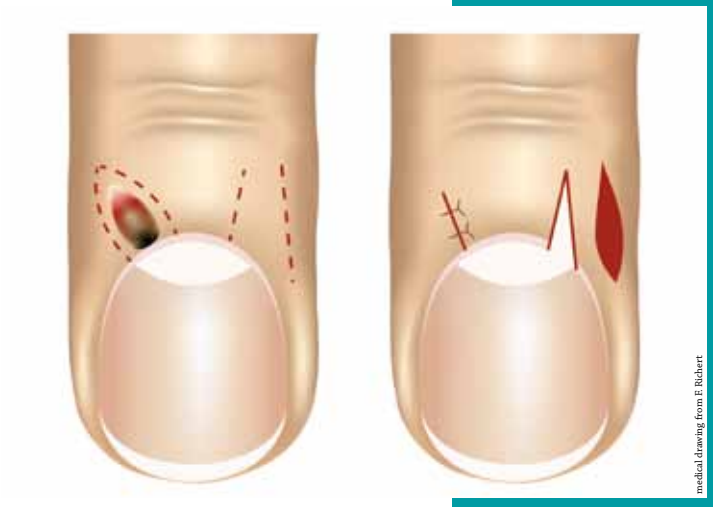
English edition 2014

n°7

The nail



medical drawing from F. Richert

What's new ?

ENS European Nail Society

The Official Journal of the European Nail Society

Pierre Fabre DERMATOLOGIE

The nail - What's new ? n° 7

THE OFFICIAL JOURNAL OF THE EUROPEAN NAIL SOCIETY
English edition 2014

EDITORIAL

Dear Friends and Colleagues,

On the initiative of Prof Luc Thomas, many of us gathered in Lyon on April 10 th, for the Meeting of the Dermatology Department, especially organized to express birthday wishes to our friend Pr. Robert Baran.

Pr. F.N. Gilly presented the medal of the University of Lyon to Pr. Baran and emphasized how much his career as a dermatologist had been quite atypical. By means of an excellent iconographic panorama, he reminded us of the extent to which Pr. Baran had contributed, over the past half-century, to progress in the field of onychology. We were invited to watch a superb 'firework display' of his findings and achievements which included congenital malalignment of hallux toe, onychomatricoma recently described with Kint, a review of the importance of the pair nail-bone with Juhlin and finally the nail degloving.

Bertrand Richert then pronounced a more intimate testimony during which all of those who were interested in nails acknowledged the fact - especially in France and maybe in Europe - that they were disciples of Robert Baran.

This outstanding physician delivered a dermatological and philosophical lecture and stressed the importance of keeping our curiosity alive when faced with clinical situations. This is undoubtedly what we should always bear in mind and this may be also a clue for longevity.

This year we celebrate the 10 th anniversary of our Journal. Ten years for a Journal denotes a well established reputation. On this occasion, we warmly welcome three new members: Dr Marie Caucanas (Belgium and France), Dr Maurice Pasch (The Netherlands) and Dr Olivier Cogrel (France).

I would also like to take the opportunity to congratulate Dr Bertrand Richert, who was nominated President of the Council of Nail Disorders during the last American Dermatology Academy in Denver. His election to this position underlines of course our Editor's qualities as a physician and a surgeon, but also how important the European Nail Society has become.

Finally, and on behalf of everyone, I would like to reiterate my thanks to both authors and readers and once again wish Pr. Baran and 'The Nail What's New' a very Happy Birthday !

Bruno Fouilloux

Robert BARAN
Honorary Professor of the University of Franche-Comté
Nail Disease Center - Cannes (France)
baran.r@club-internet.fr
baran.r@wanadoo.fr

Bruno FOUILLOUX
Dermatology-Onychology Department
University Hospital Saint-Etienne (France)
bruno.fouilloux@wanadoo.fr

Véronique BLATIÈRE
Dermatologist
University Hospital Montpellier (France)
veroblatiere@yahoo.fr

Eckart HANEKE
Professor of Dermatology
Freiburg (Germany),
Bern (Switzerland)
haneke@gmx.net

Marie CAUCANAS
Dermatologist
Brugmann University Hospital, Brussels (Belgium)
Clinique St Jean Languedoc
Toulouse (France)
marie_caucanas@hotmail.com

Jose Maria MASCARO
Emeritus Professor of Dermatology
Barcelona University Hospital (Spain)
2948jmm@comb.cat

Olivier COGREL
Dermatologist
Haut-lévêque University Hospital
Bordeaux (France)
olivier.cogrel@chu-bordeaux.fr

Marcel PASCH
Dermatologist
Radboud University Medical Center,
Nijmegen (The Netherlands)
m.pasch@derma.umcn.nl

Osvaldo CORREIA
Affiliate Professor, University of Porto
Dermatologist
Epidermis Dermatology Center
Instituto CUF, Porto (Portugal)
epidermis@epidermis.pt

Bianca Maria PIRACCINI
Division of Dermatology
Department of Experimental, Diagnostic and Specialty Medicine,
University of Bologna (Italy)
biancamaria.piraccini@unibo.it

David DE BERKER
Consultant dermatologist
Bristol Royal Infirmary
(England)
david.deberker@uhbristol.nhs.uk

Bertrand RICHERT
Clinical Professor
Brugmann, St Pierre and Queen Fabiola Children's University Hospital,
Brussel (Belgium)
bertrand.richert@skynet.be

Contents

THE OFFICIAL JOURNAL OF THE EUROPEAN NAIL SOCIETY - *The nail* - What's new ? n°7 - English edition 2014

CONDENSED SELECTED ARTICLES WITH COMMENTARY

CLINICAL CASES

CONTINUING MEDICAL EDUCATION

The nail - What's new ? n°7

Condensed selected articles with commentary

David De Berker

NAIL SCIENCE

1 Sano H, Shionoya K, Ogawa R. Finger nail configuration is influenced by mechanical forces on finger pads. J Dermatol 2013;40:1056-7.

The premise of this paper is that force upon the digit, experienced in grip and pressure, affects the shape of the nail. Specifically, pressure applied through the digit pulp results in the flattening of the nail.

The authors sought to test this idea by measuring the curvature of the thumbnail according to the equation of [nail height/nail width] x 100[%]. This was carried out on 63 carpenters, who were classified as undertaking physical work. They were compared with 63 age/sex-matched office worker controls for paired measurements. In addition to the dimensions, pinch grip was measured between finger and thumb.

The results showed that the carpenters had a significantly lower mean thumb nail curve index (14.0 +/-3.9% vs 22.6 +/-3.3%, P < 0.01) and higher mean strength (25.9 +/- 4.9 vs 21.0 +/-3.9 pounds, P < 0.01) than the office workers. The carpenters also had significantly thicker thumb nails than office workers (0.78+/-0.09 vs 0.69+/-0,09 mm, P < 0.05). The conclusion is that manual work results in flatter, thicker nails, and corresponds to having a stronger pinch grip.

2 Garzitto A, Ricceri F, Tripo L, Pescitelli L, Prignano F. Possible reconsideration of the Nail Psoriasis Severity Index (NaPSI) score. J Am Acad Dermatol. 2013;69:1053-4.

The authors of this letter were moved to make their contribution following the publication of ''Fingernail psoriasis reconsidered: A case-control study'' by van der Velden et al., who reported the Nail Psoriasis Severity Index results in the fingernails of 49 psoriatics, in comparison with age and sex matched controls. Van der Velden found leuconychia to be significantly more frequent in the control subjects than in the patients. Moreover, longitudinal ridges, nailfold involvement, and Beau's lines were more frequent in psoriatics than in controls, despite not being included in the NaPSI. Was this an isolated finding or is it generalisable to other nail psoriasis patients? Garzitto et al. compared these findings with 129 patients based on historic database records, rather than a prospective study. They found similarities, where leuconychia was more common in controls and longitudinal ridges, nailfold involvement, and Beau's lines were significantly more frequent in psoriatic patients (P \.001; P \.05; and P \. 005, respectively). They concluded that it makes no sense to have leuconychia in the NAPSI and it should be removed. Conversely, longitudinal ridges, nailfold involvement, and Beau's lines should be added. In his reply, van der Velden agrees and with the provision of 2 separate sources of patient data on this matter, it may mean that a revision of the NaPSI is due. Such a revision was cited in the Nail Summit in Marrakech in 2013.

3 Murthy SN. Iontophoresis for treating nail diseases. Ther Deliv 2013;4:647-50.

Narasimha Murthy provides a review article concerning the use of iontophoresis in the delivery of drugs to nail and subungual tissues and in particular, delivery of antifungal medication. He notes that, although systemic antifungal therapy is a common choice for a common disease, it has drawbacks in terms of side effects.

Iontophoresis has a good success record in delivery of drugs through the skin, but the nail is up to 100x thicker. Nevertheless, the hydrated nail provides a physical environment amenable to iontophoresis, which can raise the penetration of antifungal drugs several fold. This can be enhanced further by the addition of thiolytic agents, which melt the sulphur bonds between keratin molecules. A similar enhancement can be achieved with the use of low molecular weight glycerol or polyethylene glycol. A nail iontophoresis device requires electrodes, with one applied to the nail and another to some other point on the digit. The applicator probe is made of sponge or gauze with the drug embedded within. The applicator can be sized to the nail or be broader, in order to provide contact with the nail folds as well. The latter does not improve nail drug delivery and probably does not have clear advantages. Assessment of drug delivery is done through ex vivo studies using avulsed nails on an agarose gel. *In vivo* analysis is more difficult. The provision of an effective current is also a challenge, although it can be sent with a disposable battery attached to the dorsum of the foot. Other systems also work, but the duration of active delivery can require periods of up to 8 out of 24 hours/ 5 days a week for 4 weeks, as attempted through overnight

David De Berker

application with terbinafine. The final measure of value is clinical cure and in the latter study, a healthy nail margin was seen in 40% of the treatment group in comparison with 10% in the placebo.

4 Sellheyer K. Nail stem cells. J Dtsch Dermatol Ges. 2013;11:235-9.

The hair follicle and human foetus nail work has helped to evaluate the difficulties in accessing mature human nail unit for biological assessment. However, it is not possible to use radiolabelled metabolic markers in human foetal material and hence antigenic markers, assessed largely through immunohistochemistry, provide a handle on the topic. These markers, validated through work on the hair follicle stem cells, highlight 6 markers. The location of these has been mapped in the nail unit of the human embryo between weeks 12 and 23 of gestation. Markers of keratin 15 and 19 and pleckstrin-homology-like domain family A, member 1 (PHLDA1) are all found in the basal layer of the epidermis directly proximal to the embryonic nail, which evolves to become the primordium of the proximal nail fold. The nail bed, as distinct from more proximal areas, is devoid of all markers at all times. The distribution of these 3 markers in embryogenesis has not been confirmed in adult tissue, but Sellheyer concludes that it matches the hair follicle model of a germinative bulge so well, that it is likely to remain a source of stem cells in adult life.

COMMENTARY D. DE BERKER

1 Pressure on the digit results in forces that cause flattening and thickening of the nail. This seems reasonable, but the authors missed the opportunity of looking at the big toenails in the same study. It would have been interesting to attempt something similar in the big toes. I suspect that other factors also have an effect, so that the transverse curvature becomes greater with time, because of proximal changes beneath the matrix, and these forces were not taken into account. On brief evaluation, I found it difficult to determine whether the toenail and thumbnail were substantially different **(Fig 1)**. Also, the point at which you measure the difference in the longitudinal axis of the nail makes a substantial difference. Proximally, the plate is closely adherent to the

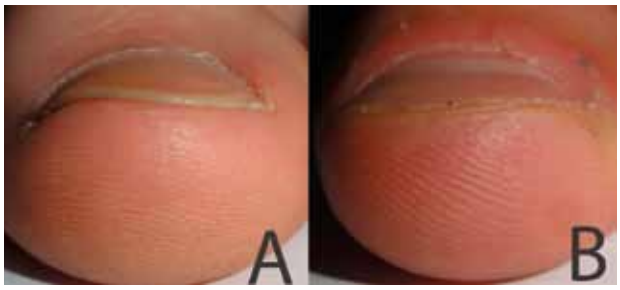


Fig1 - *This figure illustrates a toe (A) and thumb (B) end in the same young adult. It poses the question "how much does pressure on the digit pulp determine the shape of the nail?" with the assumption that pressure on the toe pulp is substantially greater and more frequent than on the thumb. © D. De Berker*

curvature of the phalanx, but this diminishes as it reaches the free edge. There is no mention in the methodology of where the authors measured the curvature. We also know that with time curvature of both toenails and thumbnails can become markedly altered. The shape of the matrix, the shape of the distal interphalangeal joint, changes in the phalanx on the distal dorsal surface, all these appear to have a possible role. Forces applied to the digit pulp will be the vector that allows expression of these different constraints and incursions upon the nail.

2 The NaPSI is due for a revision **(Fig 2)**. For a long time it was like democracy – a terrible system, but the best one we have. As it becomes more widely used, scrutiny and data provide an opportunity to improve it. It is probably best to undertake this revision soon and

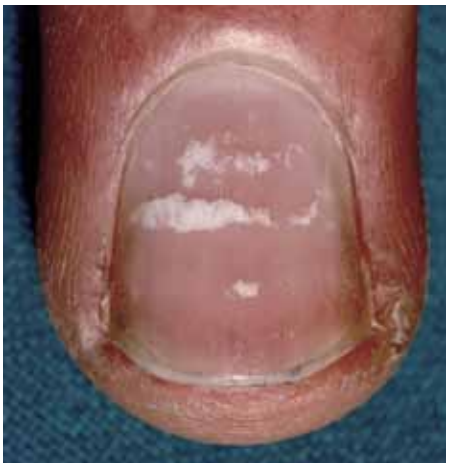


Fig2 - *Leuconychia is most often without a clear disease association and is rarely seen with nail psoriasis. © D. De Berker*

David De Berker

NAIL SCIENCE

with maximal evaluation, so that future studies can be benchmarked with an improved tool. At the time of going to press, Klaassen et al. are in Epub for the blue journal on this topic.[1] They have undertaken a review of all the current psoriatic nail scoring systems and propose the .....N-NAIL. Which is the **N**ijmegen-**N**ail psoriasis **A**ctivity **I**ndex too**L**. The naming of this tool must be hard. But, it seems likely that it will bring a new level of detail and accuracy to the scoring of nail disease.

3 Given the cost and medical supervision, topical therapy might well be preferred for onychomycosis if it were easy, safe, cheap and if it worked. Most data suggests that topical therapy meets the first three requirements, but is found wanting on the fourth. Researchers acknowledge that both the manner of delivery and the outcome are short of that required for a clinically useful tool, but the results suggest that progress is being made and clinically relevant nail iontophoresis may be available in the foreseeable future. As the technology is still in its infancy, it is not able to address the more complex issues of variation in nail thickness, subungual hyperkeratosis **(Fig 3)** and partial nail disintegration, which are common with fingernail onychomycosis.

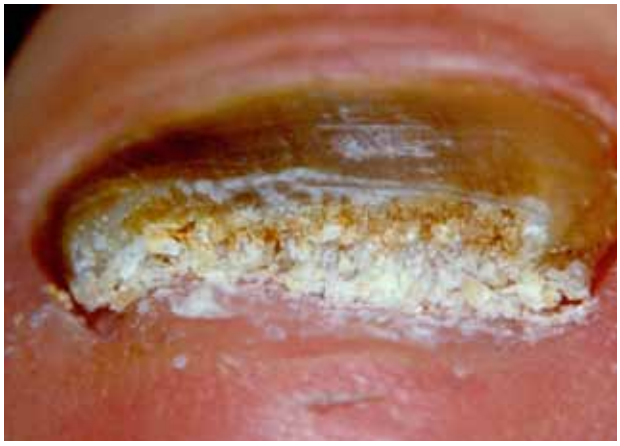


Fig3 - *Iontophoresis of the nail presents several practical difficulties and one of these is penetration of pathological subungual hyperkeratosis which is common in fungal nail disease.*
© D. De Berker

4 Nail stem cells. The location outline by Sellheyer is consistent with clinical knowledge – that proximal matrix damage has a greater chance of scarring than more distal damage. The next step will be to try and identify the persistence of these cell types into adulthood and whether they are surgically transferable with a view to autologous repair of the damaged nail matrix. The role of matrix dermis has been emphasised both in scientific and clinical reporting and experience. This suggests to me that the story is not just about keratins and their expression, but more to do with the relationship between the keratinocytes and the dermis. Follicle amputation and grafting experiments have demonstrated this interplay over many years.[2,3] In clinical terms, the interdependency may also be reflected in the ability of the nail matrix to recover well after tangential biopsy, where full thickness matrix epidermis is often removed.[4] The other element of the story, which is not explored in this work, is the difference between an appendage, that throughout life produces product (nail) continuously, and one that is always undergoing cycles of rest and regeneration. The follicle remains exceptional in this respect -whereas the nail has more in common with normal skin than the hair follicle.

References
1- Klaassen KM, van de Kerkhof PC, Bastiaens MT, Plusjé LG, Baran RL, Pasch MC. Scoring nail psoriasis. J Am Acad Dermatol 2014 Mar 31.
2- Tiede S, Kloepper JE, Bodò E, Tiwari S, Kruse C, Paus R. Hair follicle stem cells: walking the maze. Eur J Cell Biol 2007;86:355-76.
3- Matsuzaki T, Yoshizato K. Role of hair papilla cells on induction and regeneration processes of hair follicles. Wound Repair Regen 1998;6:524-30.
4- Di Chiacchio N, Loureiro WR, Michalany NS, Kezam Gabriel FV. Tangential Biopsy Thickness versus Lesion Depth in Longitudinal Melanonychia: A Pilot Study. Dermatol Res Pract. 2012; 2012:353864.

Osvaldo Correia

INTERNAL MEDICINE

1 Timolol drops causing reversible psoriatic fingernail changes. Glass LR, Nguyen M, Winn BJ, Schrier A. JAMA Ophthalmol. 2013 Sep;131(9):1134.

The authors report a case of a 81-year-old woman with fingernail changes, characterized by ridging and discoloration on her left second digit and afterwards on her third digit, 3 weeks after application of timolol maleate, 0.5% ophthalmic solution to treat glaucoma. The lesions disappeared after discontinuing the eyedrops. The authors suggest that these findings are consistent with psoriatic changes caused by β-blocker use.

2 Síndrome POPP: onicopaquidermoperiostite psoriásica (POPP syndrome: Psoriatic OnychoPachydermoPeriostitis). Romiti R, Santos D, Carvalho J, Arnone M, Takahashi MD Dermatol Online J 2013; 19(4): 6-10.

The authors described a patient aged 46, with a 2-year history of palmo-plantar psoriasis, which was moderately responsive to topical treatments. There was no family history of psoriasis or rheumatic disease. One and a half years later she developped painful swelling of the soft tissue close to the distal phalanx of both great toes, with severe nail deformity characterized by subungueal hyperkeratosis and distal onycholysis. No joint involvement was present and no other stigmata of psoriasis, behind ?– besides?? palmoplantar lesions. Magnetic resonance imaging (MRI) of the anterior feet showed an extensive periosteal reaction of both great toes, associated with bone erosion of the distal phalanx. These data were in favour of psoriatic onychopachydermoperiostitis (POPP) syndrome. Treatment with methotrexate (20 mg per week) during 4 months was unsatisfactory and acitretin (0,5 mg / kg/day) was discontinued due to side effects. Later, a 4-month trial of the fully human anti-tumor necrosis factor (TNF) antibody adalimumab 40 mg SC every 14 days was unsuccessful. They then changed to etanercept treatment (weekly 100 mg SC, for 3 months, followed by 50 mg week for a year). After 2 months of the etanercept treatment the nails began to grow regularly and a remarkable normalization of the clinical appearance was achieved. The patient was free of disease 2 years after etanercept discontinuation.

3 Karunakaran A, Ravindran R, Arshad M, Ram MK, Laxmi MK.Dyskeratosiscongenita: a report of two cases.Case Rep Dent. 2013; 2013: 845125.

