

## The Red Nail – Always Benign?

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**Abstract.** Red nail is a common disorder. However, a thorough examination of the patient's nails allows one to distinguish different diseases. For example, longitudinal erythronychia may be monodactylous or polydactylous. Only the former type can show histologically Bowen's disease or an amelanotic melanoma. Among the polydactylous type, the nosologic position of the acantholytic and dyskeratotic naevus versus Darier's disease is still controversial.

Acantholytic epidermolysis bullosa looks like bullous Darier's disease, and acrokeratosis of Hopf may present also red longitudinal streaks. Subungual warty dyskeratoma is rare, but other dermatoses such as lichen planus, psoriasis, nail melanoma and various tumours have to be ruled out.

Finally nail involvement in amyloidosis may precede the other signs of this systemic disease.

The purpose of this paper will be focused on red nails that can present principally with red lunulae, solitary longitudinal erythronychia and multiple longitudinal erythronychia. Other aspects of this feature will also be raised.

**Key words:** erythronychia, Darier's disease, acantholytic dyskeratotic epidermal naevus, acrokeratosis of Hopf, subungual warty dyskeratoma, amyloidosis.

### ERITRONIQUIA, ¿SIEMPRE BENIGNA?

**Resumen.** La eritroniquia es un trastorno frecuente. Sin embargo, una exploración minuciosa de las uñas del paciente permite distinguir distintas patologías. Por ejemplo, la eritroniquia longitudinal puede ser mono o polidactilar. En el primer caso podría corresponder histológicamente a una enfermedad de Bowen o a un melanoma amelanótico. En la forma polidactilar existe controversia acerca de la clasificación nosológica como nevus acantolítico y disqueratósico o enfermedad de Darier. La epidermolisis ampollosa acantolítica se asemeja a la enfermedad de Darier ampollosa, y la acroqueratosis de Hopf también puede presentarse como estrías longitudinales rojas. El disqueratoma verrugoso subungueal es raro y también deben descartarse otras dermatosis como liquen plano, psoriasis, melanoma ungueal y otros tumores.

Por último, la afectación ungueal en la amiloidosis puede preceder a la aparición de otros signos de esta enfermedad sistémica.

El objetivo de este artículo se centra en la revisión de la eritroniquia, que se puede presentar como lúnula roja y eritroniquia longitudinal solitaria o múltiple. También se comentarán otros aspectos relacionados con esta característica.

**Palabras clave:** eritroniquia, enfermedad de Darier, nevus epidérmico acantolítico disqueratósico, acroqueratosis de Hopf, disqueratoma verrugoso subungueal, amiloidosis.

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### Red Nails

True red nail plates are certainly extremely rare. Usually they should be attributed to exogenous agents such as fuchsin, eosin, nail enamel pigmentation, hydroquinone used in bleaching creams, etc.

In fact, red nails may be grossly divided into red lunula and (partial) redness of the nail bed. However such a classification has its drawbacks: a) the latter mainly presents as a longitudinal erythronychia band; b) it starts in the lunula region.

In addition, carbon monoxide poisoning is obviously a systemic disease with pink red nails.

### Red lunulae

Red lunulae mainly involve the thumbs where the lunula is usually clearly visible. They have been observed in patients

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**Figure 1.** Red lunula separated from the pink nail bed by a whitish crescent.

with several cutaneous or systemic disorders and, based on the etiology, have been divided by Philippe Cohen<sup>1</sup> into cardiovascular<sup>2-5</sup> (fig. 1), cutaneous<sup>4,6-10</sup> (fig. 2), endocrine<sup>3,4</sup>, gastrointestinal<sup>4</sup>, hematologic<sup>4</sup>, hepatic<sup>3,4</sup>, infectious<sup>2-4</sup>, miscellaneous<sup>3-6,8,9</sup>, neoplastic<sup>2,3</sup>, neurologic<sup>4</sup>, pulmonary<sup>3,4</sup>, renal<sup>4</sup> and rheumatologic<sup>4,5,11</sup>.

In patients with red lunulae, a narrow white band may be present at the distal lunulae proximal to the pink nail bed.

The pathogenesis of red lunulae remains undetermined. Wilkerson and Wilkin<sup>4</sup> suggested that red lunulae were caused either by a venous dilatory capacitance phenomenon of uncertain origin or by an increased arteriolar blood flow in that area.

### Monodactylous Longitudinal Erythronychia

Twenty two cases were studied: five index fingernails, sixteen thumbnails and one great toenail. In this homogenous group identical clinical features presenting with longitudinal erythronychia, with either a single (figs. 3-5) or sometimes double interrupted line (fig. 6) were found among the patients. This was composed of splinter haemorrhages and a keratinized linear expansion after removal of the nail plate, extending from the distal matrix-nail bed junction to the hyponychium where it ends in a racquet-shaped manner (fig. 7). This distal subungual keratosis is generally associated with moderate onycholysis.

At this condition usually reflects a disease of the matrix, alteration of its function reduces the thickness of nail production along the longitudinal erythronychia<sup>12</sup>.



