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ORIGINAL ARTICLE

Onychoscopic characteristics of *Trichophyton rubrum* and *Trichophyton interdigitalis* fungal infections: A multicentric study

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Abstract

Background: *Trichophyton rubrum* and *Trichophyton mentagrophytes* variant *interdigitalis* are the most frequent etiologic agents of onychomycosis. Diagnosis of certainty requires mycological examination, which often results unfeasible.

Objectives: The aim of our study is to describe pathogen specific dermoscopic features, allowing a differential diagnosis without the need for cultural examination, in order to prescribe the most appropriate treatment anyway.

Patients and methods: We conducted an observational retrospective study on 54 patients with a culture proven diagnosis of distal subungual onychomycosis of the toenail, caused by *Trichophyton rubrum* or *Trichophyton mentagrophytes* variant *interdigitalis*. Using a videodermatoscope we collected data on nail colour (white, yellow, orange, brown, dark) and on dermoscopic patterns (aurora, spikes, jagged, ruin, linear edge, dots, striae).

Results: Fifty-four patients, with a total of 72 nails, were eligible for this study. Analysing the association between discoloration of the nail plate and type of infection (*T. rubrum* or *T. interdigitalis*), no correlation turned out to be statistically significant. Instead, significant associations between spikes and *T. rubrum* infection and striae and infection from *T. interdigitalis* were identified. Finally, a 100% specificity was identified for white colour and ruin pattern for *T. rubrum* infection, and brown colour, jagged border and aurora pattern for *T. interdigitalis*.

Conclusions: Trying to find relationships between specific pathogens and dermoscopic patterns, we found out an association between spikes and striae and *T. rubrum* and *T. interdigitalis* respectively. Further larger studies are however necessary to evaluate our preliminary findings.

KEYWORDS
dermoscopy, fungal infections, mycoses, nails, onychoscopy, toenail

1 | INTRODUCTION

Onychomycosis is the most frequent nail affection, and *Trichophyton rubrum* and less commonly *Trichophyton mentagrophytes* variant *Interdigitalis* are the most frequent etiological agents. While the suspicion of onychomycosis can be formulated from anamnesis and clinical examination, a definitive diagnosis requires direct examination and culture, which may take time and often results impractical. Cultural examination, in fact, takes at least 3 weeks to provide results, with patient aesthetic discomfort.

The purpose of this study is then to identify dermoscopic features on onychomycotic nails, allowing differential diagnosis between onychomycosis caused by the two main pathogens, without waiting the necessary time for culture.

2 | PATIENTS AND METHODS

We conducted an observational retrospective study on 54 patients with a diagnosis, culture proven of distal subungual onychomycosis of the toenail, caused by *Trichophyton rubrum* or *Trichophyton mentagrophytes* variant *interdigitalis*.

For each patient were collected the following data: age, gender, toenails involvement and type of infection. All subjects reported a clinical picture, onychoscopy picture and a mycological examination (direct observation with KOH and cultural examination).

Subjects with a diagnosis of any other nail affection were excluded from the study.

Data were collected at the Department of Dermatology of the University of Bologna (Italy), at the Dermatology Clinic of São Paulo (Brazil) and in a Private Outpatient Dermatology consultation in Lugano (Switzerland) between 1 December 2021 and 30 December 2022.

The authors confirm that the ethical policies of the journal, as noted on the journal's author guidelines page, have been respected and an appropriate ethical review committee approval has been received.

Onychoscopy images were collected using a videodermatoscope (FotoFinder dermoscope, FotoFinder Systems GmbH, Bad Birnbach, Germany) with 20×, 40× and 70× magnifications. Mycological examination was performed by collecting samples at the proximal border of the onycholytic area.

During onychoscopic procedure of each affected toenail, all shades of colours between white, yellow, orange, brown and dark have been recorded.

Then we proceeded analysing the presence of seven specific dermoscopic patterns, in details:

1. Aurora discoloration: irregular pigmentation of the nail plate, distributed in horizontal striae, giving an overall impression of 'aurora borealis.'
2. Spikes: sharp structures causing indentations of the onycholytic border (proximal progression of fungi along the horny layer of the nail bed ridges).
3. Jagged: irregular border of the onycholytic area, as opposed to linear one described in traumatic onycholysis.
4. Ruin: irregular and crumbly ending of the thickened nail plate with subungual scales.
5. Linear edge: continuous and homogeneous onycholytic border.
6. Dots: nail plate spots of a certain colour.
7. Striae: nail plate structures of different colours, parallel to the major axis.