The authors reported the case of an 11-year-old girl who had been complaining of a burning sensation of the tongue for one year. The tongue showed a large leukoplakia (5 × 7 cm) with black pigmentation and well-defined borders. She had also had mild dystrophy and splitting of the fingernails for 5 years, associated with hyperkeratotic and pigmented patches on her back, feet and hands. Blood examination revealed a pancytopenia. The second patient, a 20-year-old woman presented with a 3 × 4 cm leukoplakia patch on the tongue, with a burning sensation for six months. This was previously diagnosed as lichen planus and she was treated with oral steroids. She reported a black pigmentation on the white patch that disappeared after this treatment. For three years she had had brittle and cracked nails, which were painful and sometimes discharged pus, and dryness of skin with reticular pigmentation on sun exposed areas, especially on the back and the neck, as well as the palms and soles. She had no blood alterations.

4 Sinha S, Trivedi V, Krishna A, Rao N.Dyskeratosiscongenita- management and review of complications: a case report.Oman Med J. 2013; 28(4): 281-4.

A 22-year-old man presented with a history of 7 months debilitating pain in the left hip, resulting in progressive limping and ambulating with a wheelchair. He reported a traumatic right femoral shaft fracture six years before. Since birth he had had a symptomatic diffuse brownish skin pigmentation over the chest, trunk and arms. From the age of 8 he also had white oral plaque changes in the oral mucosa and dystrophy of finger and toe nails. He had no significant blood analysis. X-rays of pelvis and both hips revealed a vascular necrosis of the femoral head on both sides and he had left hip replacement surgery. Avascular bilateral femoral heads and humeral heads is commonly associated with dyskeratosis congenital and can lead to severe restriction of hip and shoulder joint functions.

Osvaldo Correia

COMMENTARY O. CORREIA

1 Psoriasis is a common genetic disease that may be initiated (drug-induced psoriasis) or exacerbated (drug-triggered psoriasis) by some drug intakes.[1,2] Beta-blockers are well known triggers, but also lithium, synthetic antimalarial drugs, non steroidal anti-inflammatory agents and tetracyclines are well described inducers.[1,2] Systemic treatment is usually the trigger, and skin involvement the usual side effect, but sometimes nail is the main or the only target **(Fig 1-4)**.[3,4] Metoprolol has been used to treat cardiac arrhythmias and can induce nail psoriais, which proves unresponsive to topical and systemic treatments and is only resolved after the withdrawal of metoprolol.[3,4] In the clinical case reported by Glass and al it was the topical application of timolol ophtalmic solution that induced fingernail changes, limited to the digit used to apply the eyedrop and that disappeared after its discontinuation. Ophthalmologists and dermatologists must be aware of this potential side effect of topical β-blocker usage.

References

1- Dika E, Varotti C, Bardazzi F, Maibach HI. Drug-induced psoriasis: an evidence-based overview and the introduction of psoriatic drug eruption probability score. Cutan Ocul Toxicol 2006; 25 (1): 1-11

2- Basavaraj KH, Ashok NM, Rashmi R, Praveen TK. The role of drugs in the induction and/or exacerbation of psoriasis. Int J Dermatol 2010; 49 (12): 1351-61

3- Gin A, Gin D, Sinclair R. Metoprolol-induced psoriatic nail disease. Australas J Dermatol 2013; 54 (1): 59-60

4- Schmutz JL, Trechot P. Isolated ungual psoriasis and metoprolol. Ann Dermatol Venereol 2013; 140 (4): 331

Fig2 - *Psoriatic fingernail changes.© O. Correia*

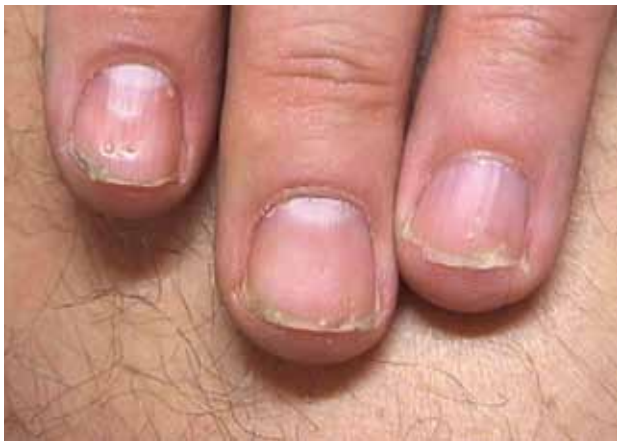


Fig3 - *Psoriatic fingernail changes.© O. Correia*

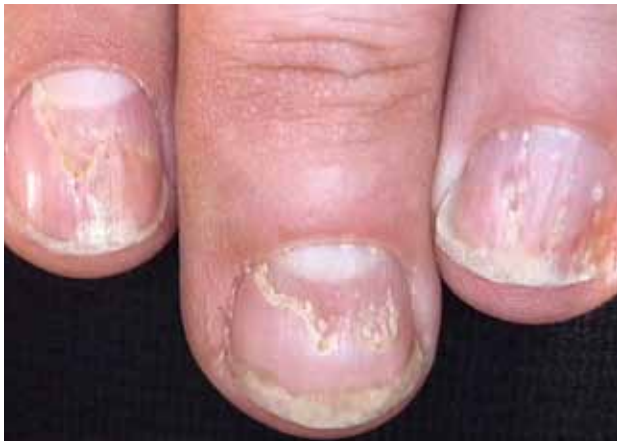


Fig1 - *Psoriatic fingernail changes.© O. Correia*

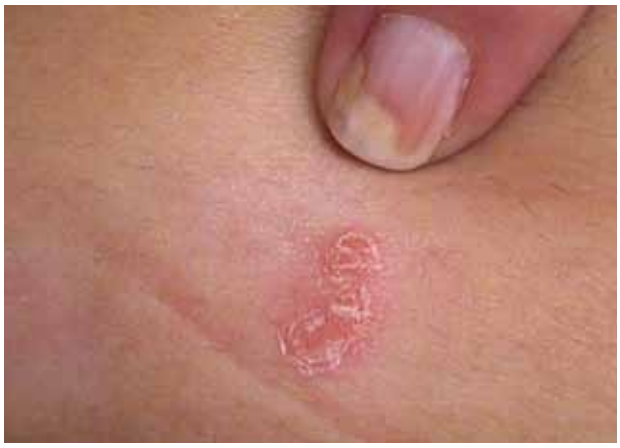


Fig4 - *Psoriatic fingernail changes.© O. Correia*

Osvaldo Correia

2 Joint and nail involvement in psoriasis is relatively common. However, bony involvement of the terminal phalanx under a psoriatic nail is rare. Psoriatic onychopachydermoperiostitis (POPP) syndrome is a rare subset of psoriatic arthritis that is characterized by psoriatic onychodystrophy, connective-tissue thickening above the distal phalanx, and a periosteal reaction. The inflammation is likely to be transmitted from the psoriatic nail to the adjacent underlying bone by the same mechanism as in enthesopathies.[1-3] Cases in children have rarely been reported.[3] In the patient reported by Romiti R et al, both great toes were affected, presenting with nail changes, painful swelling of the soft tissue close to the distal phalanx **(Fig 5, 6)**, as well as radiologic changes, including periosteal reaction and bone erosions of the distal phalanges. Joint involvement is characteristically absent and classic psoriatic lesions may be associated. The pain and inflammation limit walking and worsen the quality of life. Magnetic resonance imaging usually shows an extensive periosteal reaction of the phalangeal tuft. Treatment of POPP is difficult, with several treatment modalities possible, but with limited effectiveness. These include sulfasalazine, corticosteroids, cyclosporine and methotrexate. In recent years, biological agents have been used, including etanercept and adalimumab not always with conclusive clinical response.[5,6] The patient described by Romiti R et al, was refractory to traditional systemic treatments and adalimumab. Etanercept was effective and produced an extended period of remission. Intensive topical treatments should be considered as an additional treatment. In patients who are unresponsive or intolerant to classical treatments, biologic drugs need to be considered.

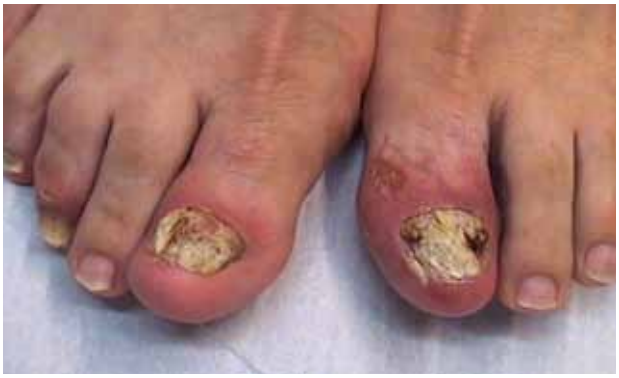


Fig5 - *Psoriatic onycho-pachydermo periostitis. © O. Correia*

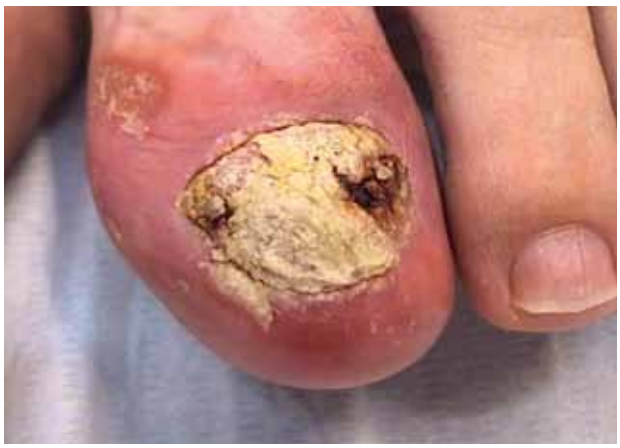


Fig6 - *Psoriatic onycho-pachydermo periostitis. © O. Correia*

References

1- Boisseau-Garsaud AM, Beylot-Barry M, Doutre MS, Beylot C, Baran R. Psoriatic onycho-pachydermo-periostitis. A variant of psoriatic distal interphalangeal arthritis? Arch Dermatol. 1996 Feb;132:176-80.

2- Schröder K, Goerdt S, Sieper J, Krasagakis K, Almond-Roesler B, Orfanos CE. Psoriatic onycho-pachydermo-periostitis (POPP). Hautarzt. 1997 Jul;48(7):500-3.

3- Srivastava M, Solomon G, Strober B. Psoriatic onycho-pachydermo periostitis. Dermatol Online J. 2007 Jan 27;13(1):20.

4- Fietta P, Manganelli P. Childhood onset of psoriatic onycho-pachydermo-periostitis (POPP). J Eur Acad Dermatol Venereol. 2005 Nov;19(6):780-2

5- Dans M, Hivnor C, van Voorhees AS. Psoriatic onychopachydermoperiostitis: improvement with etanercept. Br J Dermatol 2005; 153 (4): 858-9

6- Bongartz T, Härle P, Friedrich S, Karrer S, Vogt T, Seitz A, Müller-Ladner U. Successful treatment of psoriatic onycho-pachydermo periostitis (POPP) with adalimumab. Arthritis Rheum. 2005;52:280-2.

Osvaldo Correia

INTERNAL MEDICINE

3-4 Dyskeratosis congenita (DC) is an inherited disease, arising as a consequence of mutations in telomere biology. It occurs mostly in males and clinically manifests between 5 to 12 years of age. It is associated with nail dystrophy, abnormal skin pigmentation, oral leukoplakia, bone marrow failure and a predisposition to cancer, in particular in the keratotic white oral mucosa patches. Dermatologists, pediatricians and dentists should be aware of the nail, skin and oral mucosa alterations associated with this syndrome, developing in childhood. This syndrome has a potential multisystemic involvement and can be fatal. The only curative therapy to date for a full blown case of DC has been bone marrow transplantation. Steroids, granulocyte macrophage colony stimulating factors and erythropoietin may be helpful transiently. Gene therapy may become a feasible consideration.

References
1- Nishio N, Kojima S. Recent progress in dyskeratosiscongenita. International Journal of Hematology.2010;92:419–424
2- Nico MM, Hammerschmidt M, Lourenço SV. Oral mucosal manifestations in some genodermatoses: correlation with cutaneous lesions. Eur J Dermatol. 2013;23: 581-91

Bruno Fouilloux

INTERNAL MEDICINE

1 Gondim R.M., Neto P.B. Baran R. Pterygium inversum unguis: report of an extensive case with good therapeutic response to hydroxypropylchitosan and review of the literature. J Drugs Dermatol 2013;12:344-346.

Pterygium inversum unguis (PIU) is a rare, but not exceptional dermatological condition. Gondim et al. report the case of a 32-year-old woman who complained of pain and bleeding when she clipped her nails. The condition, which had been present for 4 years, involved all nails on both hands and spared the toenails. There were no other skin lesions, or relevant familial history. A treatment was initiated with once-daily application of a water-soluble nail lacquer containing hydroxypropylchitosan, horsetail extract and methylsulfonylmethane. Examination after 2 months of daily treatment, revealed considerable improvement in the nail changes. An overall improvement was observed after 4 months of treatment, with some persistence of the lesion on the third fingernail. PIU is a disorder consisting of a forward extension of the hyponychium anchoring to the undersurface of the nail plate and thus obliterating the distal nail groove. It may affect a single finger or multiple fingers. It may be congenital and/or familial or acquired. The first case of PIU was described by Caputo and Prandi in 1973.[1] Some cases have been described as related to systemic diseases, principally collagen diseases, allergic dermatitis, neurofibromatosis, hemiparesis, subungualexostosis and leprosy. Women are more frequently affected than men. The most common complaints are pain and bleeding, which occur when the nails are clipped. In about 50% of cases there is a history of associated collagen disease. Fingernails are more often affected than toenails. The appropriate mechanism of origin is speculative[2,3] but blood alterations and ischemia are the most acceptable hypotheses. The treatment is considered complex with poor response to topical therapies, such as keratolytics and corticosteroids.

2 Ozkan F, Ozturk P, Ozyurt K, Inci M, Kalennder A, Bakan B, Yuksel M. Frequency of peripheral arterial disease and venous insufficiency in toenail onychomycosis J Dermatol 2013;40:107-110.

Onychomycosis in toenails is a common fungal infection and vascular abnormalities of the lower extremities are thought to be one of the predisposing conditions. The aim of this study was to evaluate the predisposition effect of venous insufficiency and peripheral arterial disease on toenail onychomycosis. Onychomycosis is reported to be more prevalent in male individuals with genetic susceptibility, immunosuppression, diabetes mellitus, peripheral arterial disease (PAD) and chronic venous insufficiency (CVI).[1] The increased tendency to develop onychomycosis in elderly and diabetic patients is partly associated with the increased prevalence of PAD and CVI.[2,3] Color Duplex Ultrasonography (CDU) is a well-established technique and provides comparable results to arteriography for the evaluation of lower limb arteries. CDU can be used to detect segmental venous reflux with high accuracy. A few studies have determined the frequency of onychomycosis in patients with CVI or PAD. To the best of our knowledge, there is no study reporting the prevalence of asymptomatic PAD in patients with onychomycosis. This study was aimed at determining the frequency of asymptomatic PAD and CVI among patients with onychomycosis and to evaluate the coincidence with onychomycosis and peripheral vascular resistance by means of CDU. 33 patients with bilateral onychomycosis in toenails and 37 control subjects, who had healthy nails, were enrolled in this study. The veins and arteries of the lower extremities were examined with doppler ultrasound in terms of venous insufficiency or peripheral arterial disease. Patients with onychomycosis presented more frequent venous insufficiency than the control group (42.4% and 10.8%, respectively; P = 0.003). Although all patients had bilateral onychomycosis, the reflux was bilateral in 6 out of 14 patients with onychomycosis (42.8%).This study demonstrated a significant relationship between onychomycosis and venous insufficiency, but not with peripheral arterial disease. Also, the authors pointed out discordance with bilateral onychomycosis and unilateral venous insufficiency: in 8 out of 14 patients (57,1%) with venous insufficiency, bilateral onychomycosis was accompanied by unilateral venous insufficiency.

Bruno Fouilloux

The authors did not find PAD to be significantly more frequent among onychomycosis patients compared to the general population. In another study[4] which utilized the prevalence of nail onychomycosis and PAD in diabetic patients, no statistically significant correlation was observed between PAD and onychomycosis among diabetic patients. In contrast, Gupta et al.[5] observed an association between toenail onychomycosis and PAD in their studies. The high rate (57.1%) of discordance between bilateral onychomycosis and unilateral venous insufficiency may suggest that onychomycosis has a multifactorial etiology including genetic susceptibility and CVI is only one of the factors associated with the development of onychomycosis. This study has some limitations. Only the distal subungual type of onychomycosis was included, as it is the most common form. Also, the number of patients participating in the study was limited. Therefore, larger studies with all types of onychomycosis are called for.

3 Piraccini BM, Urciuoli B, Starace M, Tosti A, Baslestri R. Yellow nail syndrome: Clinical experience in a series of 21 patients. J German Soc Dermatol 2014 ;12:131-7.

The yellow nail syndrome (YNS) is a rare disorder characterized by the triad: yellow nails, respiratory problems and lymphedema.[1,2] Dermatologic signs diagnostic for YNS are: arrested, or slow, nail growth rate, nail plate thickening, lack of cuticles, yellow-green discoloration and increased transverse curvature of the nail plate. Dermatologists usually make the diagnosis of YNS clinically. Early diagnosis is very important in order to detect and monitor respiratory problems and other associated disorders. The authors identified 21 patients with YNS out of the patients who were treated at the Nail Clinic of Bologna from August 1985 to December 2012. There were 11 men and 11 women with mean age of 57 +/-12,3 years at the time of diagnosis. The mean duration of nail symptoms before diagnosis was 3,6 +/- 5,1 years. In 18 cases patients complained of progressive thickening and change of nail color and in 3 cases of arrested nail growth. In 15 patients all nails were involved, in 6 patients only the fingernails. In 12 patients presenting marked subungual hyperkeratosis of one or both toenails, a mycological examination was performed. Five had a positive culture for *Trichophyton rubrum*. Dermoscopy of the nail fold capillaries was performed in 15 patients and in all cases showed dilated and tortuous capillary loops. 6 patients presented with the complete triad (yellow nails, lymphedema of the lower extremities and chronic respiratory diseases) and 10 patients presented only with nail involvement and respiratory disease. The remaining 5 patients only had yellow nail alterations. Except for one case, all the other diseases were diagnosed 2 to 9 years before the onset of the YNS. Concerning the nail treatment, Piraccini reported that one patient recovered spontaneously. The other 20 patients were treated with vitamin E 1 200 IU/day. A systemic antifungal (itraconazole 400 mg/day for one week every month) was added in 9 cases for a minimum of 6 months. 10 out of the 20 patients (50 %) responded well to the therapy: 6 patients improved clinically (3 vitamin E, 3 vitamin E + itraconazole), while 4 patients recovered completely.10 patients (50 %) were non-responders (5 vitamin E, 5 vitamin E + itraconazole). In the 5 cases of onychomycosis associated with YNS, mycological regression (confirmed by negative culture) did not correlate with YNS regression. Duration of follow-up varied from 1 month to 19 years. In the 10 non-responders, the nail symptoms remained stable in 7 cases and worsened in 3. The pathogenesis of YNS remains obscure. Anatomical and functional lymphatic abnormalities have been proposed as the underlying cause. This hypothesis might explain lymphedema and pleural effusions, but yellow nails and other respiratory manifestations are more difficult to understand. Capillaroscopic observation of dilated and tortuous nail fold capillary loops suggests microangiopathy as the cause for the nail changes. The diagnosis of YNS is clinical: lymphedema and pleural effusion is enough to establish the diagnosis[1], but it is now accepted that the typical nail alterations are sufficient.[2] Chronic paronychia for fingernails and onychomycosis for toenails are the main differential of YNS. Usually all nails are affected with different degrees of severity. The main differential diagnoses of YNS are chronic paronychia for fingernails and onychomycosis for toenails. YNS is linked to a variety of underlying diseases **(Table 1)**.[3,5] 18 of the patients (85.71 %) had concomitant diseases and malignant tumors were present in 2 (9.52 %). Considering the age of the population affected by YNS and the frequency of malignant tumors, it appeared difficult for the authors to support increased tumor susceptibility in the 21 patients

Bruno Fouilloux

Table 1

Causes of Pterygium Inversum Unguis (Ventral Pterygium)
Acrylate allergy
Causalgia of the median nerve
Congenital and/or familial
Formaldehyde-containing hardeners
Idiopathic
Lenticular atrophy of the palmar creases
Leprosy
Systemic lupus erythematosus
Neurofibromatosis
Paresis
Scarring in the vicinity of the distal nail groove
Subungual exostosis
Systemic sclerosis

Adapted from Gondim R.M. et al. J Drugs Dermatol 2013;12:344-346

affected by YNS in their study. Various therapeutic regimen for the nail changes have been reported, but none have shown consistent results. Oral vitamin E at high doses is the only treatment that has been utilized in a large number of patients, even though not all had good results. Itraconazole has produced conflicting results. Complete nail recovery was seen in about 25% of the cases. It is difficult to discriminate between vitamin E and antifungal effect in the YNS, when they are administered together. Perhaps the arrested nail growth and the local immunodepression due to the lymphatic deficit may explain the predisposition to fungal infection in YNS.