**Figure 2.** Punctate redness of the lunula in lichen planus.



**Figure 3.** A. Isolated longitudinal erythronychia. B. Same patient showing the keratinized ridge involving the end of the lunula and the nail bed.



**Figure 4.** Isolated longitudinal erythronychia with distal black end.

Most of the patients showed a common histological pattern. There was acanthosis of the epithelium of the nail bed with a slight extension to the lunula and a

marked distal longitudinal papillomatosis of the nail bed (figs. 3B, 5B).

In the latter, marked fusiform eosinophilic cells were seen. The nuclei were flattened and hyperchromatic with smooth and regular contours. Frequently, these eosinophilic cells formed superficial, wide, stratified layers of cells with a V-shape arrangement at the base. This prominent eosinophilic zone and the absence of the granular layer rendered these foci of keratinisation comparable to the keratogenous zone of the matrix as defined by Zaias<sup>13</sup> (fig. 5C). The transverse sections of the avulsed nail plates showed a thinned area above the epithelial ridge in the distal lunula and nail bed region. In the distal nail bed, a cavity was formed, filled with cornified, sometimes thick layers that consisted of highly intertwined cells, stained weakly, or not at all, by eosin. In addition, in some foci pyknotic nuclear debris was observed. Therefore, these cornified cells presented with a morphology which was very close to that of onychocytes. On the avulsed plates, the nail bed epithelium was not adherent to the cornified mass and the granular layer was not visible. Small brown haematogenic deposits, and accumulations of exudates stained by PAS, before and after the addition of diastase, were found. In some cases, the keratogenous zone of the nail bed was only focal and the papillomatosis, at the junction between nail bed and hyponychium, showed an intermittent granular layer giving rise to a laminated keratin, filled with PAS-positive exudates. The vascular tissue of the papilla was hyperplastic, without any stroma in the distal matrix and, by contrast associated



**Figure 5.** A. Interrupted longitudinal erythronychia composed of splinter haemorrhages with splinting of the free edge. B. Exposed subungual tissue showing a longitudinal ridge with distal expansion in hyponychium area. C. This prominent eosinophilic zone is comparable to the keratogenous zone of the matrix (Histology: Ch. Perrin, Nice, France).

with thick collagen fibres and discrete inflammatory infiltrates at the distal portion of the nail bed.

A red longitudinal streak found in the nail plate or longitudinal erythronychia, may also be associated with glomus tumour, lichen planus and amyloidosis. More rarely, it may accompany localized multinucleate distal subungual keratosis<sup>14</sup> and even subungual warty dyskeratoma<sup>15,16</sup>. It is wise to rule out Bowen's disease when performing a longitudinal biopsy from the lunula to the hyponychium<sup>17-19</sup> (figs. 8, 9).

### Polydactylous Longitudinal Erythronychia of the Fingers

Six cases allowed us to exclude this condition<sup>20</sup> from the much more frequent monodactylous longitudinal erythronychia.

Examination of the terminal phalanges of several fingers showed single splinter haemorrhages (fig. 10). In one patient, they were replaced two years later by longitudinal



**Figure 6.** Double banding made of proximal erythronychia and distal haemorrhages.



**Figure 7.** Onychopapilloma: keratinized expansion after removal of the distal nail plate.

erythronychia with some streaks running the whole length of the nail and finishing on a distal subungual keratosis with a tendency to fissuring at the free edge. Pain was experienced by this patient, a concert pianist, and when he was playing it became progressively worse. In some other cases this symptom was not confirmed.

There are certainly some similarities between this type of longitudinal erythronychia which is an entity different from the one described as monodactylous longitudinal erythronychia: a) the redness may appear after splinter haemorrhages; b) the free edge is often fissured in both types; c) the distal subungual keratosis could be present in either type.

There are however some differences:

1. In one of our patients the splinter haemorrhages were restricted for two years to the base of the nails.
2. The histology of monodactylous lesions shows a keratin mass of pseudo nail with multinucleate cells in some cases while the pathology in the polydactylous case which we have biopsied was that of a lichenoid reaction.

3. The polydactylous type has never been clearly associated with malignancy in contrast to some cases presenting with single longitudinal erythronychia<sup>17-19</sup>. Nevertheless the case report of a patient with longitudinal streaky pink erythronychia of the thumb revealing a melanoma in situ and one dark red longitudinal line of a finger of the same hand<sup>19</sup> indicates that the relationship between idiopathic polydactylous longitudinal erythronychia and idiopathic single or double monodactylous longitudinal erythronychia banding still remains uncertain.

## Darier's Disease

Darier's disease is inherited in an autosomal dominant fashion. Penetrance of the gene is high. The nail signs diagnostic of Darier-White disease or dyskeratosis follicularis are very common. In a study on 163 patients, they were found in 92% by Burge and Wilkinson<sup>21</sup> and in 95% of a smaller number in a similar study<sup>22</sup>. Ronchese<sup>23</sup>, Bingham and Burrow<sup>24</sup>, Munro and MacLeod<sup>25</sup> reported the occurrence of nail changes in the absence of other evidence of disease.



**Figure 8.** Longitudinal erythronychia showing Bowen's disease after subungual biopsy.



**Figure 9.** Longitudinal erythronychia with distal onycholysis presenting with Bowen's disease after biopsy of the nail bed.