All data were analysed using the QuickCalcs function of the GraphPad online software (https://www.graphpad.com/quickcalcs). The association analysis was made using chi-square test, considering two-tailed *p*-values <.05, <.01, <.001 to be statistically significant.

3 | RESULTS

A total of 54 patients were enrolled, 26 women (48.15%) and 28 men (51.85%). Median age was 51.26 ± 17.20 (range: 19–88 years).

In this study was analysed a total of 72 nails (36 patients presented single nail involvement and 18 patients showed multiple nail affection).

In particular, 30 patients had only one big toe affected (55.56%), while 10 subjects had both big toes (18.52%). Four subjects had one big toe and another one nail (7.40%), while 10 patients revealed only other nails involvement (different from big toenails) (18.52%).

Culture examination revealed a positivity for *Trichophyton rubrum* in 46 toenails (63.89%), and for *Trichophyton mentagrophytes* variant *interdigitalis* in the other 26 toenails (36.11%) (See Table 1).

Analysing the association between discoloration of the nail plate and type of infection (*T. rubrum* or *T. interdigitalis*), no correlation turned out to be statistically significant (See Table 2).

TABLE 1 Demographic and clinical characteristics of study participants.

Number of patients	54	100%
Age		
Mean	51.27	
Range	19–88	
Gender		
Female	26	48.15%
Male	28	51.85%
Toenails involved	72	
Toenails involvement		
1 big toe	30	55.56%
Both big toes	10	18.52%
Big toe + other nail	4	7.40%
Other nails	10	18.52%
Type of infection		
Rubrum	46	63.89%
Interdigitalis	26	36.11%

Instead, analysis of onychoscopic patterns associated with each pathogen revealed a significantly association between the presence of spikes and *T. rubrum* infection ($p = .01$), with a sensitivity of 54.35% and a specificity of 76.92%.

Less statistical evidence was denoted in the correlation between dermoscopic presence of striae and infection from *T. interdigitalis* ($p < .05$, $p = .03$). Sensitivity in this case appeared to be 65.38% and specificity came out 60.87% (See Table 2). Interestingly, trying all possible combinations between discolorations and patterns we discovered a statically significant specificity of 100% for *T. rubrum* infection and the presence of both white colour and ruin pattern at onychoscopy (p-value = .01) (Figure 1).

Very significant turn out to be also the specificity for *T. interdigitalis* with onychoscopy showing brown colour, jagged border and aurora pattern (Sp = 100%, p-value = .002; See Table 2 and Figure 2).

TABLE 2 Study results with lamina discoloration and onychoscopic pattern in relation with the type of fungal infection.

	Rubrum					*Interdigitalis*				
	N	%	Sensitivity	Specificity	*p*-Value	*N*	%	Sensitivity	Specificity	*p*-Value
White	16	61.5	34.78	61.54	.75	10	38.4	38.46	65.22	.75
Yellow	42	66.67	91.3	19.23	.19	21	33.33	80.77	8.69	.19
Orange	26	79.27	56.52	57.7	.25	11	29.73	42.3	43.48	.25
Brown	10	52.63	21.74	65.38	.23	9	47.37	34.61	78.26	.23
Dark	7	77.78	15.22	92.31	.35	2	22.22	7.69	84.78	.35
Aurora	18	72.00	39.13	98.44	.3	7	28.00	1.55	60.87	.3
Spikes	25	80.65	54.35	76.92	.01	6	19.35	23.08	45.65	.01
Jagged	32	69.57	69.56	46.15	.18	14	30.43	53.85	30.43	.18
Ruin	26	72.22	56.52	61.54	.14	10	27.78	38.46	43.48	.14
Edge	5	41.67	10.87	73.08	.08	7	58.33	26.92	89.13	.08
Dots	7	77.78	15.22	92.31	.35	2	22.22	7.69	84.78	.35
Striae	18	51.43	39.13	34.61	.03	17	48.57	65.38	60.87	.03
White + Ruin	10	21.74	21.74	100	.01	0	0	0	78.26	.01
Brown + Aurora + Jagged	0	0	0	80.77	.002	5	19.23	19.23	100	.002

FIGURE 1 Clinical and dermoscopic (10× and 40× magnification) images of *Trichophyton rubrum* infection: the presence of both white colour and ruin pattern at onychoscopy reached 100% specificity for *T. rubrum* infection.