COMMENTARY B. FOUILLOUX

1 Gongim reports a case of pterygium inversum unguis (PIU), which is a rare disease of the hyponychium. The author focused on this pathology and especially on causes Table 1. Concerning the mechanism of PIU, the author's hypothesis is that in PIU there is no parallelism between the nail plate and nail bed growth. However, the cause of this discrepancy of growth is uncertain. Because of the risk of association with systemic diseases and the good therapeutic response achieved in this case, the authors suggest the use of a flowchart for screening patients with other disorders, treatment of associated diseases, follow-up, and establishment of therapeutic proof. The author proposes to use a surgical technique, with replacement of a strip of nail bed and hyponychium 3 to 4 mm wide by a split-thickness graft[4] in idiopathic cases where local hydroxypropylchitosan has failed.

References
1- Caputo R, Brandi G. Pterygium inversum unguis. Arch Dermatol 1973;108:817-818
2- Vadmal M, ReyterI ,Oshtory S. Hensley B, Woodley DT. Pterygium inversum unguis associated with stroke. J Am Acad Dermatol 2005;53:501-503.
3- Sherber NS, Wigley FM, Scher RK. Autoimmune disorders: nails signs and therapeutic approaches. Dermatol Ther 2007;20:17-20.
4- Zook EG. The perionychium. In: Green DP, Ed. Operative hand surgery New York, New York : Churchill Livingstone 1990:1331-1375

2 In the study from Ozkan, the authors demonstrate that the prevalence of venous insufficiency increases in patients with onychomycosis, whereas the prevalence of peripheral arterial disease does not. This study is based on 33 patients compared with 37 controls, and the patients were explored by color duplex ultrasonography, which is a well established technique to appreciate lower limb arteries and detect segmental venous reflux. They point out the discordance of bilateral onychomycosis and unilateral venous insufficiency. Therefore, further investigations with larger samples sizes should be carried out.

References
1- Thomas J, Jacobson GA, Narkowicz CK, Peterson GM, Burnet H, Sharpe C. Toenail onychomycosis: an important global disease burden. J Clin Pharm Ther 2010;35: 497–519.
2- Gupta AK, Gupta MA, Summerbell RC et al. The epidemiology of onychomycosis: possible role of smoking and peripheral arterial disease. J Eur Acad Dermatol Venereol 2000;14:466–469.
3- Shemer A, Nathansohn N, Kaplan B, Trau H. Toenail abnormalities and onychomycosis in chronic venous insufficiency of the legs: should we treat? J Eur Acad Dermatol Venereol 2008;22: 279–282.
4- Saunte DM, Holgersen JB, Haedersdal M et al. Prevalence of toenail onychomycosis in diabetic patients. Acta Derm Venereol 2006;86:425–428.
5- Gupta AK, Konnikov N, MacDonald P et al. Prevalence and epidemiology of toenail onychomycosis in diabetic subjects: a multicentresurvey. Br J Dermatol 1998;139: 665–671.

Bruno Fouilloux

INTERNAL MEDICINE

3 In a detailed study in an important series of 21 patients, Piraccini et al. made a complete focus on YNS. This pathology is relatively rare, but not exceptional, and dermatologists and internists should be aware of it. The diagnosis is above all clinical. The authors emphasize the association with others diseases and especially respiratory diseases **(Table 2)**. According to the literature, pleuropulmonary symptoms and lymphedem have been found respectively in 63% and 80% of patients with YNS.[3,4] The data of the 21 patients of this study differ markedly from that reported in the others, since 16 of them (76.19%) had respiratory diseases, while only 6 (28.57%) presented with lymphedema. On the contrary to what is found in the literature, they found no correlation between the evolutivity of the disease and the absence of response to the treatment. Indeed, nail abnormalities have been reported to improve or regress, when the associated respiratory disease is successfully treated. Nevertheless, the authors note that 5 of their patients (23.81%) showed a resolution of the nail symptoms; 6, an improvement (28.57%); 7, no changes (33.33%); and 3, a worsening (14.29%), and only 1 of the 5 cured patients had a lasting remission of the respiratory symptoms. This study shows that much progress can be made in YNS, both in physiopathology and treatment. The authors insist on the difficulties of establishing a reference treatment.

References
1- Hiller E, Rosenow EC, Olsen AM. Pulmonary manifestations of the yellow nail syndrome. Chest 1972;61:452-8.
2- Bourcier T, Baudrimont M, Borderie V et al. Conjunctival changes associatedwithyellownail syndrome. Br J Ophtalmol 2002;86:930.
3- Norklid P, Kroman-Andersen H, Struve-Christensen E. Yellow nail syndrome-the triad of yellow nails, lymphedema and pleural effusions. Acta Med Scand 1986;219: 221-7.
4- Beer DJ, Pereira W Jr, Snider GL. Pleural effusion associated with primary lymphedema: a perspective on the yellow nail syndrome. Am Rev Respir Dis 1978; 117:595-9.
5- David-Vaudey E, Jamard B, Hermant C, Cantagrel A. Yellow nail syndrome in rheumatoid arthritis: a drug-induced disease? Clin Rheumatol 2004;23:376-8.

Table 2

Malignancies	Carcinoma of the larynx, lymphoma, melanoma, adenocarcinoma of the endometrium, anaplastic undifferentiated tumor, carcinoma of the breast, fibrosarcoma of the skin, mycosis fungoides, carcinoma of the gallbladder, renal carcinoma, lung adenocarcinoma
Endocrine disorders	Diabetes mellitus, thyroid dysfunction
Rheumatoid arthritis	
Myocardial infarction	
Nephrotic syndrome	
Connective tissue diseases	Raynaud phenomenon, polymyalgia rheumatica, eosinophilia-myalgia syndrome
Associations reported as single case report	Pyelonephritis, systemic lupus erythematosus, psoriasis, intestinal lymphangectasia, sleep apnea, mental retardation, hemochromatosis, Guillain Barré syndrome, hypoplastic kidney, thromboembolic disease, cerebral aneurysm, immunological disorders (hypogammaglobulinemia, pancytopenia, IgA deficiency), sarcoidosis, bullous stomatitis, anydrosis, pectus excavatum, immunodeficiency states, chronic chemosis and conjuctival degenerative lesion

Adapted from Piraccini BM et al. Yellow nail syndrome: Clinical experience in a series of 21 patients. J German Soc Dermatol 2014;12:131-7.

Jose Maria Mascaro

SELF-INDUCED NAIL DISORDERS

1 Borges-Costa J, Sacramento Marques M. Median nail dystrophy associated with ritonavir. Int J Dermatol 2013; 52: 1581-2.

The authors report the case of a 38-year-old HIV positive male who suffered a two year duration median thumb nail dystrophy, developed two months after highly active antiretroviral therapy (HAART) with lamivudine, tipranavir, ritonavir, enfuvirtide, and raltegravir. No injuries, tic habits, other drugs or familial cases were noticed. Retinoid-like side-effects on the nails (paronychia, pyogenic granuloma, ingrown toe nails) have been described for many of the drugs used in HAART.[1-4] However, median nail dystrophy (MND) has only previously been reported associated to isotretinoin.[5,6] Since virological response was good in their patient, ritonavir dosage was reduced from 600 mg twice daily to once per day and complete resolution of the nail alterations was observed within six months. Due to this evolution the authors consider that MND was a ritonavir side effect, as no other taken medications could be considered responsible for that manifestation.

2 Pacan P, Grzesiak M, Reich A, Kantorska-Janiec M, Szepietowski JC. Onychophagia and Onychotillomania: Prevalence, Clinical Picture and Comorbidities Acta Derm Venereol 2014; 94: 67-71.

Onychophagia is a chronic nail biting conduct, that usually begins in childhood, with an estimated prevalence of 20% to 45% of adolescents. Recurrent picking and over manicuring of the finger and/or toenails, with shortening and/or removal of nails is named onychotillomania. The authors studied the prevalence of onychophagia and onychotillomania in young adults and the comorbidity of these conditions with anxiety and obsessive compulsive disorders (OCD), as well as with other factors related to this behaviour. A total of 339 voluntary university students (131 male and 208 female) were interviewed with a specific structured questionnaire and were later examined by a psychiatrist. Onychophagia was present in 46.9% (19.2% active and 27.7% past nail biters). Most (86.2%) started before the age of 13 and 47.2 % reported a lifetime habit. The majority of subjects (92.2%) described nail biting as an automatic comportment. Tension before nail biting (65.7%) and pleasure after it (42%) was described. 22.5% of the participants with lifetime onychophagia met criteria for anxiety and 3.1% for OCD. The most common disorders were specific phobia (14,1%), panic (5%), social phobia (4.4%) and OCD (4.4%). There was no gender difference in frequency or mean duration of NB. However, in women it was not usually an intentional activity, while in most men it was, interrupting other activities. The authors conclude that multiple psychological factors are involved in these conditions.

3 Ghanizadeh A, Derakhshan N, Berk M. N-acetylcysteine Versus Placebo for treating Nail Biting, a Double Blind Randomized Placebo Controlled Clinical Trial. Anti-Inflammatory Anti-Allergy Agents in Medicinal Chemistry 2013; 223-228.

The authors studied the possible action of N-acetylcysteine (NAC), a powerful glutathione and glutamate modulator, for management of chronic nail biting (CNB) in youth. 42 children and/or adolescents suffering from CNB were treated with either 800 mg/day NAC or a placebo in a double blind trial. The patients were evaluated before, then one month and two months after the beginning of the study. Nail length was the objective outcome. Throughout the trial, mean nail length progressively increased in both groups, and after the first month of the trial a statistically significant difference between the two groups regarding increased nail length was noted. However, after two months no difference was observed. Regarding NAC side effects, two patients of that group discontinued the medication due to adverse events (headaches and agitation for one and change of behavior with aggressiveness for the other). The authors conclude that NAC decreases nail biting tendency in youth during a relatively short term treatment. NAC is reasonably well tolerated and severe adverse effects are uncommon. New long duration studies are required to confirm these results.

Jose Maria Mascaro

SELF-INDUCED NAIL DISORDERS

COMMENTARY JM MASCARO

1 As emphasized by Jorges-Costa and Sacramento Marques, longitudinal median nail dystrophy (classically named Heller's canaliform dystrophy) **(Fig 1)** is usually the result of a repeated voluntary or involuntary mechanical trauma or is due to the presence of a tumor (usually glomus tumor) on the nail matrix or underlying the proximal nail bed. Familial cases have not been documented frequently. It has also been reported concomitant with isotretinoin treatment.[5,6]

Systemic retinoids, due in part to their ability to modify keratinization, have been reported as being able to originate many mucous membranes and temporary skin changes; on the nails they may particularly produce fragility, paronychia, granulomatous proliferations, ingrown toe nails, onycholysis, elkonyxis and other alterations.[7-9] Occasionally, normal nail regrowth after treatment with retinoids may originate a transversal dystrophy-like appearance, that could be misinterpreted by non-experts as a side-effect and not as a sign of good response **(Fig 2)**.

Retinoid-like effects have been described with HAART drugs, most of them related to indinavir. Diverse mucocutaneous manifestations resembling adverse effects of systemic retinoid therapy have also been noted, including possible nail alterations. The use of indinavir appears to be related to a significant risk (4-9%) of ingrown toe nails.[4] In the reported case, as median nail dystrophy resolved after a dose reduction of ritonavir, it appears reasonable to assume that this drug was responsible for that peculiar alteration.

Taking into consideration the frequency of paronychia in patients treated with indinavir and also the possibility of nail side effects with other concomitant HAART medications, it seems relevant that patients who receive these treatments should be instructed to take meticulous care of their nails, particularly their toe nails, in order to prevent bacterial or candida superinfection of the mentioned nail side effects.

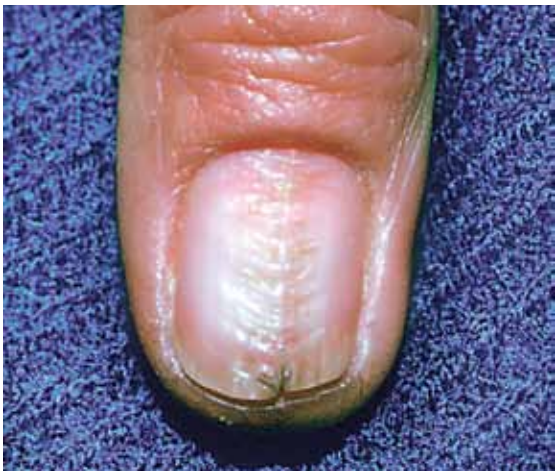


Fig1 - *Longitudinal median nail dystrophy (or Heller's canaliform dystrophy). © JMM. Mascaro*

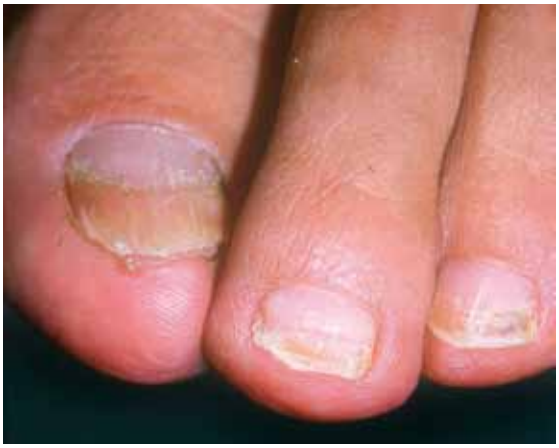


Fig2 - *Normal nail regrowth after treatment with retinoids inducing a transversal groove. © JMM. Mascaro*

References

1- Blanes M, Belinchón I, Portilla J. Cutaneous drug reactions in HIV-infected patients in the HAART era. Actas Dermosifiliogr 2009;100: 253-265.

2- Sass JO, Jakob-Sölder B, Heitger A, Tzimas G, Sarcletti M. Paronychia with pyogenic granuloma in a child treated with indinavir: the retinoid-mediated side-effect revisited. Dermatology 2000; 200:40-42.

3- Bourezane Y, Thalamy B, Viel JF, Bardonnet K, Drobacheff C, Gil H, Vuitton DA, Hoen B. Ingrown toenail and indinavir: case-control study demonstrates strong relationship. AIDS. 1999;13:2181-2182.

4- Garcia-Silva J, Almagro M, Peña-Penabad C, Fonseca E: Indinavir-induced retinoid-like effects: incidence, clinical features and management. Drug Saf 2002;25:993-1003.

5- Bottomley WW, Cunliffe WJ. Median nail dystrophy associated with isotretinoin therapy. Br J Dermatol 1992;127:447-448.

6- Dharmagunawardena B, Charles-Holmes R. Median canaliform dystrophy following isotretinoin therapy. Br J Dermatol 1997;137:658-659.

7- De Raeve L, Willemsen M, De Coninck A, Roseeuw D: Paronychia and the formation of granulation tissue during isotretinoin therapy. Dermatologica 1986;172:278-280.

8- Onder M, Oztaş MO, Oztaş P. Isotretinoin-induced nail fragility and onycholysis. J Dermatolog Treat 2001;12:115-116.

9- Yung A, Johnson P, Goodfield MJ. Isotretinoin-induced elkonyxis. Br J Dermatol. 2005;153: 671-672.

Jose Maria Mascaro

SELF-INDUCED NAIL DISORDERS

2 Some years ago I was asked to write a foreword for a Monograph on Dermatology and Psychiatry. I titled it "*Hand in hand and not giving back to the others*" ,meaning that practitioners in these two branches must cooperate and not treat patients, who have problems in both fields, self-sufficiently. Probably psychiatry is one of the lesser known medical specialties for those who have not properly trained in that area. Nevertheless, many of the patients seen by dermatologists have not only so-called "somatic" problems, but have a combination with psychological implications producing or produced by their basal disease. For this reason it is relevant to comment the summarized papers on onychophagia/nail biting that are comportments associated with nail alterations, but which particularly involve a complex psychological background. If we look at most textbooks of Dermatology there is only a small space devoted to these conditions, focused on describing nail modifications, short allusions to probable psychological implications and reference to the possible help of unpleasant taste topical preparations, bandages and administration of anxiolytics. The papers summarized here, written by psychiatrists, maybe appear exceedingly meticulous and redundant for dermatologists, who are used to short reports for topics that may appear as minimal problems. They also deal with some subjective manifestations (such as feelings of tension or pleasure), which are difficult to evaluate accurately, even though dermatologists are used to trying to do so ,when assessing pruritus, pain or burning sensations.

It is well known that babies and little children explore everything with their mouths. They can easily reach and perceive the structure of fingers and nails. They suck, and when teeth grow out, they start to bite when they feel that their background is unpleasant. There is an estimation that more than half of the school-aged population frequently or occasionally bites fingernails. Biting nails exteriorizes their energy or helps concentration, as well as their doing other minor compulsive self-actions (tics, picking, scratching) and psychiatrists mention that it could occur by either over-stimulation (stress, excitement) or lack of stimulation (inactivity, boredom).
However self-aggression, severe or minimal, could originate from different factors. As an example, I remember a patient who was suffering from Lesch Nyhan syndrome (LNS) and due to his behavior and self-aggression, he was initially referred to a pediatric psychiatrist, who later forwarded him to me. This syndrome is characterized by hyperuricemia, changes of behavior, mild to severe neurological manifestations (choreoatetosis) and self-aggression, sometimes producing extremely severe mutilations (they may destroy their lips, fingers or other reachable areas). In fact this neurogenic syndrome is due to deficiency of hypoxanthine-guanine-phospho-ribosil transferase by a mutation of the HPRT1 gene on the chromosome X. More than 300 mutations have been reported and the severity of clinical phenotype is variable. There is also a LNS type called Kelley-Seegmiller syndrome characterized by hyperuricemia, nephrolithiasis and severe gout, but presenting no neurological manifestations.

3 In relation to nail biting treatment, different medications have been used, such as serotonin uptake inhibitors and tricyclic antidepressants. However, on the other hand, modulation of the glutamate system appeared as an interesting strategy and then N-acetylcysteine (NAC), at the dosage 800 mg/d, has been used for autism, compulsive behaviour and psychiatric problems involving oxidative stress or impulsivity. NAC has also been reported to be effective in a case of nail biting and it was for that reason than Ghanizadeh et al. tried the drug with the interesting results summarized here; however new trials must be carried out to confirm NAC usefulness for this common condition.

Marcel Pasch

PSORIASIS

Nail psoriasis may have a profound impact on the quality of life of patients. Current treatment options are limited and poorly investigated. Fortunately, new treatments are being explored and may offer new opportunities in the near future.

1 de Vries AC, Bogaards NA, Hooft L, Velema M, Pasch M, Lebwohl M, Spuls PI. Interventions for nail psoriasis. Cochrane Database Syst Rev. 2013 Jan 31.

The authors reviewed all relevant randomized controlled trials (RCTs) to assess evidence for the efficacy and safety of treatments for nail psoriasis. From 1946 to March 2012 only 18 studies, involving 1266 participants, could be included, but the results could not be pooled due to the heterogeneity of many of the studies. Therefore, the primary outcomes were defined as "Global improvement of nail psoriasis as rated by a clinician", "Improvement of nail psoriasis scores", "Improvement of nail psoriasis in the participant's opinion". Secondary outcomes were "Adverse effects (and serious adverse effects)"; "Effects on quality of life"; and "Improvement in nail features, pain score, nail thickness, thickness of subungual hyperkeratosis, number of affected nails, and nail growth". Short-term (3 to 6 months), medium-term (6 to 12 months) and long-term (>12 months) treatments were assessed separately if possible.

