typical honeycomb aspect of onychomatricoma and highlight the vascular alterations of this tumor, especially in the proximal region.

Moreover, in case of a longitudinal fissure of the nail plate with a periungual mass, the red-light of the new prototype allows the differential diagnosis between a fibrokeratoma, which is characterized by the absence of signs of vascular mass, and a digital mucoid cyst, whose location of the lesion can be easily identified

Additionally, the red-light modality enables an excellent observation of the main superficial alterations of the nail plate. It's known that in alopecia areata pits are regular in shape, size and distribution, while in psoriasis they appear large deep and irregular in shape, size and distribution.¹⁰ Using the red-light, the visual resolution of the pits is very high and the contrast with the healthy nail can be further highlighted.

The prototype also allows an optimal visualization of the pustules, often not visible with the naked eye, and of the capillaries of the hyponychium, which appear irregularly distributed, dilated, tortuous and elongated. Capillary density is positively correlated with the disease severity and response to treatment, so they are important to find and monitor over time.¹¹ Generally, these vascular alterations are never seen with small magnifications like those of manual dermoscopy, but they are quite visible with the new prototype, reinforcing a presumptive clinical diagnosis.

Conclusions

The addition of the red-light seems to enable a greater clarity of the main nail lesions features, and their respective vascular alterations. Its use was proven in this study to enhance differential diagnosis between nail diseases, usually difficult to distinguish at standard clinical observation. The red-light for vascular pattern onychoscopy seems to represent a

valid enhancement to the onychoscopy investigational tool, evidencing nail vascular pattern visualization, without having to use higher resolutions.

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Figures legends

Figure 1. Subungual hematoma with the sharp contoured hematoma shape, the multiple blood globules and the splinter hemorrhages.

Figure 2. Frictional pyogenic granuloma with white discoloration in the center of the lesion and a red color at the periphery, associated with irregular vessels, peripheral necrotic material and blood clots.

Figure 3. Glomus tumor with vascular abnormality, in sharp contrasts with the pale pink of the nail bed or the white color of the lunula.

Figure 4. Onychopapilloma well-defined longitudinal red band with splinter hemorrhages, starting from the lunula and reaching to the distal margin (a). Onychomatricoma with the characteristic vascular alterations, in addition to view its typical honeycomb aspect.

Figure 5. Muroid cysts well visible in the periungual tissue.

Figure 6. Fibrokeratoma visible such as periungual mass without signs of vascular mass at the level of periungual tissues.

Figure 7. Irregular pitting well visible on the nail plate typical of nail psoriasis.

Figure 8. Small pustules and alteration of the capillaries of the hyponychium, which appear irregularly distributed, dilated, tortuous and elongated diagnosed of nail pustular psoriasis.

Table 1. Features of common nail disorders as visualized at Onychoscopy white light 10x, white light 40x and red light 10x, according to a scale of clarity.

<i>Nail disorder, n</i>	<i>Features visualized at Onychoscopy</i>	Assessment Scale*	White light (10X)	Magnified white light (40X)	Red light (10X)	p-value
Traumatic onycholysis, 3	Linear line of detachment	1	1	1	0	0.549
		2	3	3	4	
	Normal pale pink bed, without hyperkeratosis	1	1	1	0	0.549
		2	3	3	4	
	Whitish to yellow subungual space	1	1	4	0	0.012
		2	3	0	4	
Subungual hematoma, 3	Round shape and homogeneous pigmentation	2	4	4	4	
	Color ranging from red-purple to black, often surrounded by multiple small blood globules of paler color	2	4	4	4	
Frictional pyogenic granuloma, 3	Red discoloration with a milky-red veil and a regular pattern of the vessels	1	1	1	0	0.017
		2	3	3	0	
		3	0	0	4	
Glomus tumor, 3	Deep red-purple subungual mass with blurred borders, or Band of longitudinal erythronychia that does not	1	1	4	0	0.001
		2	3	0	0	

	usually reach the distal margin	3	0	0	4	
Onychopapilloma, 3	Longitudinal red band, starting from the lunula and reaching to the distal margin, often associated with splinter hemorrhages	1	1	3	0	0.005
		2	3	1	0	
		3	0	0	4	
	Fissure of the distal nail plate and subungual filiform hyperkeratotic mass	1	4	0	0	0.002
		2	0	4	4	
	Honeycomb holes at the free distal margin	2	4	4	4	
Onychomatricoma, 3	Yellowish discoloration with longitudinal striae	1	0	3	0	0.018
		2	4	1	4	
	Splinter hemorrhages or vascular alterations	1	1	2	0	0.012
		2	3	2	0	
		3	0	0	4	
		0	4	4	0	0.017
Digital mucoid cyst, 3	Periungual mass	1	0	0	0	
		2	0	0	3	
		3	0	0	1	
	Longitudinal furrow	1	0	4	0	<0.001
		2	4	0	0	
		3	0	0	4	
Fibrokeratoma, 3	Longitudinal furrow	1	4	4	0	0.017

		2	0	0	3	
		3	0	0	1	
Alopecia areata, 3	Regular and homogeneously distributed pitting	1	1	0	0	0.045
		2	3	4	1	
		3	0	0	3	
Nail psoriasis, 3	Slightly dented margin of the onycholytic area surrounded by a yellow-orange band and splinter hemorrhages	1	0	1	0	0.336
		2	4	3	4	
	Diffuse subungual hyperkeratosis	1	0	3	0	0.018
		2	4	1	4	
	Irregular pitting	2	4	4	0	0.002
		3	0	0	4	
Pustular nail psoriasis, 3	Small papules	1	4	3	0	0.008
		2	0	1	0	
		3	0	0	4	
	Tortuous and elongated capillaries of the hyponychium	0	4	0	0	0.002
		1	0	0	0	
		2	0	4	4	
	Nail plate surface alteration	1	2	2	0	0.223
		2	2	2	4	

Onycholysis	0	0	1	0	
	1	0	3	0	0.017
	2	4	0	4	

*Assessment scale: 0=absent, 1=visible but unclear, 2=visible and partially clear, 3=visible and fully clear