FIGURE 2 Clinical and dermoscopic (40× magnification) images of *Trichophyton interdigitalis* infection: brown colour associated with jagged border and aurora pattern turned out to be highly specific for this pathogen.

4 | DISCUSSION

Distal lateral subungual onychomycosis (DLSO) is the most common clinical subtype of onychomycosis, accounting for approximately 90% of toenail infections globally, with a prevalence increasing with age.[1,2] It is characterized by subungual hyperkeratosis, discoloration of the nail plate and onycholysis and sometimes involvement of the adjacent skin.[1]

Data reported in literature highlight a slight prevalence in the male sex and a preferential involvement of big toenails.[3] Our study falls in line, having 51.85% of males and presenting a single big toe involvement in 55.56% of subjects, both toes involved in 18.52% of cases and a combined affection of big toe and other nails in 7.40% of patients.

DLSO is usually caused by *Trichophyton rubrum* and less commonly by *Trichophyton mentagrophytes interdigital* variant, and rarely, by *Epidermophyton floccosum*.[4]

This type of onychomycosis is often associated with tinea pedis (70% of cases). Among other etiological agents there are also moulds, especially *Scopulariopsis brevicaulis*, *Aspergillus* sp. and *Acremonium* sp.[5]

Differential diagnosis between nail affections is sometimes not possible with clinical evaluation alone, and traditionally culture has always been used to identify the presence or not of a fungus.

In agreement with current guidelines, clinical suspect of onychomycosis must be confirmed with pathogen identification, using direct microscopic examination with KOH and cultural exam from a nail plate sample and subungual debris.[6]

The main issue with direct and culture examination is that sometimes fungi are difficult to isolate because of their low number and viability. Microscopy may be negative in up to 10% of cases and culture in up to 30% of cases. Moreover, to obtain results from culture we should wait at least 3 weeks delaying treatment prescription. However, identification of the pathogen is important not only from an epidemiological perspective, but also to prescribe the most appropriate treatment to patients. We could obtain information regarding the fungal species (but not about their viability) through a PCR analysis, faster but extremely expensive and requiring specialized laboratories.

For these reasons, trying to identify a responsible fungal species through clinical and dermoscopic examination would be of benefits in certain context.

Several steps forward have been made in the dermatoscopic diagnosis of onychomycosis.[7–14] Piraccini et al. suggested an algorithm to diagnose DLSO with the aid of onychoscopy. They firstly proposed to exclude onychomycosis in the presence of a linear onycholytic border and instead search for spikes if dealing with a jagged one.[15] In the presence of both spikes and striae, a onychoscopic diagnosis of onychomycosis was suggested.[15]

Our study goes deeper confirming these results: in fact, both spikes and striae resulted statistically associated with onychomycosis, and farther found a relation between each characteristic and the specific pathogen. In particular, spikes resulted associated with *T. rubrum* with high specificity (Sp = 76.92%, $p = .01$), while striae obtained a discrete correlation with *T. interdigitalis* in terms of sensibility and specificity (Sn = 65.38, Sp = 60.87, $p = .03$).

The appearance of spike and striae are directly connected to onychomycosis pathogenesis. Fungal invasion begins at the level of the hyponychium or at lateral nail folds, and then progresses to involve the nail bed and proceeds longitudinally, towards lunula and overlying lamina. Migration then proceeds proximally across the nail plate, causing the appearance of linear striae and spikes.[3,5]

Interestingly, searching for the association of multiple patterns with each infection we discovered a 100% specificity for *T. rubrum* infection and presentation with white colour and ruin pattern ($p = .01$) and the same grade of specificity (Sp = 100%) for *T. interdigitalis* showing brown colour, aurora pattern and jagged border ($p = .002$; Figures 3 and 4 respectively).

5 | CONCLUSIONS

We conducted this multicentric retrospective and observational study with the aim of strengthen the use of onychoscopy as a tool to make diagnosis of onychomycosis, avoiding more costly and time consuming procedures such as microbiological examinations, furthermore not always feasible.

In addition to this, we tried to evaluate if specific pathogens were correlated with dermoscopic patterns and found a statistical association with spikes and striae (respectively with *T. rubrum* and *T. interdigitalis*).