The quality of the trials was generally poor. Only two systemic biologic studies and three radiotherapy studies reported significant results for the first two primary outcomes. Infliximab 5 mg/kg showed 57% nail score improvement versus -4% for placebo ($P < 0.001$); golimumab (50 mg and 100 mg every four weeks), another anti-TNF biologic, showed 33% and 54% improvement respectively, versus 0% for placebo ($P < 0.001$), both after medium-term treatment. Both also showed significant results after short-term treatment. From the three radiotherapy studies, the superficial radiotherapy study (given as 3 fractionated doses of 150 cGy every 2 weeks) showed a moderate 20% versus 0% nail score improvement ($P = 0.03$) after short-term treatment, but only on non-hyperkeratotic nails. Grenz rays (5 Gy) on ten occasions at intervals of 1 week induced moderate improvement at 10 weeks in 8 out of 22 patients, and electron beam (6 Gy given in 8 fractions over 8 weeks) also induced significant nail improvement compared to the comparative treatment: three months after treatment, electron beam showed a significant reduction ($P < 0.05$) compared to the other hand; however, not at 6 months ($P > 0.5$) or 1 year ($P > 0.5$).

Studies with ciclosporin, methotrexate, and ustekinumab did not show significantly better results than their respective comparators etretinate, ciclosporin, and placebo. Nor did studies with topical interventions (5-fluorouracil 1% in Belanyx lotion, tazarotene 0.1% cream, calcipotriol 50 µg/g, calcipotriol 0.005%) and their respective comparators: Belanyx lotion (urea, propylene glycol), clobetasol propionate, betamethasone dipropionate with salicylic acid, or betamethasone dipropionate. Concerning the secondary outcomes, not all included studies reporting adverse events. Only one study reported the effect on quality of life, and two studies reported nail improvement per feature.

The authors conclude that although the quality of trials was generally poor, the review may have some implications for clinical practice. Infliximab, golimumab, superficial radiotherapy, grenz rays, and electron beam caused significant nail improvement compared to the comparative treatment. Although infliximab and golimumab, as powerful systemic treatments, have been shown to be beneficial, they may have serious adverse effects. This review reported only mild adverse effects, recorded mainly for systemic treatments. However, because of their design and timescale, RCTs generally do not pick up serious side-effects. Therefore, infliximab and golimumab are not realistic options for people troubled with nail psoriasis, unless these systemic treatments are prescribed for the patient because of cutaneous psoriasis or psoriatic arthritis or the nail psoriasis is severe, refractory to other treatments, or has a major impact on the person's quality of life. Radiotherapy for psoriasis is not used in common practice. The results with superficial radiotherapy, Grenz rays, and electron beam did show significant improvement, but often in a minority of treated patients and for only a limited time. The evidence for the use of topical treatments is inconclusive and of poor quality; however, this does not imply that they do not work.

Marcel Pasch

Future trials need to be rigorous in design, with adequate reporting. Trials should correctly describe the participants' characteristics and diagnostic features, use standard validated nail scores and participant-reported outcomes, be long enough to report efficacy and safety and include details of effects on nail features.

2 Al-Mutairi A, Elkashlan M. Nail psoriasis treated with pulse dye laser. Indian J Dermatol. 2013;58:243.

Pulse dye laser (PDL) has proved effective for plaque psoriasis, but it has not been evaluated in nail psoriasis. The authors report PDL treatment of 10 psoriatic nails in one patient. This 40- year-old female had been suffering from nail psoriasis with pitting, onycholysis and subungual hyperkeratosis of ten finger nails for the past two years. No lesions were detected on the body.

The nails were treated with PDL (595nm) once monthly for three months. The pulse duration was 1.5 milliseconds, the beam diameter was 7 mm, and the laser energy was 8.0 to 10,0 J/cm. Stacking technique was used. The nails were evaluated before treatment and one month after the last session **(Fig 1)** using the Nail Psoriasis Severity Index (NAPSI) score. The NAPSI scores were not shown, but had markedly decreased. Both nail matrix and nail bed features improved.

Fig1 - *The upper panel shows left hand nails before treatment and the lower panel the same nails one month after treatment.*
© Indian Journal of Dermatology

The effectiveness may be due to destruction of abnormal vasculature. Authors believe that PDL would be an effective, convenient treatment option for nail psoriasis. However, more studies are needed to objectively judge its effect.

3 Goldust M, Raghifar R. Clinical Trial Study in the Treatment of Nail Psoriasis with Pulsed Dye Laser. J Cosmet Laser Ther. 2013 Oct 16.

Nail psoriasis has a high incidence among psoriasis patients, with reported incidences varying from 10-78%. The treatment options for nail psoriasis are limited and the management of nail psoriasis is challenging for physicians. Many studies have proven the efficacy of pulse dye laser (PDL) in the treatment of plaque psoriasis. The pulse durations in these studies varied between 0.35 and 1.5 milliseconds (ms). This study aimed at evaluating the effect of different pulse durations in the treatment of nail psoriasis with the 595nm PDL to determine the optimal pulse duration. To investigate this, forty patients with bilateral fingernail psoriasis were recruited and completed a 6-month trial. PDL was applied in two passes on the lunula, proximal and lateral nailfolds based on random assignment. Eighty nails were treated with 6-ms pulse duration and 9 J/cm^2, whereas 80 nails on the opposite hands were treated with 0.45-ms and 6 J/cm^2. The spot size in both modalities was 7-mm. Contiguous layers of spots were applied with 10% overlap, once a month for 6 consecutive months. The Nail Psoriasis Severity Index (NAPSI) was used to assess the clinical outcome from pre-treatment and post-treatment photographs.

All forty patients completed the 6-month protocol. During the first 3 months of treatment, mean total NAPSI and mean nail matrix NAPSI scores significantly decreased from baseline. The significant reduction in mean total NAPSI and mean nail matrix NAPSI scores was observed as early as after the first month of treatment, in both the longer and shorter pulse duration groups ($P < 0.005$). There was no significant difference between the longer and shorter pulse duration ($P > 0.05$). For the mean nail bed NAPSI score, a significant reduction from baseline was observed in the third and fourth month of treatment in

Marcel Pasch

PSORIASIS

both groups (P< 0.05). No significant difference between both groups was observed, except after the first month of treatment. After 6 months of the first treatment, there was a significant reduction in overall NAPSI, nail matrix NAPSI, and nail bed NAPSI scores from baseline in both groups; however, no significant difference was found between the two pulse duration groups. Side effects were mild, including transient petechiae in almost half of the nail folds and hyperpigmentation in about 30% of the nail folds. A higher level of pain was found in the longer pulse duration group.
The authors conclude that both the longer 6-ms and shorter 0.45-ms pulses of PDL (595 nm) have been clinically proven to be effective for the treatment of nail matrix and nail bed psoriasis. This is likely to have been caused by its effect on angiogenesis and vascularity within the psoriatic nail unit.

4 Al-Mutairi N, Nour T, Al-Rqobah D. Onychomycosis in patients of nail psoriasis on biologic therapy: a randomized, prospective open label study comparing Etanercept, Infliximab and Adalimumab. Expert Opin Biol Ther 2013;13:625-9.

Some patients with nail psoriasis have nail changes, such as subungual hyperkeratosis, pitting, yellowish or white discoloration of the nails, or thickening of the nail plate, which morphologically resemble onychomycosis. In a psoriasis patient with nail changes it can be difficult to decide whether this is due to psoriasis, onychomycosis, a combination of both or due to another cause. Psoriasis of the nail may lead to a higher susceptibility for nail infection with dermatophytes. In contrast, an infection with dermatophytes might, hypothetically, induce a local Kœbner reaction. The aim of this prospective study was to determine the incidence of onychomycosis among patients with nail psoriasis, who were being treated with anti-TNF therapy (infliximab, etanercept, and adalimumab).
315 patients and 180 controls with nail psoriasis were enrolled after ruling out the presence of exclusion criteria: positive fungal scraping, systemic illness, systemic psoriasis medication in the past 3 months, no-show after screening, contra-indications for anti-TNF, or refusal to participate. Patients were randomly divided into 3 groups (Group A: infliximab, Group B: etanercept and Group C: adalimumab). Control patients did not receive biologics. The patients were followed up every 4 weeks for 24 weeks. Nail scrapings were repeated at week 24. The target NAPSI of the most involved digit was assessed at the base line and then every 4 weeks until the end of the treatment period. The results of the biologic treated patients were compared with the controls. All patients and controls underwent mycological evaluation of the involved nails at the end of the study using potassium hydroxide (KOH) direct microscopic examination and fungal culture using Sabouraud's dextrose agar with cycloheximide and chloramphenicol. Both the KOH and the culture needed to be positive to include the data.
In total, in 64 out of 315 patients both KOH examination and mycological culture was positive at the end of 24 weeks (20.3%) in comparison to 25 out of 180 (13.9%) of the controls. When comparing the three groups, the results were as follows: 33% (33/100) of the patients on Infliximab, 15.5% (17/110) of the patients on etanercept, and 13.3% (14/105) of the patients on adalimumab had developed a positive fungal state. The difference between the mycological results in patients on infliximab versus controls was statistically significant (P<0.01). The differences between etanercept, adalimumab, and controls were statistically not significant (P>0.01). Dermatophytes (*T. rubrum* and *T. mentagrophytes*) were the most encountered fungi, responsible for 64% of positive cultures. Yeast (C. albicans, C glabrata, and Rhodotorula rubra) was cultured in 26%. The remaining 10% consisted of molds (*Penicillium sp. and Mucor sp.*).
Onychomycosis in association with nail psoriasis was more common in males on anti-TNF (M:F–53:11) and in controls (M:F–19:6). The effects of the biologics on the NAPSI is not mentioned.
This study revealed statistically significant association between fungal infections of the nail in patients with psoriasis on treatment with infliximab. The difference in occurrence of fungal nail infection between systemically treated nail psoriasis patients and controls, could explain why studies focusing on the prevalence of onychomycosis in nail psoriasis patients have conflicting results. The authors advocate fungal evaluation in all psoriasis patients with nail involvement.

Marcel Pasch

PSORIASIS

COMMENTARY M. PASCH

Nail psoriasis can have a profound impact on the quality of life of psoriasis patients, even more than plaque-psoriasis has.[1] All summarized papers express the increased recognition of this fact. The first three papers focus on therapeutic options, while the fourth paper confronts us with the potential side-effects of our attempts to help patients with nail psoriasis.

1 The Cochrane Review of De Vries et al. is a beautiful attempt to supply us with evidence-based data on treating nail psoriasis. In spite of the high ambitions of the authors, it turned out that the quality of almost all the studies on nail psoriasis treatment was too low to fulfill the criteria for inclusion in a Cochrane review. Infliximab, golimumab, superficial radiotherapy, Grenz rays, and electron beam are not realistic options for people troubled with nail psoriasis. In daily practice we are used to working with topical formulations, intralesional steroids, and conventional systemic therapies, and know the positive effects of intralesional steroids for nail matrix psoriasis or methotrexate for nail bed and nail matrix psoriasis. De Vries has also recognized this and is currently working on a review about non-RCT's for nail psoriasis. However, the challenge for future trials is to design protocols which do fulfill criteria for RCT's, in order to provide the most serious data for the future.

2-3 The publications of Al-Mutairi and Elkashlan, and of Goldust and Raghifar focus on pulsed dye laser treatment of nail psoriasis. The first case-report describes a single patient whose both hands were treated with PDL for three months and showed some improvement. The work of Goldust and Raghifar has a nice prospective character and compares two treatment regimes using a right/left comparison in forty patients. This study design is promising in order to obtain trustworthy results. They did not find differences between 6-millisecond and 0.45-millisecond pulses of PDL. The lack of difference can show equal effectiveness of both pulse durations or can demonstrate ineffectiveness, and therefore emphasizes the urgent need for a gold standard topical therapy to compare with. Limited effectiveness is suggested by the fact that the NAPSI values after treatment were not shown in this study. Also, other previous studies on PDL treatment for nail psoriasis did not include controls.[2,3] A recent study by Huang et al.[4] compared the efficacy of pulsed dye laser, plus topical tazarotene versus topical tazarotene alone, in psoriatic nail disease in a left-to-right controlled study. Unfortunately, they used some unusual endpoints, but concluded that pulsed dye laser plus topical tazarotene is more effective than tazarotene alone. However, the question - if PDL is a realistic option for nail psoriasis - remains unanswered and depends on the extent of the obtained improvement: are significant improvements also clinically relevant improvements?

4 The assumed interrelationship between nail psoriasis and onychomycosis has been subject to many studies, which have recently been systematically reviewed.[5] According to this systematic review, the estimated prevalence of onchomycosis in nail psoriasis was 18%, assumably higher than in the general population. Al-Mutairi et al. demonstrate the clinical relevance of awareness regarding onychomycosis in psoriasis patients that receive infliximab. A decreased resistance for many fungi during infliximab therapy has been reported previously.[6] According to the study of Al-Mutairi, this mycosis promoting effect is limited to infliximab and cannot be extended to etanercept and adalimumab. However, reduced immune response for fungal infections appear to be particularly reduced by infliximab, but is assumed to play a role in all patients on anti-TNF therapy.[7] These data should motivate us to repeat fungal cultures in psoriasis patients being treated with anti-TNF biologics in which improvement of the nails appears to be disappointing.

References

1- Klaassen KM, van de Kerkhof PC, Pasch MC. Nail Psoriasis, the unknown burden of disease. J Eur Acad Dermatol Venereol 2014 Jan 15.
2- Oram Y, Karincaoğlu Y, Koyuncu E, Kaharaman F. Pulsed dye laser in the treatment of nail psoriasis. Dermatol Surg 2010;36:377–81.
3- Fernández-Guarino M, Harto A, Sánchez-Ronco M, García-Morales I, Jaén P. Pulsed dye laser vs.photodynamic therapy in the treatment of refractory nail psoriasis: A comparative pilot study. J Eur Acad Dermatol Venereol 2009;23:891–5.
4- Huang YC, Chou CL, Chiang YY. Efficacy of pulsed dye laser plus topical tazarotene versus topical tazarotene alone in psoriatic nail disease: a single-blind, intrapatient left-to-right controlled study. Lasers Surg Med 2013;45:102-107.
5- Klaassen KM, Dulak MG, van de Kerkhof PC, Pasch MC. The prevalence of onychomycosis in psoriatic patients: a systematic review. J Eur Acad Dermatol Venereol 2013 Aug 19.
6- Marie I, Guglielmino E. Infections opportunistes non tuberculeuses au cours des traitements par les anti-TNFα. Rev Med Interne 2010;31:353-60.
7- Rychly DJ, DiPiro JT. Infections associated with tumor necrosis factor-alpha antagonists. Pharmacotherapy 2005;25:1181-92.

Véronique Blatière

ONYCHOMYCOSIS

1 Rich P. Topical treatment of onychomycosis with efinaconazole solution 10%. Cutis. 2013 Jun;91(6):305-7. PubMed PMID: 23837154.

In this article, Phoebe Rich reports a case of onychomychosis treated with Efinaconazole 10%, a new topical agent. The patient was enrolled in one of the two recent phase III, multicenter, randomized double blind studies of Efinaconazole 10%.[1] The patient had suffered from onychomychosis of the great toenail for more than 5 years and 50% of the total nail surface was involved. Five toenails were infected and the culture was positive for *Trichophyton rubrum*. Efinaconazole solution 10% was applied once daily to the clean nail plate surface, lateral and proximal folds, hyponychium and undersurface of the free edge of the nail plate. The patient was assessed for efficacy and safety at weeks 12, 24, 36, 48, and at 52, as a post treatment follow-up. By the end of the treatment the target nail had 0% involvement and both KOH and fungal cultures had been negative since week 36. No adverse effect was reported. Based on this case, Phoebe Rich informs physicians that Efinaconazole 10% solution is encouraging as a treatment of moderate distal lateral subungual onychomycosis.

2 Del Rosso JQ, Reece B, Smith K, Miller T. Efinaconazole 10% solution: a new topical treatment for onychomycosis: contact sensitization and skin irritation potential. J Clin Aesthet Dermatol. 2013 Mar;6(3):20-4. PubMed PMID: 23556032; PubMed Central PMCID: PMC3613269.

The authors studied the potential of Efinaconazole 10% and its corresponding vehicle to induce delayed skin sensitization and skin irritation. They used two methodologies:

For contact sensitization, they conducted a single-center study of 239 healthy adults, based on Jordan and King's principles.[2] All subjects were exposed to applications of both test solutions. The study was divided into 3 phases: induction, challenge and an optional re-challenge phase, which is required in case of skin reactivity during the challenge phase. Signs of dermal reactions were graded using a 6-point grading scale:

0 (none); 0.5 (barely perceptible); 1 (mild); 2 (moderate); 3 (marked) ; 4 (severe). 207 patients completed the study; three went on to complete the re-challenge phase. Efinaconazole 10% produced a patch test irritancy response of 0 (67%) or 0.5 (91.6%); the worst score of 3 was observed in four patients (1%). The vehicle solution also produced a score of 0 or 0.5 in the majority of cases (71% and 95% respectively) with a worst score of 3 in four subjects (2%). The re-challenge procedure was carried out on the three subjects; there was no evidence of induced contact sensitization under occlusive, semi-occlusive and open rub-in applications of Efinaconazole 10% solution. The reactivity observed with Efinaconazole solution was not considered evidence of induced contact sensitization. However, the skin reactivity observed with the vehicle was probably allergic in nature, under occlusive testing conditions. No severe adverse event was related to the medication; one non severe adverse event (burning sensation) possibly was.

For skin irritation, they used, the so-called *21-day cumulative irritation procedure based on* Lanman et al's work on a *single-center study of 37 adults*.[3] This is a predictive test for comparing the irritation potential of mild to moderately irritating topically applied skin care products. They evaluated the irritation potential of three concentrations of Efinaconazole solution (1%, 5% and 10%), its vehicle, and two controls, - 0.2% sodium lauryl sulfate in deionized water (w/v) as a positive control and dionized water as a negative one. The tested substances were applied on occlusive patches, which were placed on the same spot of the upper back of the subject. The spot location was randomized. Responses were assessed on the importance of the erythema, pruritus, and burning/stinging sensation of the test article and compared to the controls. A Total Cumulative Irritation Index for each subject and a Mean Cumulative Irritancy Index were calculated. Overall, 70.5% of the subjects reported no, or mild, erythema with Efinaconazole 10% solution. Scores for pruritus, burning and stinging were similar with all concentrations of Efinaconazole solution, vehicle and the negative control. All test articles showed similar responses to tape reaction.

Véronique Blatière

ONYCHOMYCOSIS

3 **Sigurgeirsson B, van Rossem K, Malahias S, Raterink K. A phase II, randomized, double-blind, placebo-controlled, parallel group, dose-ranging study to investigate the efficacy and safety of 4 dose regimens of oral albaconazole in patients with distal subungual onychomycosis. J Am Acad Dermatol. 2013 Sep;69(3):416-25. doi: 10.1016/j.jaad.2013.03.021. Epub 2013 May 22. PubMed PMID: 23706639.**

This article relates to a phase II double blind, placebo-controlled dose-ranging, multicentre, parallel group study investigating the efficacy and safety of four-dose regimens of albaconazole in a distal lateral subungual onychomychosis. Albaconazole is a broad-spectrum azole antifungal. In vitro it is effective against yeasts and a broad range of filamentous fungi and dermatophytes. It inhibits CYP3A4, so the concomitant use of albaconazole and drugs metabolized by a CYP3A4 pathway needs careful attention. Its long half-life may allow for weekly dosing. Plasma and toenail albaconazole exposure increase proportionally with dose. Albaconazole remains detectable in toenails, with a consequent mean concentration 16 to 28 weeks after the cessation of treatment.

582 patients were assigned to one of four once-weekly albaconazole capsule dose regimens: 100 mg (36 weeks), 200 mg (36 weeks), 400 mg (36 weeks), 400 mg (24 weeks + 12 weeks of placebo) or placebo 36 weeks.

The proportion of patients who reacted effectively to treatment (mycologic cure and clear /almost clear nail < 10 %of the nail plate affected) at week 52, increased with dose and was higher compared to placebo, respectively 54% (400 mg-36 W), 38% (400 mg-24 W), 39 % (200 mg-36 W), 21% (100 mg-36 W), 1% (placebo). Results for complete cure at week 52 were respectively 27%, 22%, 21%, 10%, and 1%. 71% experienced at least one adverse effect. The most frequent treatment–related, treatment-emergent adverse effects (TEAE) reported, were headache (3%), nausea (3%), diarrhea (2%), upper respiratory tract infection (2%), elevated ALT (2%) elevated creatine phosphokinase (2%).

In conclusion, and at this stage of development, albaconazole resulted in high complete cure rates. It is not possible to compare the safety profile with approved oral antifungals. A once weekly regimen is expected to improve patients' adherence.