The number of abnormal nails ranges from two or three to all nails in a minority of patients. Toenails are involved but less often and less severely than fingernails<sup>21</sup>. The nail lesions (54 out of 56 patients) and palmar pitting (49 out of 56 patients) are earlier and more consistent evidence of the presence of the gene than is the characteristic rash<sup>25</sup>.



**Figure 10.** Polydactylous longitudinal erythronychia of the fingers (Courtesy of Krayenbühl B. Switzerland).

Nail features include longitudinal, subungual, red or white streaks, or both, associated with distal wedge-shaped subungual keratosis<sup>26</sup>. The single or multiple red longitudinal streaks may, with time, develop into white ones. Such changes extending through the nail and crossing the lunula are most characteristic. Where a streak meets the free edge of the nail a V shaped notch is usually present originating from the distal nail bed and hyponychium. The wedge-shaped subungual keratosis may massively thicken the nail plate in severe cases<sup>27</sup>.

The red longitudinal streak in Darier's disease may also be mimicked by the warty dyskeratoma<sup>15,16</sup> and the multinucleate distal subungual papilloma<sup>14</sup>.

### **Acantholytic Dyskeratotic Epidermal Naevus as a Mosaic form of Darier's Disease (ADEN)**

The nosologic position of the acantholytic and dyskeratotic naevus (ADEN) versus Darier's disease is still controversial.

Munro and Cox<sup>28</sup> reported the case of a patient affected by an ADEN with ipsilateral involvement of the palm and the dorsum of the hand, of the left third and fourth fingernails and left great toenail with red streaks terminating in notches, on the free edge.

Cambiaghi et al<sup>29</sup> described a patient affected by ADEN showing an ipsilateral palmar involvement and dyschromia on the left third and fourth fingernails as red and white ridging. At the end of the broad white streak, the free edge of the third fingernail had a V-shaped nick with a longitudinal split.

More recently, Venencie and Dallot<sup>30</sup> reported on a patient with keratotic erythematous itching papules on the lateral aspect of the trunk. The nails of the three first fin-

gers showed longitudinal red or white bands with a V shaped notch of the free margin.

These three observations of ADEN following Blascko lines are a plea for considering them so far, as a mosaic form of Darier's disease.

An article on acantholytic epidermolysis bullosa describes a new variant of epidermolysis bullosa and elucidates the clinical, histological and ultrastructural features of this condition<sup>31</sup>. This form displays an autosomal dominant inheritance pattern, characterised by acral bullae on the dorsal aspect of the fingers. Nails show red and white longitudinal bands and distal splitting, very reminiscent of bullous Darier's disease<sup>32</sup>.

## Acrokeratosis of Hopf

Keratotic papules on the dorsal portion of the nail fold may resemble acrokeratosis verruciformis<sup>32,33</sup> but, histologically, they demonstrate the features of Darier's disease. The nails in the former are pearly white in childhood and become horny, brown and grooved later in life. Red longitudinal streaks have been observed by Macfarlane et al<sup>34</sup> in a family presenting with acrokeratosis verruciformis in whom they identified a mutation in the ATP2A2 gene which is defective in Darier's disease. A solitary longitudinal white or red line may occur in persons with a tumour in the nail matrix or nail bed. More equivocal could be acantholytic epidermolysis bullosa presenting with white and red streaks mimicking bullous Darier's disease<sup>35</sup>.

## Subungual Warty Dyskeratoma

Longitudinal erythronychia may be the presenting sign<sup>15</sup> in subungual warty dyskeratoma. We have seen a longitudinal reddish ridge on a fingernail originating also in the lunula. It was bordered by splinter haemorrhages<sup>16</sup>. The nail plate was slightly fissured at its free margin. Nail avulsion revealed a longitudinal ridge on the nail bed. Histology showed nail bed papillomatosis with long thin digitations penetrating the underlying connective tissue almost horizontally. Numerous multinucleate cells were seen. A crateriform impression existed at the hyponychium with epithelial digitations containing dyskeratotic cells, *corps ronds* and grains as well as a suprabasal acantholysis.

## Other Dermatoses

Lichen planus may present with red subungual tissue<sup>36</sup>; psoriasis (oily spots), nail melanoma<sup>19</sup>, tumors (glomus tumor, neurofibroma, etc.), hemangiomas congenital or acquired.

## Systemic Diseases

Amyloidosis may mimic lichen planus and nail involvement may precede the other signs of this condition.

## Conclusion

Our studies on red nail have opened new paths. We have shown that multiple giant cells even observed in serial sections are not the privilege of Darier's disease and seem to be only a mode of reaction of the nail bed to unknown mechanism. We have also demonstrated a relationship between monodactylous longitudinal erythronychia and Bowen's disease and even melanoma. Finally we have isolated an idiopathic polydactylous longitudinal erythronychia, a variant that may be a new entity.

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I am proud to have been asked to contribute to this centenary issue as an Honorary member of the Spanish Academy of Dermatology.

## Conflict of interests

Author has no conflict of interests to declare.

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