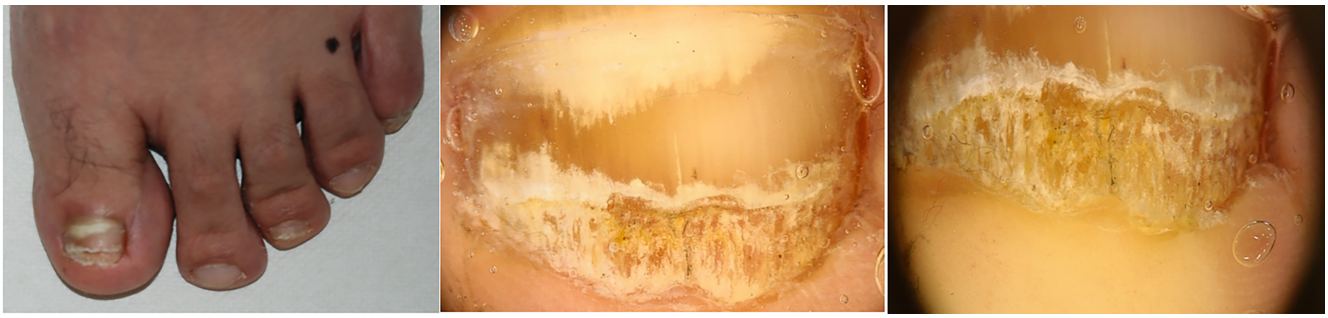

FIGURE 3 Clinical and dermoscopic (10× and 40× magnification) images of *Trichophyton rubrum* infection: the presence of white, yellow and orange colour with patterns jagged, striae and ruin.

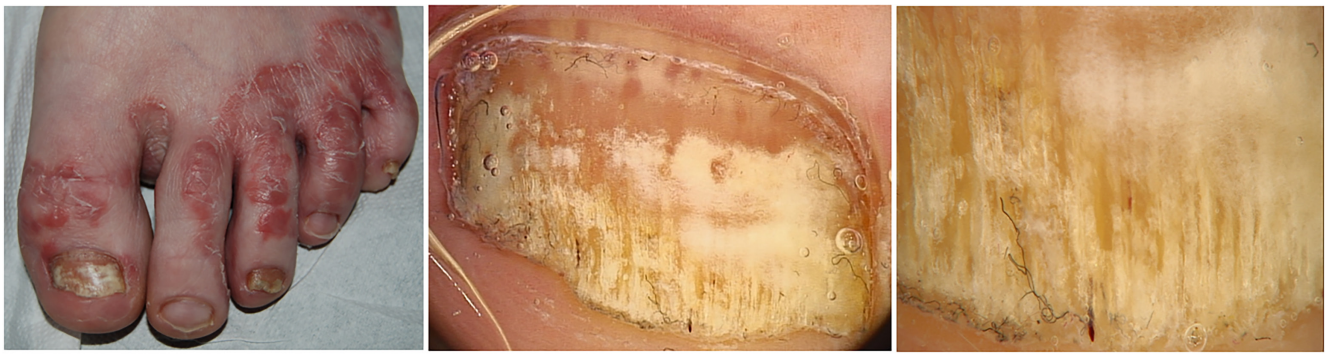

FIGURE 4 Clinical and dermoscopic (10× and 40× magnification) images of *Trichophyton interdigitalis* infection: the presence of white and yellow with patterns jagged and striae.

Lastly, being multicentric our study reduces patient selection bias, even if sample size is still small to draw definitive conclusions. Further larger studies are needed to corroborate our results.

AUTHOR CONTRIBUTIONS

Michela Starace: Conceptualization; validation; supervision; project administration; methodology; funding acquisition. **Elisa Milan:** Writing – original draft; writing – review and editing; methodology; formal analysis. **Giovanni Summa:** Formal analysis; data curation; software. **Aurora Maria Alessandrini:** Data curation; supervision; project administration; investigation. **Andrea Sechi:** Software; data curation; validation. **Matilde Iorizzo:** Data curation; investigation; validation. **Nilton Gioia Di Chiacchio:** Data curation; validation; investigation. **Nilton Di Chiacchio:** Investigation; validation; data curation. **Bianca Maria Piraccini:** Visualization; validation; project administration; resources; supervision; funding acquisition.

CONFLICT OF INTEREST STATEMENT

None declared.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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