COMMENTARY V. BLATIÈRE

Considerable progress has been made in the management **(Figs 1 & 2)** and the treatment of onychomycosis over the past decades, following the introduction of the oral antifungals terbinafine and itraconazole. Topical agents like amorolfine 5% and ciclopirox 8%, formulated as lacquers, have improved drug delivery to nails, but cure rates are lower than with systemic therapy and re-infection or relapse often occurs, as with oral antifungal therapy. The drug efficacy depends upon the vehicle, as shown in Lusiana et al. study with an infected nail plate model.[4] Efficacy also relies on host related factors, the importance of nail invasion, nail thickness…[5]

The inadequacies of the current treatments mean that there is still a need to develop new effective topical

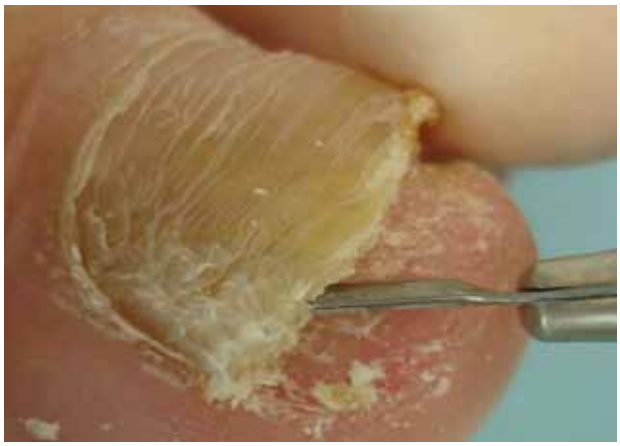


Fig1 - *Management of onychomychosis: nail sampling.*
© V. Blatière

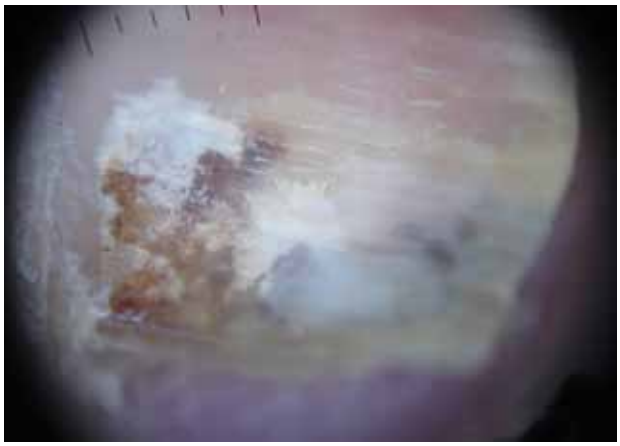


Fig2 - *Management of onychomychosis: dermoscopy.*
© V. Blatière

Véronique Blatière

ONYCHOMYCOSIS

antifungal treatment for onychomychosis, that will allow site-specific administration and minimize the systemic exposure of the therapeutic agent.
Several on-going studies are testing different products, which means that we may expect new or innovative topical reformulations and films on the market, and these should improve the management of onychomychosis in the coming years.

1-2 **Efinaconazole 10% solution** is the first triazole antifungal developed specifically for the topical treatment of distal lateral subungual onychomychosis. The Phase III study was completed recently, assessing good outcomes and could be an alternative to oral treatment options in mild to moderate onychomychosis.[1]
Because of the slow growth rate of toenails, treatment of toe onychomycosis is more challenging than finger onychomycosis and it may take up to 18 months of therapy to achieve clearance. This means that to be effective, a long-term topical treatment should be prescribed This requires good patient compliance and/or tolerance of the drug and its vehicle. The evaluation reported in Del Rosso's article showed that efinaconazole 10% solution did not cause sensitization and exhibited only minimal skin irritation.

3 **Albaconazole**, a new triazole, prevents the conversion of lanosterol to ergosterol by inhibiting fungal 14◊-demethylase, thus disrupting the formation of the fungal cell membrane. Albaconazole has demonstrated in vitro activity against a broad spectrum of species and has an interesting toxicity profile compared to other triazoles.[6]
In a Phase I study, the authors[7] compared the bioavailability and bioequivalence of albaconazole tablets with albaconazole capsules. It was shown that exposure to albaconazole and 6-hydroxyalbaconazole (its primary metabolite) after a single 400-mg dose of albaconazole, was higher with the capsule formulation than with the tablet. Albaconazole is metabolized by CYP3A4. The concomitant use of albaconazole and drugs metabolized by the CYP3A4 pathway would therefore need careful attention. In Sigurgeirsson's article, a once-weekly albaconazole capsule resulted in high complete cure rates (33% in the 400-mg 36-week group) with a good safety profile. It could be considered a potential alternative to terbinafine and itraconazole.

References

1- Elewski BE, Rich P, Pollak R, et al. Efinaconazole 10% solution in the treatment of toenail onychomycosis: two phase III multicenter, randomized, double-blind studies J Am Acad Dermatol. 2013;68:600-608.
2- Jordan WP, King sE. Delayed hypersensitivity in females. The development of allergic contact dermatitis in females during comparison of two predicative patch tests. Compare Dermatitis. 1977;3:19-23.
3- Lanman BM, Elvers WB, Howard Cs. The role of human patch testing in the product development program. Proceed Joint Conf Cosmet Sci Toilet Goods Assoc. 1968:135-145.
4- Lusiana, Reichl S, Müller-Goymann CC. Infected nail plate model made of human hair keratin for evaluating the efficacy of different topical antifungal formulations against *Trichophyton rubrum* in vitro. Eur J Pharm Biopharm. 2013 Aug;84(3):599-605.
5- Baran R and Kaoukhov A, Topical antifungal drugs for the treatment of onychomycosis: an overview of current strategies for monotherapy and combination therapy J Eur Acad Dermatol Venereol. 2005 ; 19:21-29
6- Cao X, Sun Z, Cao Y, Wang R, Cai T, Chu W, Hu W, Yang Y. Design, Synthesis and Structure-Activity Relationship Studies of Novel Fused Heterocycles-Linked Triazoles with Good Activity and Water Solubility. J Med Chem. 2014 Mar 7. [Epub ahead of print] PubMed PMID: 24564525.
7- Van Rossem K, Lowe JA. A Phase 1, randomized, open-label crossover study to evaluate the safety and pharmacokinetics of 400 mg albaconazole administered to healthy participants as a tablet formulation versus a capsule formulation. Clin Pharmacol. 2013;5:23-31.

Marie Caucanas

LASERS & ONYCHOMYCOSIS

Up to now, the US FDA laser system approval relates to the innocuity of these devices for the patient in the treatment of onychomycosis. It does not correlate with efficacy.

1 Carney C, Cantrell W, Warner J et al. Treatment of onychomycosis using a submillisecond 1064-nm neodymium:yttrium-aluminum-garnet laser. J Am Acad Dermatol. 2013; 69(4):578-82.

An Nd :YAG 1064 nm laser was used for onychomycosis treatment in this 4-part in vitro and in vivo study.

In the first part of the *in-vitro* study, the authors intended to assess the level of heat and the time required to obtain a fungicidal effect, on three different suspensions containing respectively *Trichophyton rubrum*, *Epidermophyton floccosum* and *Scytalidium dimidiatum*.

7 tubes of each species were exposed to different heat and time exposures, one was kept as control and then plated on potato dextrose agar for incubation at 30°C. Efficacy of the thermal treatment was estimated by counting the number of Colony Forming Units (CFU) growing on the dish. A fungicidal effect on *T. rubrum* and *E. floccosum* was seen at 50°C with exposure times of 15 minutes and 10 minutes respectively. S. *dimidiatum* showed only a lighter growth after 5 minutes at 55°C.

In the second part of the *in vitro* study, the authors assessed the efficacy of submillisecond 1064 nm Nd :YAG laser on *T. rubrum* fungal elements dropped onto four Petri dishes containing potato dextrose agar with four different parameters and a fifth Petri dish served as control. They were all then incubated.

In the third part of the *in vitro* study, the authors directly assessed the efficacy of the four different laser parameters on *T. rubrum* plugs of mycelium inserted in a potato dextrose agar plate. One plate was not irradiated (control). No growth inhibition was seen at each of the specified laser exposures in both the second and third phases. The temperature of the agar plate reached 40°C.

The fourth part was a 24-week *in vivo* pilot study of 10 patients (5 men, 5 women), between the ages of 19-65 years, with clinically diagnosed distal lateral subungual onychomycosis of at least one great toenail, culture-proven dermatophyte onychomycosis (9 *T. rubrum*, 1 *E. floccosum*) and at least 2 mm of healthy nail growth measured from the proximal nail fold. Subjects were treated with the same Nd :YAG laser (16 J/cm^2, 0.3 ms, 5 mm, 2.0 Hz), without local anesthesia, at weeks 0, 1, 2, 3 and 7. Assessment included: calculation of the Onychomycosis Severity Index (OSI) score, digital photographs, potassium hydroxide and mycological culture. At 24 weeks, the authors evaluated the clinical improvement as measured by healthy nail growth from the proximal nailfold, the percentage of disease involvement and the OSI score; the secondary outcome measure was mycological cure. 2 patients were not included and the remaining 8 patients showed only mild clinical improvement. None of them experienced mycological or clinical cure. Side effects were qualified as minimal, although one treatment-related onycholysis was reported.

2 Nenoff P, Grunewald S, Paasch U. Laser therapy of onychomycosis. J Dtsch Dermatol Ges. 2014; 12(1):33-8.

The authors review the *in vitro* and *in vivo* aspects of the treatment of onychomycosis with lasers.

Rationale for laser treatment:

Infrared lasers (780-3000 nm) deliver heat according to various parameters (spot size, fluence, pulse duration, repetition rate), though visualization of thermal effects showed that nail temperature only increases for a very short time after 1064 nm and 980 nm laser treatment. 405/635 nm and 870/930 nm lasers give rise to the production of Adenosine Triphosphate (ATP) and toxic levels of Reactive Oxygen Species (ROS) disrupting the mitochondrial membrane potential (MMP). Q-switched lasers (532 nm, 694 nm, 1064 nm) attempt to destroy the fungal hyphae with extremely short pulses.

***In vitro* effects:**

Irradiation with the 1064 nm long-pulsed Nd:YAG laser induced a histological dissection of the nail plate from the nail bed and electron microscopy showed shrinking, fractionation and formation of holes, thus providing evidence for the destruction of the cell walls in the hyphae of *T. rubrum*. 808 nm laser application generated coagulation due to absorption of approximately 50% of the energy. These observations indicate an *in vitro* partial efficacy of such laser devices.

***In vivo* studies:**

Clinical data suggest an improvement as shown in **Table 1**, but the very short follow-ups are the major weakness of the studies.

Marie Caucanas

LASERS & ONYCHOMYCOSIS

Table 1. *Clinical data from Nenoff et al. minireview on laser and onychomycosis.*

WM	LASER	Wavelength	Parameters	Local anesthesia	NT; interval	Results
Heat	Nd :YAG sp	1064 nm	0.65 ms 2 mm 223 J/cm^2	No	3	Initial clearing up of the nail in 87.5% within 3 weeks
Heat	Nd :YAG lp	1064 nm	40 ms, 70 J/cm^2 3 passes	Cooled ultrasonic gel	4 ; 4 weeks	Clear nail growth starting at week 16
Heat	Diode	980 nm	12 ms, 12x12mm 30 J/cm^2 3 passes	No cooling	4 ; 4 weeks	Clear nail growth starting at week 16
ROS ATP	Diode	870/930 nm			4	Considerable clinical improvement

WM = working mechanism NT = number of treatments sp = short pulse lp = long pulse

Discussion about laser therapy of nails:
The authors point out that the decisive advantage of laser therapy is the possible transungual approach allowing treatment of the nail matrix, although it remains unclear whether this latter should be treated or not. At the moment, there is no consensus on the most effective practical approach, particularly when dealing with the management of pain, the need for additional interventions or co-medication and how the patient should be warned about the potential risks and side effects. Among them, nail loss has been reported following overheating. As a result, the authors do not recommend anesthesia, thus providing the patient with an opportunity to signal an excessive rise of temperature.

3 de Morais OO, Costa IMC, Gomes CM et al. The use of the Er:YAG 2940nm laser associated with amorolfine lacquer in the treatment of onychomycosis. Anais Brasileiros de Dermatologia 2013; 88(5):847-849.

Another approach of laser treatment in onychomycosis consists in increasing the penetration of topical antifungals in the nail plate using a fractional laser. The authors compared two groups of patients with hand and foot distal lateral onychomycosis, caused by *T. rubrum* and T. mentagrophytes: one group was treated with 2940 nm Er: YAG laser and amorolfine lacquer and the other group had to apply amorolfine lacquer alone. In the laser-treated group, a single session of Er:YAG laser was performed on the damaged nail plate area with 2 to 3 mm overflowing (50 MJ/mtz, 2 ms, 1 Hz) as shown in **Fig 1a, 1b**. The authors admitted that there was a large variation in the average number of pulses delivered per nail treated, depending on pain tolerance, the variable extension of affected nail areas and the degree of subungual hyperkeratosis. Overall, patients reported mild discomfort during laser treatment. Moderate bleeding at the site of treatment was a frequent adverse effect, following damage to the nail bed by the laser. Partial results showing clinical improvement were observed. The authors concluded that nails treated with Er:YAG laser and amorolfine lacquer presented greater clearing rates than those treated with amorolfine alone.

COMMENTARY M. CAUCANAS

Data about laser and onychomycosis is spreading in the medical literature and even beyond the scientific community. Patients are informed about this new form of treatment, through fashion magazines and other media (TV, Internet...). Available approved local and oral treatments are limited. Antifungal nail lacquers have limited efficacy. Systemic antifungal agents can lead to potential serious side effects, drug interaction, compliance difficulties, significant failure rate and relapses.[1] They should not be prescribed to pregnant or breastfeeding women and are off-label indications in children. As a consequence, new laser applications have emerged, providing *in vitro* and *in vivo* studies, with varying levels of methodology.

1 Intending to objectively assess the treatment response, Carney et al.[2] are the first to use the OSI score, though the major drawback of this study is the very small number of patients treated (8) and the use of parameters that had not shown any conclusive result in the *in vitro* second and third parts. Nevertheless, the most interesting finding relies on the materialization of the resistance of

Marie Caucanas

LASERS & ONYCHOMYCOSIS

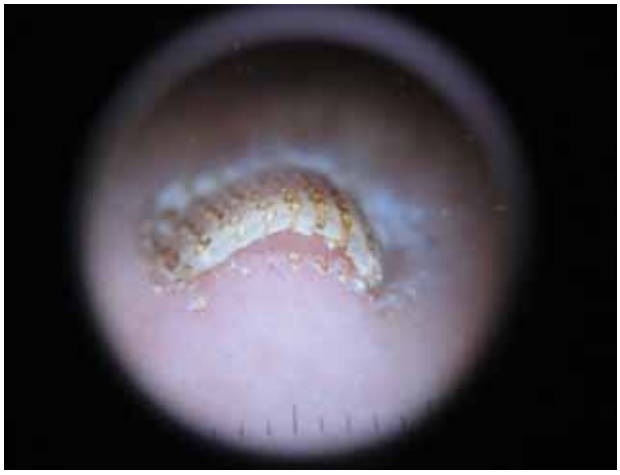


Fig1a - *Laser perforations passing through the whole thickness of the nail plate, eventually reaching the nail bed. © O. Oliveira de Morais*

Fig1b - *Clinical aspect of the nail plate after the laser session. © O. Oliveira de Morais*

dermatophytes up to 50-55°C according to the species, implying that the real dilemma is to figure out if or how it is possible to reach such a temperature within the nail plate, in terms of pain tolerance and without a risk of burning the underlying tissues. The authors suggest that mechanisms other than heat could intervene, notably the denaturation of the keratin proteins feeding the dermatophyte or through an immunologic effect in the host.

2 Indeed, heating the nail plate does not appear to be the unique working mechanism as described in the mini review from Nenoff et al.[3] Other means include the targeting of the fungal mitochondria (combined diode lasers) and the photomechanical disruption of the hyphae (q-switched).

3 de Morais et al.[4] offer a novel approach in combining fractional Er:YAG laser with the application of amorolfine lacquer. However, the results shown are incomplete, without any precise data, indicating very weak methodology.

Up to now, the Nd-YAG laser is the most studied device in onychomycosis, but the methodology and parameters used in the in vivo studies differ considerably, preventing any conclusion to be drawn from these results.[5] Many questions are still pending, the first dealing with the laser parameters themselves: the most appropriate laser and the most effective parameters limiting discomfort are still unknown. Would this treatment be efficient on any type of onychomycosis and any kind of infecting species? Other practical details include the optimal number of treatments and interval delays. Should a difference be made between toenails and fingernails which grow faster? Should we perform mechanical debridement on hyperkeratotic onychomycosis before laser treatment?[6] Potential side-effects are not well defined and even more important is if there is a risk of permanent dystrophy when treating the lunula and or/the proximal nail fold.

In conclusion, an *in vivo* laser effect on onychomycosis is not a figment of the imagination. However, as long as no randomized controlled trials emerge from this continuous cumulative data, the indication can only remain as "cosmetic" and will not attain a legitimate "therapeutic" expectation.

References

1- Gupta AK, Ryder JE, Johnson AM. Cumulative meta-analysis of systemic antifungal agents for the treatment of onychomycosis. Br J Dermatol. 2004; 150(3):537-44.
2- Carney C, Cantrell W, Warner J et al. Treatment of onychomycosis using a submillisecond 1064-nm neodymium:yttrium-aluminum-garnet laser. J Am Acad Dermatol. 2013; 69(4):578-82.
3- Nenoff P, Grunewald S, Paasch U. Laser therapy of onychomycosis. J Dtsch Dermatol Ges. 2014; 12(1):33-8.
4- de Morais OO, Costa IMC, Gomes CM et al. The use of the Er:YAG 2940nm laser associated with amorolfine lacquer in the treatment of onychomycosis. Anais Brasileiros de Dermatologia 2013; 88(5):847-849.
5- Gupta AK, Simpson FC. Medical devices for the treatment of onychomycosis. Dermatol Ther. 2012; 25(6):574-81.
6- Kalokasidis K, Onder M, Trakatelli MG, Richert B, Fritz K. The Effect of Q-Switched Nd:YAG 1064 nm/532 nm Laser in the Treatment of Onychomycosis In Vivo. Dermatol Res Pract. 2013; 2013:379725.

Bianca Maria Piraccini

ONYCHOMYCOSIS

Every year, the literature provides us with studies on new methods for diagnosing onychomycosis, suggested by dermatologists, microbiologists, dermatopathologists and even engineers! These studies propose diagnostic techniques that give results in an easier, cheaper, quicker and more sensitive way than the 'classic' KOH+ culture. Some new techniques are even performed in vivo, avoiding any invasive procedure.

1 Tsunemi Y, Takehara K, Miura Y, Nakagami G, Sanada H, Kawashima M. Screening for tinea unguium by Dermatophyte Test Strip. Br J Dermatol 2014; 170: 328-31.

The study tested the detection capacity of the Dermatophyte Test Strip in the diagnosis of onychomycosis and assessed the minimum nail sample amount required for good testing. The Dermatophyte Test Strip is an immunochromatography test that uses a monoclonal antibody that reacts with *Trichophyton* species and after 15 minutes gives a positive signal when in contact with one of these dermatophytes. It comes as a ready-to-use kit and is easy to perform.
The technique had already been tried in a small series on onychomycosis with poor results, indicated by a low specificity (58.3%).[1] In this study nail samples were tested for dermatophytes, both with the Dermatophyte Test Strip and with direct microscopy. Nail samples were homogenized and diluted, in order to determine the minimum sample required for positive testing.
The results showed 97.8% sensitivity and 78.4% specificity of the Dermatophyte Test Strip. The minimum sample amount required for good results was considerably variable and the amount of 1 mm in edge length (1 mg) was considered valid.
The Authors concluded that the Dermatophyte Test Strip has a very high negative predictive value. Therefore, if it is negative, the final diagnosis excludes onychomycosis. If, on the contrary, the Test is positive, direct microscopy is necessary, as the positive predictive value is not sufficiently high.

2 Idriss MH, Khalil A, Elston D. The diagnostic value of fungal fluorescence in onychomycosis. J Cutan Pathol 2013;40:385-90.

The study evaluated the use of a fluorescent microscope to detect fungal elements in nail clippings. The idea comes from the fact that in hematoxylin and eosin-stained specimens, fungal hyphae will fluoresce when examined under a fluorescence microscope.[2] This characteristic of fungi is known to help in the histopathological diagnosis of superficial and deep fungal infections, but has never been tested on nails.

The Authors examined nail clippings from suspected onychomycosis, stained with periodic acid-Schiff (PAS), under a fluorescent microscope; 48 of them were PAS positive and 23 were PAS negative and used as controls. Low power magnification was initially used, followed by higher power magnification, if the first view did not allow visualization of fungi. The diagnosis of onychomycosis seen by fluorescent microscope was based on the finding of tubular structures with a rim of bright green fluorescence at the periphery.
Examination with the fluorescent microscope permitted diagnosis of onychomycosis at medium power view (10X and 20X objectives) in 74% of the PAS positive specimens. In the remaining 26% of the specimens, fluorescence showed ambiguous patterns or required higher power view of multiple fields to identify the hyphae. In 2 PAS positive cases, fluorescence was not detected. Three of the PAS negative specimens showed fluorescence that could be misinterpreted as fungal elements, but in fact was due to eosin-filled clefts surrounded by parakeratotic cells. These specimens were considered false-positive.
The ease in detecting fluorescence of fungi was related to their density, while the difficulties in detecting fluorescent fungi was mainly due to the background fluorescence of keratin. Fluorescence microscopy is not able to distinguish between the different species of fungi and does not allow identification of alive or dead hyphae.

The authors concluded that the advantages of fluorescent microscopy for diagnosis of onychomycosis in nail clippings were its quick availability, compared to special stains, and the cost, which is cheaper than that of PAS stain. The disadvantages are the need for well trained personnel to examine the specimens, the difficulties in

Bianca Maria Piraccini

ONYCHOMYCOSIS

the interpretation of specimens with high background fluorescence and the lower specificity compared with PAS and other special stains.

3 Smijs TG, Jachtenberg JW, Pavel S, Bakker-Schut TC, Willemse-Erix D, de Haas ER, Sterenborg H. Detection and differentiation of causative organisms of onychomycosis in an ex vivo nail model by means of Raman spectroscopy. J Eur Acad Dermatol Venereol 2013 Nov 28. [Epub ahead of print].

The study evaluated the use of Raman spectroscopy in the diagnosis of onychomycosis, also assessing if this technique permits the identification of the causative species.
Raman spectroscopy is a vibrational spectroscopic technique that allows the investigation of the molecular composition of samples, based on molecular specificity of spectral bands in a vibration spectrum.
The Authors created ex vivo models of onychomycosis infecting human nail clippings with microconidia of several fungi, including dermatophytes, the non-dermatophyte mold *Scopulariopsis brevicaulis* and the yeast *Candida albicans*. It should be noted that one of the tested dermatophyte was *T. tonsurans*, which is an extremely rare cause of nail invasion! The different fungi gave various Raman spectra, and observation of them permitted identification of the species.
The Authors' conclusions are that *in vivo* studies will prove the possible application of Raman spectroscopy in the diagnosis of onychomycosis.

4 Villaseñor-Mora C, Vega AG, Garay-Sevilla ME, Padilla-Medina JA, Arteaga-Murillo LI. Procedure to diagnose onychomycosis through changes in emissivity on infrared images. J Biomed Opt 2013 ; 18:116005.

The Authors tested infrared (IR) image analysis as a possible method to diagnose onychomycosis *in vivo*.
All parts of the body, including the nail, emit energy through radiation. The nail radiates energy corresponding to the heat transmitted from the nail bed by conduction. The degree of energy radiated from the nail depends on 1) temperature and 2) nail plate emissivity.
1- Temperature of the feet is therefore a key factor and peripheral vascular diseases may greatly decrease nail emission of energy. Nail plate temperature is also influenced by alterations of its structure and there are several nail dystrophies that decrease it. Onycholysis, for example, impairs temperature conduction from the nail bed to the nail plate. For the same reason, the nail plate free margin radiates lower energy than the attached nail plate. A thick nail plate has poor heat conduction and therefore emits low energy.
2- Nail plate emission of energy is decreased when the nail is invaded by fungi, due to impaired radiant emissivity.
The technique utilized to measure the energy emitted by the nail plate uses an IR camera that obtains digital images of the nail and of the periungual skin in standard environmental conditions. The pixel gray levels of the different areas directly correspond to the intensity of the energy emitted. To quantify the damage of the nail, and exclude interpersonal variations due to peripheral vascular problems, it is necessary to subtract the skin value from the nail value.

The study described in the article was carried out on 141 people, who underwent IR imaging and then mycology sampling for KOH and cultures. The areas of the nails affected by onychomycosis appeared as dark areas in the IR images, suggesting the diagnosis. Moreover, nails with lower energy than the adjacent skin indicated a very high possibility of suffering from onychomycosis.
The authors concluded that IR Image study allows diagnosis of onychomycosis, as the affected nails emit less energy than non-affected nails, and that the more the nail is invaded, the less energy it emits. In contrast, nails with dystrophic changes not due to onychomycosis appear normal in the IR images (although the normal picture shown for this nail does not show any dystrophy!!). Possible confusion in interpretation of the IR images comes from long nails, where the free edge has a low temperature. Having the patient cut the nails and repeating the imaging 20 minutes later can solve the problem. Other problems may come from dystrophic nails in patients with impaired distal perfusion or from nails with onycholysis. In these cases, characterized by low energy emission of the nails,

Bianca Maria Piraccini

ONYCHOMYCOSIS

the Authors suggest adding the data obtained from clinical examination of the nails to the results of IR imaging. Another problem of the technique comes from the fact that the evaluation of the degree of energy emission is completely subjective.

COMMENTARY BM PIRACCINI

The way in which I evaluate new testing procedures is mainly based on the needs of a clinician, who encounters a patient with a nail dystrophy of possible mycotic origin. The best technique would be the one that allows immediate confirmation of the clinical diagnosis in a cheap and quick manner! In fact a technique that then permits us to identify if the fungus that is invading the nail is a dermatophyte, a non-dermatophyte mold or a yeast would really be the best.

Identification of the responsible agent might not be necessary in mild cases of distal subungual onychomycosis, where treatment is based on topical agents. In these cases, a technique that confirms the mycotic origin of the onychodystrophy is more than enough. Mild cases of distal subungual onychomycosis **(Fig 1a)**, should be differentiated from traumatic onycholysis **(Fig 2a)**, which is indeed much more common! Dermoscopy can be helpful in these cases, as in onychomycosis it shows a typical fringed proximal margin **(Fig 1b)**, while in traumatic onycholysis it shows a linear proximal rim of the detachment **(Fig 2b)**.[3] I always advise removal of the onycholytic nail plate in order to speed up the cure of onychomycosis, and keep the material for mycology, but I must admit that female patients often do not want their nail cut, especially before summer!

Mycology with identification of the responsible agent is, on the other hand, mandatory in patients with a suspected onychomycosis with diffuse nail involvement **(Fig 3)**, where the choice of therapy depends on the results of culture. In general, non-dermatophyte molds do not respond to systemic antifungals and in these types of onychomycosis the best choice is topical therapy, associated with periodic removal of the affected nail plate. If the onychomycosis is caused by *Candida* sp., the drug of choice should not be terbinafine, as the yeast is not sensitive to it. Moreover, the isolation of *Candida* from a nail should always suggest a careful evaluation of the patient, as *Candida* onychomycosis is frequently associated with diabetes or immunodepression.

"Classical" mycology, with KOH and culture cannot always be performed, as it requires availability of a mycology laboratory, 1-2 months to receive the results, and a clinician who finally has to associate the mycological outcome with the nail symptoms. However, KOH and culture still remain the gold standard for the best management of onychomycosis. Histopathology of nail clippings with PAS stain is definitely easier, as histopathology laboratories are more numerous than mycology labs! The finding that sensitivity of PAS stain is maintained when using subungual debris and not the nail plate, makes this technique easier to perform, even by laboratories that are not used to processing nail specimens.[4]

2 The article by Idriss and colleagues suggests the use of fluorescent microscopy as a possible alternative to PAS stain, due to its lower cost. Although fluorescent microscopy requires training and experience, in order to have observers able to rapidly discriminate false positive from true fungal fluorescence, I think that this technique is very interesting and should be considered as a possible alternative to special stains.

3 In one of the other papers that I reviewed, Smijis and colleagues tested the possible use of Raman spectroscopy for diagnosis of onychomycosis. They showed only preliminary results, as the study was performed on nail clippings infected by fungi *in vitro*. It is therefore not clear if and how Raman spectroscopy can be applied *in vivo*. Will the procedure be carried out directly on the patient or on nail clippings? There are no details concerning cost and availability of the instrument, duration and easiness of the procedure and its possible application as a routine diagnostic procedure for onychomycosis.

4 Infrared (IR) image analysis has been applied in nails *in vivo* by Villaseñor-Mora and colleagues, who have come to the conclusion that IR image analysis allows diagnosis of onychomycosis and permits evaluation of the severity of invasion. I am personally quite skeptical about the specificity of the technique, as all the conditions that should be clinically differentiated by onychomycosis are among those that reduce nail emission of energy! Differential diagnosis of distal subungual onychomycosis includes in fact traumatic onycholysis, where nail emission of energy is reduced, due to the impaired temperature conduction from the nail bed to the detached nail plate,

Bianca Maria Piraccini

ONYCHOMYCOSIS

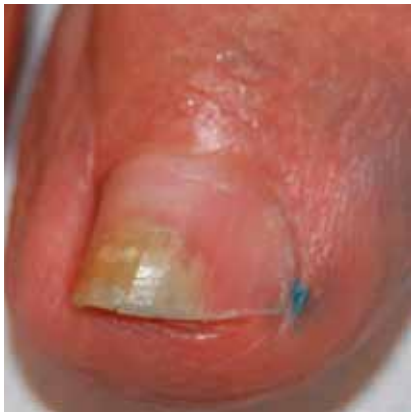


Fig1a - *Distal subungual onychomycosis due to T. rubrum of the great toenail, producing mild lateral onycholysis and subungual hyperkeratosis. © B-M. Piraccini*

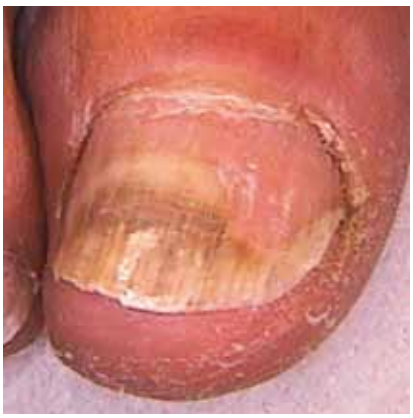


Fig2a - *Traumatic onycholysis of the great toenail: nail detachment is more marked on the lateral side. © B-M. Piraccini*

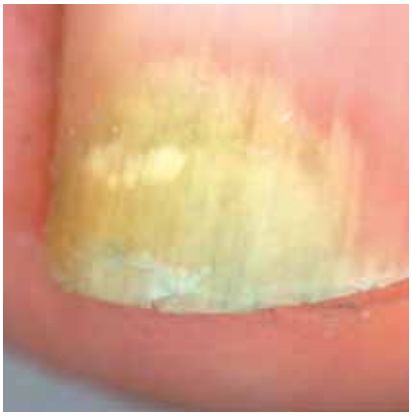


Fig1b - *Dermoscopy of figure 1a, showing a fringed (jagged) margin of the onycholysis suggesting onychomycosis. © B-M. Piraccini*

Fig2b - *Dermoscopy of figure 2a, showing a typical linear margin of the onycholysis suggesting a traumatic cause. © B-M. Piraccini*

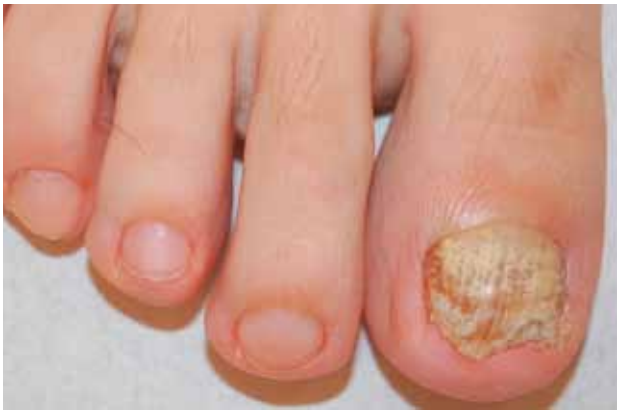


Fig3 - *Massive thickening and discoloration of the great toenail. Mycology with detection of the causative fungus is necessary to decide the best treatment option. © B-M. Piraccini*

Bianca Maria Piraccini

ONYCHOMYCOSIS

and onychogryphosis - or other forms of nail thickening -, where the thickened nail plate has poor heat conduction and therefore emits low energy. Moreover, the technique does not seem to be quick and easy to perform: the patient must wait for 20 minutes, with feet uncovered, to avoid the influence of shoes and conditions of arrival; the temperature of the examination room must be kept at around 20°C; the nail that has to be examined should be free of any kind of ointment, body lotion or any other substance and well trimmed... How many of our patients would be willing and ready to have such an examination performed?

1 The tool that I personally like very much is the Dermatophyte Test Strip, which is very quick, easy to perform and inexpensive. The test has a highly sensitive and negative predictive value, so it can be used to rule out onychomycosis in all doubtful cases.

A wide use of the test by general practitioners and dermatologists would considerably decrease the number of wrong diagnoses of onychomycosis and incorrect prescriptions of antifungals. In fact, a great number of doctors tend to consider all nail dystrophies characterized by onycholysis and/or nail thickening as onychomycosis, without carrying out any kind of mycological examination. This leads to poor treatment outcome and considerable patient disappointment and also to a great waste of private or public money.

If doctors could be provided with an easy and quick tool that allowed them to exclude the diagnosis of onychomycosis, they would no doubt examine dystrophic nails differently and be able to make more precise diagnoses.

References

1- Higashi Y, Miyoshi H, Takeda K, et al. Evaluation of a newly-developed immunochromatography strip test for diagnosing dermatophytosis. Int J Dermatol 2012; 51: 406–9.
2- Rao S, Rajkumar A, Ehtesham M, Prathiba D. Autofluorescence: a screening test for mycotic infection in tissues. Indian J Pathol Microbiol. 2008; 51(2): 215-7.
3- Piraccini BM, Balestri R, Starace M, Rech G. Nail digital dermoscopy (onychoscopy) in the diagnosis of onychomycosis. J Eur Acad Dermatol Venereol. 2013; 27(4): 509-13.
4- Nagar R, Nayak CS, Deshpande S, Gadkari RP, Shastri J. Subungual hyperkeratosis nail biopsy: a better diagnostic tool for onychomycosis. Indian J Dermatol Venereol Leprol. 2012; 78: 620-4.

Robert Baran

AUTO-IMMUNE DISEASES

1 Clinical study of nail changes in vitiligo. Anbar T, Hay RA, Abdel-Rahman AT et al. J Cosm Dermatol. 2013; 12: 67-72.

Vitiligo is an acquired dyschromia of the skin in which there is a loss of epidermal melanocytes. The prevalence of vitiligo is approximately 0.1-2% world-wide.
Previous studies suggested that the pathogenetic mechanisms of vitiligo could be a systemic event, as vitiligo is associated with other autoimmune disorders, particularly Hashimoto thyroiditis, Graves disease, alopecia areata (AA), and autoimmune polyglandular syndrome.
Nail pitting is the commonest nail abnormality associated with AA. Trachyonychia, onychorrhexis, punctuate leukonychia, spotting of the lunula, onycholysis, and onychomadesis are other reported nail changes. It has been proposed that the nails are targeted by the same type of inflammatory cells that target hair follicles in AA. As vitiligo and AA are commonly associated, the authors hypothesized that nail changes can be found in vitiligo patients. On revising the literature, only two types of nail changes were described in association with vitiligo, nail dystrophy and red lunula. A common autoimmune insult to the nail matrix and melanocytes was proposed as the possible cause of this correlation.
The aim of this work was to study the frequency and types of nail changes among patients with vitiligo in comparison with nail changes in normal healthy volunteers.

2 Dermatoscopy of nail lichen planus. Nakamura R, Abrego Broce AA, Cantillo Palencia DP et al. Int J Dermatol. 2013; 52:684-87.

Nail lichen planus affects 10% of all patients with lichen planus. It was therefore interesting to examine these cases with dermatoscopy.
Dermatoscopic photographic data of 11 patients having 79 nails affected with nail lichen planus, seen in a specialized nail disease facility, were selected and analysed. The data was confirmed with histopathological analysis.

Dermatoscopy showed abnormalities of the nail matrix, with trachyonychia in 40.51% and pitting in 34.18%. Concerning nail bed anomalies, there was chromonychia in 55.70%, fragmentation of the body of the nail in 50.63%, splinter haemorrhage in 35.44%, onycholysis in 27.85%, and subungual keratosis in 7.59%. Concerning anomalies that involved the nail matrix, bed, and the perionychia region together, there were longitudinal streaks in 82.28% and anonychia in 1.27%. Paronychia was present in 31.55% of the cases.

3 Nail trichrome vitiligo: case report and literature review. Di Chiacchio NG, Ferreira FR, De Alvarenga ML, Baran R. Br J Dermatol. 2013; 168:668-69.

A 10-year-old boy, phototype V, presented with a 6-month history of a dark macula on his second right toenail. The patient had been under treatment for vitiligo for the previous 3 years with topical and systemic corticosteroids and phototherapy (ultraviolet B narrowband radiation). The lesions on the skin fluctuated with periods of improvement and deterioration. During the last four months only topical steroids had been used. During the last month of treatment the pigmentation changed and light brown patches appeared, intermixed with areas of a deeper brown colour and associated with deterioration in the skin lesions. On examination there was a light brown macula surrounding a darker brown macula on the second right toenail. The proximal nail fold presented achromic areas alternating with a dark-brown pigmentation.
Dermoscopic examination showed an achromatic macula surrounded by normal skin on the medial part of the proximal nail fold **(Fig 1)**. The lateral nail folds and periungual tissues did not show any abnormal pigmentation. The distal portion of the medial side of the nail plate showed a pigmentation that was subdivided into two different bands: a light-brown band and a more usual darker-brown band. The remaining part of the nail plate had no abnormal pigmentation. Onycholysis was observed in the distal medial part of the nail plate. Histopathological examination by haematoxylin and eosin and periodic acid schiff stains did not show blood or fungi. In the Ziehl-Neelsen stain melamine was highlighted. After a thorough clinical history and dermatological, dermoscopic and histopathological examination, the diagnosis was trichrome vitiligo. Three months later, a regression of the light-brown and darker-brown band beneath the nail plate was observed and an achromic area appeared in its place **(Fig 2)**.

Robert Baran

AUTO-IMMUNE DISEASES

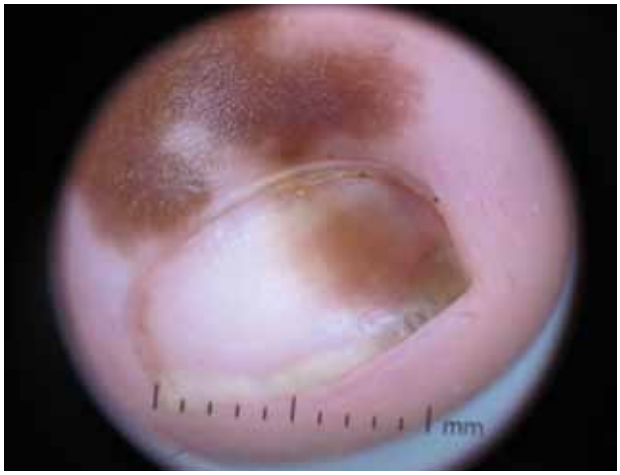


Fig1- *Dermoscopy examination: achromic macula surrounded by normal skin on the medial part of the proximal nail fold. © R. Baran*

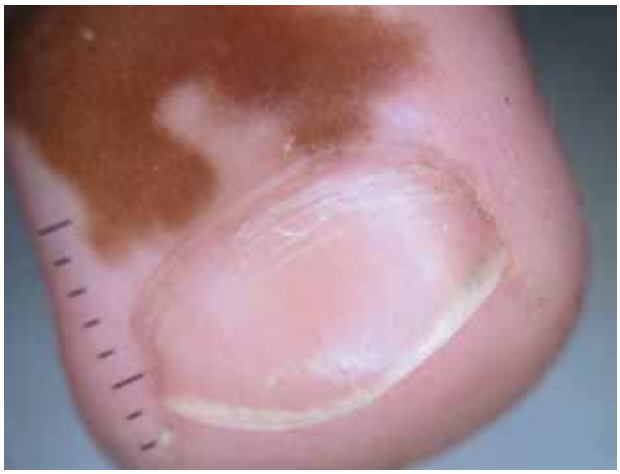


Fig2- *Dermoscopy examination: a regression of the light-brown and brown band beneath the nail plate producing an achromic area. © R. Baran*

COMMENTARY R. BARAN

1 A few previous case reports were concerned with the association between vitiligo and nail changes, such as twenty nail dystrophy (TND), red lunula and onychodystrophy.

The most common and significant nail abnormality in vitiligo patients was the longitudinal striations, which were seen in 40 patients.

The second significant (p=0.037) observation in the current study was absent lunula, which was seen in 15 patients (16.5%) and six controls (6.6%). Although the lunula is not often visible on all fingers and toes, it is most consistently observed on the thumb, the index finger, and the great toe.

Another reported nail abnormality in the current study was punctate leukonychia, this was seen in the study in 18 patients (19.8%).

Pitting was seen in 9.9% of the patient group and was found in 3.3% of the control group.

Alkiewicz and Pfister[1] thought that the pitting of AA had a different pathological appearance. The suggestion by Dotz[2] et al on the similarity of pitting in psoriasis and AA is questionable. This could explain their disagreement with Alkiewicz and Pfister, who did not find parakeratotic cells in cases of AA with pitted nails.

In the current study, three patients showed AA in association with vitiligo and two of them had nail changes (one had leukonychia and the other had longitudinal ridging).

2 Considering that nail lichen planus is an underdiagnosed disease with severe consequences, early diagnosis is essential. This descriptive study of dermatoscopic characteristics of nail lichen planus highlights some key changes in the course of the disease, which will contribute to early diagnostic suspicion, early treatment, and could improve prognosis.

Nail abnormalities	Total	%
Nails, *n*	79	
Nail matrix, *n*		
Pitting		34.18
Trachyonychia		40.51
Red lunulae		3.80
Dorsal pterygium		21.52
Nail bed, *n*		
Onycholysis		27.85
Subungual keratosis		7.59
Chromonychia		55.70
Splinter haemorrhage		35.44
Nail plate fragmentation		50.63
Matrix and nail bed, *n*		
Longitudinal red streaks		82.28
Anonychia		1.27
Paronychium, *n*		
Paronychia		31.65

Robert Baran

3 The clinical classification of vitiligo can be presented as localized (focal, segmental, mucosal), generalized (vulgaris, acrofacial, mixed) or universal.[3] Clinical variants are known in vitiligo, such as vitiligo ponctué, trichrome vitiligo, quadrichrome vitiligo, pentachrome vitiligo and the isomorphic Koebner phenomenon. The term trichrome vitiligo was first suggested in 1964 by Fitzpatrick. The lesions have an intermediate zone of hypochromia located between the achromic centre and the peripheral unaffected skin. This results in three shades of colour – brown, tan and white – in the same patient. The trichrome lesion evolves naturally to a typical vitiligo macula.

No citations of trichrome vitiligo of the nail unit were found in the literature, but this does not mean that it does not occur.

References

1- Alkiewicz J, Pfister R. Atlas der Nagelkrankheiten. Schattauer Verlag, 1976.

2- Dotz WI, Lieber CD, Vogt PJ. Leukonychia punctata and pitted nails in alopecia areata. Arch Dermatol. 1985; 121:1452-4.

3- Ortonne JP. Vitiligo and other disorders of hypopigmentations. In: Dermatology (Bologna JL,Jorrizzo JL, Rapini RP eds) 2nd edn. St Louis MO; Elsevier, 2008; 913

Olivier Cogrel

TUMOURS & NAIL SURGERY

1 Jellinek NJ, Cordova KB. Frozen sections for nail surgery: avulsion is unnecessary. DermatolSurg 2013; 39 :315-316.

Mohs micrographic surgery (MMS) has been proposed for malignant tumors of the nail unit, especially for squamous cell carcinoma (SCC).[1, 2, 3] Indeed, it is usual in routine to perform nail plate avulsion before surgical removal of nail unit tumors, especially because the nail plate can be difficult to cut. However, nail bed superficial epithelium is sometimes missing in histologic specimens and complete analysis of the whole epithelium is therefore impossible. In fact the authors propose to perform an "en bloc" excision, as is done for lateral longitudinal nail biopsy. The nail plate is softened beforehand by soaking the digit in a mixture of warm water and an antiseptic solution for at least 15 minutes. The tissue is laid flush, so that the plate and attached bed and matrix epithelium are mounted en face. The tissue is mounted directly on a frozen stainless steel chuck. Once frozen, the tissue is cut at a typical thickness (3-5 µm) and stained in standard fashion.
This technique preserves the superficial epithelial layers of the nail bed or nail matrix and allows an entire surgical margin examination of histologic specimens and is more precise than the one traditionally used.

2 Turkmen I, Alpan B, Soylemez S, UnluOzkan F, Unay K, Ozkan K. OsteoidOsteoma of the Great Toe Mimicking Osteomyelitis: A Case Report and Review of the Literature. Case rep Orthoped. 2013; ID 234048. Andalib A, Sajadie-Khajouei. Osteoidosteoma of distal phalanx: a rare disorder and review of literature. J Res Med Sci. Mar 2013; 18: 264–266.

Osteoidosteoma is a relatively frequent benign bone tumor mostly occurring in the 2nd and 3rd decade of life, accounting for about 11% of all benign bone tumors. The most common location is in the long bones of lower limbs (especially femur and tibia), where it occurs in 50% of the cases.

The first case report was a 23-year-old male patient who had previously undergone surgery for an ingrown toe nail and had undergone a second operation due to intractable pain, which was mostly assumed to be caused by osteomyelitis and yet was found to be related to osteoidosteoma in a pathological examination in the distal phalanx of the toe.

The second case report was a 27-year-old man who presented a 4 year history of gradual increase in size and deformity of the distal part of his left middle finger which clinically looked like an isolated clubbed digit. Pain was a marked feature that disabled his life and was only relieved temporarily by analgesics and was aggravated at night. Radiographs revealed soft tissue edema on the volar and dorsal side of the finger. An oval shaped sclerotic mass in the base of the volar aspect of the distal phalanx with tinny radiolucent border was seen. Based on clinical and radiographic findings, the presumptive diagnosis of osteoidosteoma was made. En bloc excision and bone curettage was performed and histological examination confirmed the diagnosis of osteoidosteoma, since the typical nidus was found in the histological specimen.
Osteoidosteoma is a small tumor usually measuring less than 1,5 cm, composed of a central zone named nidus, which is an atypical bone completely enclosed within a well-vascularized stroma. Prostaglandins are found in the nidus at levels 100 to 1 000 times that of normal tissue. They induce vasodilation and the resultant increased capillary permeability in the surrounding tissues are believed to mediate tumor related pain, classically

Olivier Cogrel

TUMOURS & NAIL SURGERY

described as night pains relieved by salicylates. These lesions are rare in the distal phalanx, but when they do appear, they present unusual diagnostic difficulties due to:

1- Atypical radiological appearance: radiographs most commonly demonstrate a lytic lesion rather than the classic appearance of reactive sclerosis surrounding a central lucent nidus. CT scan is of considerable value when there is no evidence on plain films to localize the nidus of osteoidosteoma
2- Presence of soft tissue enlargement and nail deformity (clubbing)
3- The small size of the distal phalanx and consequent close approximation of lesions to the nail, growth plate and distal interphalangeal joint.

Histopathological examination of osteoidosteomas demonstrates variably mineralized fine trabeculae of woven bone inside a central nidus. The caliber of trabeculae may vary. Benign osteoblastic border cells and multinucleated osteoclast-like giant cells are seen, dispersed in a fibrovascular stroma. Outside the nidus, fibrovascular tissue is surrounded by sclerotic lamellar bone.

Pain and swelling in the distal phalanx of the great toe may be attributed to a wide spectrum of diseases, such as benign and malignant bone neoplasms, cellulitis, and osteomyelitis. The literature describes etiologic factors causing enlargement of toes as intraosseous epidermoid inclusion cysts, pseudomonas osteomyelitis, subungual squamous cell carcinoma and subungueal keratoacanthoma, macrodystrophia lipomatosa, chondrosarcoma, fibrolipoma and osteoidosteoma.

COMMENTARY O. COGREL

1 The publication from Jellinek and Cordova raises several questions for me:

A- Is nail plate avulsion necessary before nail bed or nail matrix surgery?
B- Is it necessary to perform frozen sections or modified Mohs' Micrographic Surgery (MMS) with rush paraffin sections? What kind of sections (vertical or horizontal) are appropriate in this location?
C- And finally a crucial and provocative question for the Mohs' surgeon that I am: is MMS really the best option for malignant tumors of the nail apparatus?

A- Is nail plate avulsion necessary before nail bed or nail matrix surgery?

It is possible to perform surgery, while the nail plate is still in place. When the plate is thin, atrophic or dystrophic, which is actually frequent regarding *in situ* squamous cell carcinoma of fingernails, cutting the plate and the underlying tissues is quite easy and softening, which is useful when the nail plate is very thick or hyperplasic, is unnecessary. The advantage of maintaining the nail plate, is that it is possible to see what is going on in the upper part of the epidermis. This is the reason why lateral longitudinal excision is performed to achieve a diagnosis, particularly for inflammatory nail disease. I do agree with Jellinek and en bloc lateral longitudinal excision-biopsy for very lateral (invasive or *in situ*) tumors of the nail apparatus **(Fig 1)** is possible (in our experience, we usually prefer to take a punch biopsy to confirm the diagnosis before performing a larger excision). Horizontal sections from the bottom to the top of the histologic specimen give the opportunity, not only to diagnose carcinoma, but also to see the entire margins. However, very limited and lateral tumors remain exceptional and the authors did not experiment such excisions on the medial part of the nail unit, which would probably be the hardest. They did not say if margin involvement was noted histologically after excision and if another excisional stage had to be taken.[4] I am personally convinced that a clear exploration of the nail matrix or the nail bed after partial avulsion is preferable, in order to determine the clear limits of malignant tumors and to perform a very selective excision.

Fig1 - *Lateral invasive squamous cell carcinoma. © O. Cogrel*

Olivier Cogrel

TUMOURS & NAIL SURGERY

B- Is it necessary to perform frozen sections or modified MMS with rush paraffin sections? What kinds of sections (vertical or horizontal) are more appropriate in this situation?

In our experience, frozen sections are very time-consuming for the pathologist and the dermatologist, and they are performed only for infiltrative tumors or when a complex reconstructive procedure is planned. This is not really appropriate for nail surgery (healing by secondary intention, primary closure, advancement flap that does not modify the anatomy). Therefore, for limited SCC we propose a modified MMS with a three dimensional approach and rush paraffin vertical sections of the margins and vertical sections on debulking **(Fig 2 & 3)**.

C- Is mohs micrographic surgery really the best option for malignant tumors of the nail apparatus particularly for SCC?

Currently, no standardized approach to therapy for SCC has been established. Some authors have considered MMS as a gold standard for achieving high cure rates and sparing uninvolved skin, but no comparative trial has been published.[1, 2, 3] Three major features must be pointed out to propose optimal treatment: extent and localization of the SCC (medial or lateral part), depth of the SCC and the presence of Human Papillomavirus. In case of bone infiltration, digit amputation is the reference treatment. For limited lateral tumors, MMS is an option and we do recommend modified MMS with

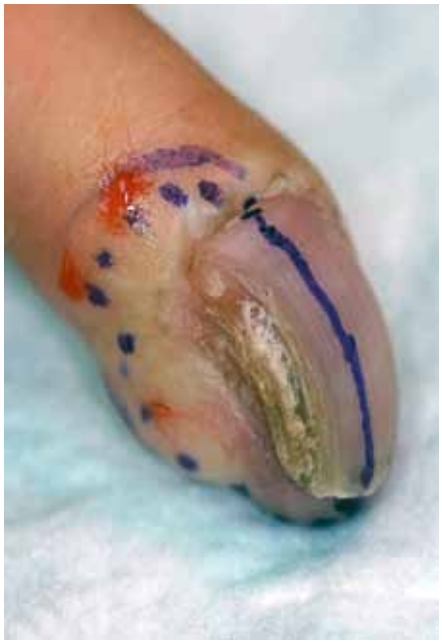


Fig2 - *Modified MMS. © O. Cogrel*

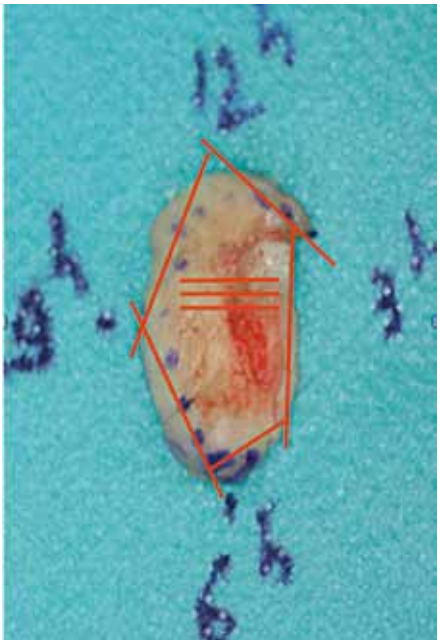


Fig3 - *Modified MMS. © O. Cogrel*

Olivier Cogrel

TUMOURS & NAIL SURGERY

en face sections. For larger tumors **(Fig 4a, b, c)**, MMS becomes very challenging as it is difficult to obtain good horizontal sections providing an accurate evaluation of the depth of the tumor. Moreover, complete extirpation of SCC cannot ensure the elimination of HPV from the area of the tumor or its surroundings. Conservation of a small part of the nail or a dystrophic nail is often found to be a poor benefit. When the SCC involves more than 50% of the nail unit, complete avulsion of the whole nail apparatus is actually the treatment of choice.[5] For very limited medial tumors, combining tangential excision followed by imiquimod or photodynamic therapy, would probably be a good option. For melanocytic lesions, there is no indication for micrographic surgery.

References:
1- Lecerf P, Richert B, Theunis A, André A. A retrospective study of squamous cell carcinoma of the nail unit diagnosed in a Belgian general hospital over a 15-year period. J Am AcadDermatol 2013; 69:253-61.
2- Dika E, Piraccini BM, Balestri R, Vaccari S, Misciali C, Patrizi A, Fanti PA. Mohs surgery for squamous cell carcinoma of the nail: report of 15 cases. Our experience and a long-term follow-up. Br J Dermatol 2012; 167: 1310-1314.
3- YoungLC, Tuxen AJ, Goodman G. Mohs' micrographic surgery as treatment for squamous dysplasia of the nail unit. Austr J Dermatol 2012; 55: 123-127.
4- Joseph AK. Commentary: nail avulsion before nail surgery: is it always necessary? DermatolSurg2013 ; 39:315-6.
5- Dalle S, Depape L, Phan A, Balme B, Ronger-Savle S, Thomas L. Squamous cell carcinoma of the nail apparatus: clinicopathological study of 35 cases. Br J Dermatol2007;156: 871-874.

2-3 The two recent case reports of subungual osteoid osteoma emphasize that this bone tumor has to be well known by dermatologists even if lesions arising in the distal phalanx are unusual.

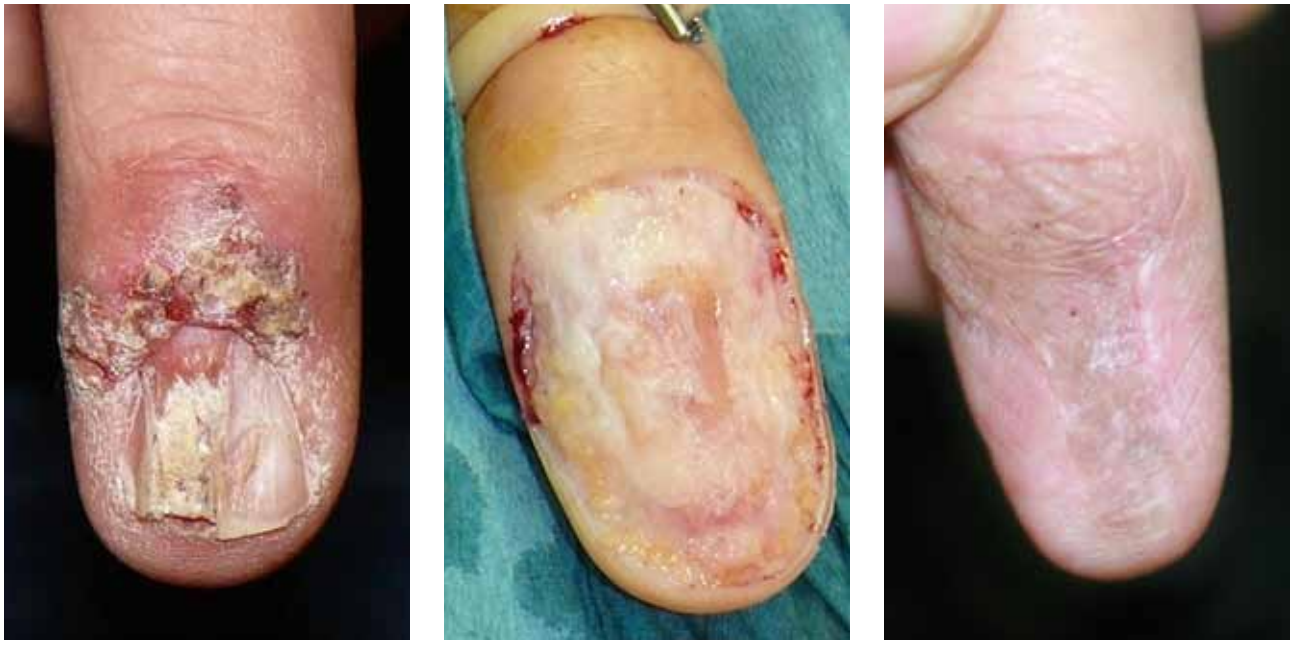


Fig4a, b, c - *Avulsion of the whole nail apparatus for in situ SCC (before, during and after). © O. Cogrel*

Eckart Haneke

TUMOURS & NAIL SURGERY

1 Richert B, Theunis A, Norrenberg S, André J. Tangential excision of pigmented nail matrix lesions responsible for longitudinal melanonychia: Evaluation of the technique on a series of 30 patients. J Am Acad Dermatol 2013;69:96-104

Thirty longitudinal melanonychias were treated with Haneke's tangential matrix excisional biopsy technique. 20 patients were female and 22 streaks were located on fingers. Half of the patients had a band wider than 6 mm, 2 had a total melanonychia. The tangential excision of the melanocyte focus of the matrix was performed after retraction or reflection of the proximal nail fold and partial detachment of the proximal third of the nail plate over the lesion. A shallow incision around the lesion with a 1 – 2 mm margin was performed, and the lesion then horizontally removed with saw-like back-and-forth movements of a Teflon-coated #15 scalpel. The thin tissue slice was placed between filter paper and cardboard stapled together and fixed in formalin. Sections were made for histopathology and stained with H&E, Fontana, MelanA and HMB45. It was possible to make a diagnosis in all the cases. Diagnoses were melanocyte activation (n=10), lentigo (n=4), nævi (n=10: 8 junctional, 1 compound, 1 blue), intraepithelial atypical melanocyte proliferation (n=2), in situ melanoma (n=3), and invasive melanoma with Breslow index of 0,16 mm (n=1). The 4 melanomas and one atypical melanocyte proliferation were treated with complete ablation of the nail apparatus. Of all the cases, 23 were left for postoperative evaluation of the tangential biopsy result: 17 had no postoperative nail dystrophy, 1 had discrete, 4 had moderate and 3 had severe dystrophy. However, 16 patients developed recurrence of pigmentation 8 to 12 months after tangential excision. If there was re-excision, it was successful with other horizontal excisions.

Ungual melanomas often have a poor prognosis due to a late diagnosis. An early correct diagnosis, which is possible with the tangential biopsy technique, would prevent thick tumours and fatal cases.

2 Neczyporenko F, André J, K. Torosian K, Theunis A, Richert B. Management of in situ melanoma of the nail apparatus with functional surgery: report of 11 cases and review of the literature. J Eur Acad Dermatol Venereol 2014, EPub ahead of publication

Melanomas of the nail are said to be rare and have a poor prognosis, due to late diagnosis and treatment. Diagnosis of early ungual melanoma is assumed to be difficult. Few cases of in situ melanoma of the nail have been described. Pigmented in situ melanoma usually starts in the matrix, whereas nail bed melanoma may cause a lichen planus like aspect of the nail without pigmentation. The brown band very slowly enlarges and periungual pigmentation may occur, a situation that often exists for years or even decades before an invasive melanoma develops, which is again proof of year-long neglect of the brown nail. A longitudinal melanonychia is not easy to diagnose clinically in young people, even though dermatoscopy of the nail plate and matrix during surgery, as well as confocal reflectance microscopy, may be of help. Early subungual melanoma is also difficult to diagnose histologically, as it often requires immunostains.

The authors present their experience with functional surgery in 11 patients with in situ and early invasive nail melanoma seen and operated over a period of 13 years. There were 8 women and 3 men. The mean age was 48 years with a range from 30 to 66 years. Two thirds were localized on fingers, of which 4 were on the thumb. Eight patients had skin type II, three had type III. One patient reported a previous trauma and one had a family history of melanoma. Nine patients presented with a longitudinal melanonychia of variable colour intensity and with blurred borders, one had a total melanonychia. The width was from 1.5 to 7 mm. One patient had a Hutchinson sign and two a micro-Hutchinson sign. The mean diagnostic delay was 5 years, but the longest was 20 years. In the 8 cases where dermatoscopy was performed, it was suspicious. Punch (3), tangential (5) and lateral longitudinal (1) biopsies were performed, prior to definitive surgery, with total ablation of the entire nail apparatus, and including a 6 mm safety margin. A full thickness skin graft was used in 6 patients, 5 wounds were left for second intention healing.
An acral lentiginous melanoma was diagnosed in eight

Eckart Haneke

TUMOURS & NAIL SURGERY

cases, and in three, the diagnosis of atypical melanocytic proliferation, with possible in situ melanoma, was made. In two cases local recurrence was observed after 7 and 11 years. It was invasive and treated by distal phalanx amputation and sentinel lymph node excision, which did not reveal metastases.

Up to now there have been four series of subungual in situ melanomas, for a total of 29 cases. Thumbs and big toes were most commonly affected. Women were more often affected. Although a width of > 6 mm was typically seen, this was not always the case. One patient with a melanonychia only 3 mm wide had a microHutchinson, a history of sudden widening and a positive family history of melanoma. One patient had an amelanotic in situ melanoma.

3 Lecerf P, Richert B, Theunis A, André J. A retrospective study of squamous cell carcinoma of the nail unit diagnosed in a Belgian general hospital over a 15-year period. J Am Acad Dermatol 2013;69:253-261

Squamous cell carcinoma (SCC), also called epidermoid carcinoma, of the nail is the most frequent malignant nail tumour. Since 1850, about 200 cases have been reported. From 1995 to 2011, 58 patients with probable SCC of the nail unit were seen. Fifty-one patients, of which 72% were men, met the criteria for evaluation and were included in the study. Two patients had 2 ungual SCCs and one patient had 3. Except for one SCC, all other carcinomas were localized on fingers, 62% on the right hand. The nail bed was most frequently involved, followed by the periungual region. Almost two thirds were in situ, 32% were invasive with a maximum thickness of 8 mm. The delay until diagnosis was over 6 years. The clinical diagnosis was only rarely suspected by general physicians and other non-dermatologists and the initial diagnosis was always a wart. Subungual hyperkeratosis, onycholysis, oozing, and nail plate destruction were the most common signs. An X-ray showed bone erosion in 1 of the 14 cases examined. The treatment comprised surgical excision, amputation, photodynamic therapy, curettage with or without fluorouracil 5% or imiquimod 5% cream, and bleopuncture with imiquimod cream. Surgical therapy was either partial ablation of the nail unit, en block ablation of the nail unit with 6-mm margins, amputation, and limited excision with full orientation of the specimen and evaluation of the lateral and deep margins to obtain clear margins. Follow-up data of 38 patients were available with an average time of 40 months (range: 4-177 months). The mean recurrence rate for all techniques was 30.6%, with 28.57% for lateral and deep margins to obtain clear margins. No patient died from the disease.

This largest study on nail carcinoma has shown thus far that the diagnosis is usually delayed for many years, but that the prognosis is still good. Risk factors are trauma, arsenic ingestion, ionizing radiation, and particularly high-risk human papillomaviruses. In this study, the right index and middle fingers were most frequently involved, which is in agreement with a genito-digital transmission of HPV, but different from other studies. Metastases are rare, although progression to an invasive tumour is frequently seen. However, the recurrence rate is relatively high, with 28.5% for local surgery. This may be due to the aetiology of HPV that are not completely eradicated with surgery.

4 Abbade LP, Silva F, Guiotoku MM, Miot HA. Banana: a new simulation model to teach surgical techniques for treating ingrown toenails. Dermatol Surg 2013;39:1274-1276

Clinicians' attention continues to be drawn to ingrown toenails. More than a hundred different techniques have been described in the literature and new ones are forever being invented. These authors devised a model to train young staff in the surgical treatment of ingrown toenails, using a banana as a model. They show the digital block and tourniquet, how to partially avulse the nail plate and finally a wedge excision, correlating the banana and a real big toe.

Eckart Haneke

TUMOURS & NAIL SURGERY

COMMENTARY E. HANEKE

1 After our first description of an excisional tangential matrix biopsy in 1999, many dermatological surgeons adopted this procedure for the diagnosis of longitudinal melanonychias, mostly with very good results. Depending on the localization of the excision within the matrix, perfect restitution of the nail or only a slight nail dystrophy is the rule. A pterygium was possible when both the apical matrix and the most proximal portion of the overlying proximal nail fold had to be excised. Even with insertion of a silicone sheet between the shallow defects of the matrix and eponychium, these may heal together before new matrix epithelium can re-form. The reviewer cannot confirm the relatively high percentage of pigment recurrence. As shown in the Fig 2 and 3 of their article, the authors have oriented their biopsy rather transversely **(Figs 1a, 1b,1c)**, whereas the long axis of our biopsies is usually longitudinal as the lesions are also oval, stretching more from proximal to distal than lateral to medial.

2 An acquired longitudinal melanonychia in a fair-skinned adult Caucasian has to be considered as a melanoma. Treatment with ablation of the nail apparatus with a 6 mm safety margin around the nail unit, has a very good prognosis in subungual *in situ* melanomas, as was shown for the first time in 1978 and confirmed in a large series 25 years later in 2003.

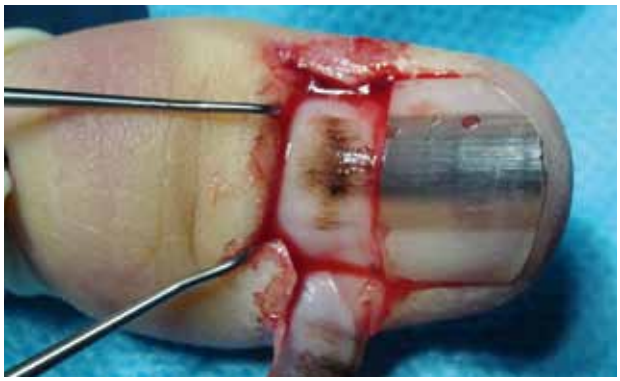


Fig1a - *Pigmentation on the matrix spreading transversally. © B. Richert*

Fig1b - *After tangential excision of the pigmentation. Note the oval shaped defect. © B. Richert*

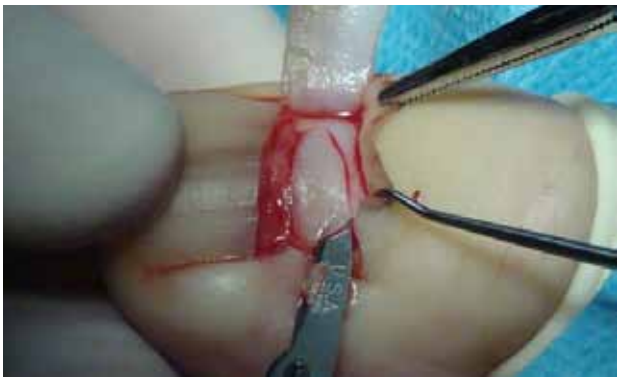


Fig1c - *A transverse oval shape in drawn to remove a broad pigmentation on the matrix. © B. Richert*

Eckart Haneke

TUMOURS & NAIL SURGERY

3 The series of 54 ungual SCCs in 51 patients, seen over a period of 15 years, is the largest hitherto published. Most of the results correspond to other case series, but the main localization differs. This is not surprising as the total number of patients is not as big. It is also our experience that most SCCs are still in situ, even when they are grossly hyperkeratotic and lift the nail. The clinical impression of a wart **(Fig 2)** is also often seen histopathologically with a verrucous appearance of the carcinoma.

Fig2 - *Warty hyperkeratosis lifting up the distal plate: Bowen's disease. © B. Richert*

4 Whereas the idea of developing a model for ingrown nail surgery is good, unfortunately, the concept and drawings are wrong. I am afraid that if young adepts do their ingrown nail surgery as shown, the rate of recurrence will be even higher.

A- The real shape of the nail is not as shown properly in the scheme of their publication (the plate is as wide proximally as distally with the proximal lateral corner extending proximally).

B- The illustration of the matrix horn phenolization is not clear, as they have not created a cavity corresponding to the matrix horn.

C- The authors propose to teach nail avulsion as this "can help the resident learn how to treat other nail diseases and ungual trauma". Nail avulsion is the most frequent nail trauma and is by no means a treatment of nail diseases, although in some very rare cases it may be the start of a treatment.

D- Their "classical matricectomy" is intended to show the partial lateral nail avulsion with removal of the corresponding lateral nail fold. They claim to widen their incision with an epidermal stitch. An "epidermal stitch" is virtually impossible, and inadequate, as the epidermis is very thin and cannot hold any tension, and how could a stitch widen the incision? What they in fact illustrate is the wedge excision that is known to have a recurrence risk of between 20% and 75%. The tip of their wedge turns inward (towards the centre of the nail), thus the most lateral proximal matrix portion will be left in place giving rise to a spicule or clear-cut recurrence. In their figure 4, third row left, one can see that the nail is still in place and no matrix portion has been excised. They finally stitch the wound in order to bring the rest of the lateral nail fold to the nail plate again. This increases the imbalance between a wide nail plate and a narrow nail bed.

Although a model on how to operate an ingrown nail would most certainly be welcome, this particular proposal will do more harm than good. A saying from the advertising industry claims that a picture is worth 10,000 words; alas, wrong pictures may be worse than 100,000 words.

Bertrand Richert

MISCELLEANOUS

1 Baran R. Proximal nail fold intralesional steroid injection responsible for Hoigné syndrome. J Eur Acad Dermatol Venereol. 2013 Oct 25.

R. Baran herein describes the case of a 38 year-old male who developed a Hoigné syndrome after an intralesional injection of steroids in the proximal nail fold. Hoigné's syndrome is characterized predominantly by neuropsychiatric alterations, including severe psychomotor agitation with confusion, sensations of disintegration, depersonalization and derealization, perceived changes of body shape, visual and auditory hallucinations, panic-like anxiety, including fear of death, as well as alterations of consciousness and seizures. The neuropsychiatric symptoms tend to be accompanied by tachycardia, hypertension, dyspnoea and numbness of the extremities. Most reported cases involve reactions to intravenous or more often intramuscular administrated penicillin. The characteristics of acute symptoms and clinical course of Hoigné's syndrome depend upon the size of the particles of the drug that accidentally penetrate a blood vessel and reach the temporo-limbic structures of the brain. Dermatologists routinely inject steroids in the skin. They should be aware of this syndrome, that has a spontaneously favourable issue within a few minutes. It should be differentiated from anaphylactic manifestations.

2 Guero S. Benefits of an ungual prosthesis in traumatology and reconstructive surgery of the nail. Tech Hand Up Extrem Surg. 2014;18(1):20-4.

Lesions of the nail apparatus can leave aesthetic and sometimes functional sequelae. Many sequelae are the result of incorrect growth of the nail plate. During the acute phase, in the absence of a nail plate, the nail bed may keratinize or form a pyogenic granuloma, compromising harmonious regrowth of the nail plate. The ideal is to reinsert the plate if it is available, but if it has been lost, an ungual prosthesis must be inserted to act as a temporary implantable splint. This implant must have the same shape and structure as the nail plate. Many ideas have been used in the past, including suture pack, infusion tubing, or x-ray film. However, these techniques are no longer acceptable as, in many countries, all types of implants require a documented recorded identification or "traceability." The implants used by the authors are manufactured and stored individually in a sterile packaging. They are immediately available in traumatology departments treating hand emergencies. These prostheses are also very useful in reconstructive surgery of the hands and feet, particularly when the nail bed has to be reconstructed. In this case, the implant is used to flatten the nail bed, whether it is sutured, grafted, or reconstructed with flaps, during the slow regrowth of the nail plate. The author reports his own experience in emergency or secondary repair of the nail unit.

Bertrand Richert

MISCELLEANOUS

3 Cronin LJ, Mildren RP, Moffitt M, Lauto A, Morton CO, Stack CM. An investigation into the inhibitory effect of ultraviolet radiation on *Trichophyton rubrum*. Lasers Med Sci. 2014;29(1):157-63.

Onychomycosis, is predominantly caused by *Trichophyton rubrum*. This infection is an important public health concern, due to its persistent nature and high recurrence rate. Alternative treatments are urgently required. One such alternative is phototherapy, involving the action of photothermal or photochemical processes. The aim of this novel study was to assess which wavelengths, within the ultraviolet (UV) spectrum, were inhibitory and nail transmissible. The first step studied the transmission of UV and visible light through normal avulsed nail plates. All radiations between 200 and 317 nm were blocked. The light transmission increased as the wavelength became longer (> 317nm). The second step was the irradiation of *T. rubrum* spore suspensions using a tunable wavelength lamp system (UVC to UVA) to evaluate which wavelengths prevented fungal growth. Inhibitory activity was observed only for the sample irradiated at 280 nm with a fluence of 3,1 J/cm^2. Light-emitting diodes (LEDs) of defined wavelengths with different fluence were then used on the cultures. These experiments demonstrated that exposure at 280 nm using a LED with a fluence as low as 0,5 J/cm^2 (this means a 5 minute treatment) was inhibitory, while exposure to longer wavelengths was not. A key requirement for the use of phototherapy in the treatment of onychomycosis, is that it must be nail transmissible. To conclude, the authors indicate that the treatment with UVC is not feasible, given that there is no overlap between the antifungal activity observed at 280 nm and transmission through the nail plate. However, a potential indirect application of this technology could be the decontamination of reservoirs of infection, such as the shoes of infected individuals, thus preventing reinfection.

4 Le QV, Howard A. Dexamethasone iontophoresis for the treatment of nail psoriasis. Australas J Dermatol. 2013;54(2):115-9.

Iontophoresis is a technique using a small electric charge to deliver medications through the skin. Dexamethasone iontophoresis (DI) has been widely used in various concentrations for the treatment of musculoskeletal disorders. This is a retrospective study of 27 patients treated with dexamethasone iontophoresis weekly for at least 3 months, between 1996 and 2011. The treatment involved immersing all fingernails of the affected hand or hands into 100 ml of distilled water with a 3-mL dexamethasone sodium solution (8 mg in 2 ml). Electrodes were placed on the dorsum of the hands and 4 mA of current applied through the solution for 20 minutes at each treatment. Response to treatment was assessed on clinical photographs taken before treatment, during reviews, and at the end of the treatment, using the nail psoriasis severity index (NAPSI) scoring. In this case series, DI resulted in improvement in most patients, with complete clearance in individual nails in some of them. Patients were often using other topical treatments as well (betamethasone, calcipotriol, clobetasol, oral methotrexate, intralesional corticosteroid injection, grenz ray...). DI is easy and economical to set up and administer and is associated with minimal side effects. However, it is a time-consuming procedure (20-min session every week in the clinic). In most patients it took at least 3 months before they started to see any improvement.

COMMENTARY B. RICHERT

1 Hoigné's syndrome is an extremely interesting, but frightening condition when you are unaware of it. If you look in the literature, you will find that this syndrome is frequently considered as a pseudoanaphylactic or pseudoallergic reaction following intramuscular and aqueous procaine penicillin administration. Following Baran's publication, the etiology should be completely revisited. It is indeed an accidental embolization of tiny crystals that may reach various organs according to their size. Robert Baran knows a lot about it, as in 1964, he published the first case of amaurosis secondary to

Bertrand Richert

MISCELLEANOUS

insoluble steroid injection for alopecia.[1] Microcrystals of procaine penicillin may reach the brain through the blood stream up to the limbic structures, where they cause the neurologic disturbance within a few minutes. Some other authors claim that some crystals may dissolve when they penetrate the blood flow and only the bigger ones (> 8 µm) may be trapped in the pulmonary capillaries, then causing dyspnoea. Blocked there, they cannot go further and will not cause any neurologic symptoms. Humbert et al. reported another case of Hoigné's syndrome, after an injection of 0.5 cm^3 of triamcinolone 40 mg/ml mixed with half a cc of lidocaine into a keloid of the abdomen of a 13 year-old girl.[2] Robert Baran contacted the manufacturer for information about the steroid solution he had used, and was told that the crystals were 2 to 4 µm in diameter, thus explaining the neurologic symptoms.

More recently another Hoigné's syndrome was reported following an intravenous injection of ceftriaxone.[3]

All physicians injecting drugs, especially those containing crystals, should be aware of this particularly distressing, but rapidly self-healing side effect. Injection sustained-release drugs such as steroids, are especially a risk **(Fig 1)**. The reaction may occur after an injection in any place, even with a very small amount of drug in a very peripheral location with tiny vessels, such as the proximal nail fold.

References

1- Baran R. The risk of amaurosis during local treatment of alopecia with injectable corticotherapy. Bull Soc Fr Dermatol Syphiligr 1964;71:25-8.

2- Humbert P, Girardin P, Aubin F. Fear of dying after intra-keloid injection of triamcinolone acetonide and lidocaine: Hoigné's syndrome. Ann Dermatol Venereol 2001;128:762.

3- Landais A, Marty N, Bessis D, Pages M, Blard JM. Hoigné syndrome following an intravenous injection of ceftriaxone: A case report. Rev Med Interne 2014;35:199-201.

2 We expected a lot from the paper of Guéro, a famous French hand surgeon in Paris. He is well known in the nail field, as he studied the ligamentary system of the nail apparatus.[1] The dorsal expansion of the lateral ligament of the distal inter-phalangeal joint arising from the intermediate phalanx and ending in the matrix and the lunula, is now called the Guéro ligament.

Unfortunately, we did not learn anything new. This paper is a review of 153 reconstructions over a period of 20 years. The main issue is that any trauma, any reconstruction should be covered by a splint, in order to avoid any distortion of the nail bed or synechia between the ventral part of the proximal nail fold and the matrix. The ungual prosthesis should be kept in place for at least 2 months. If the nail is lost or kept for the lab, it should be replaced by a sterile artificial nail. And in this case there may be a conflict of interest, as there is a picture of the device he routinely uses...

We recently learned from a communication of Beth Ruben, a San Francisco based dermatopathologist, that in some instances the nail plate should be sent to the lab: when performing a plate avulsion, the most superficial layers of the bed and matrix are ripped off and remain attached to the undersurface of the plate **(Fig2)**. She reported a case where the diagnosis of melanoma *in situ* was made not

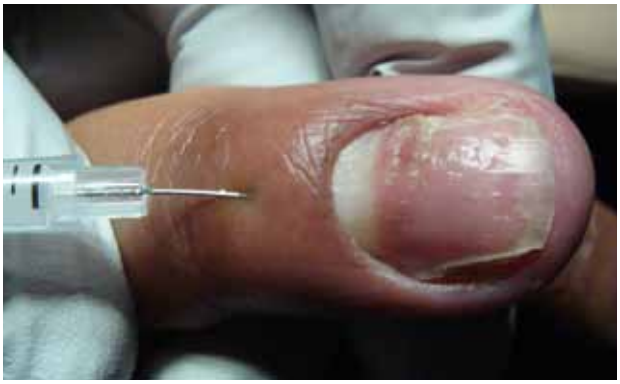


Fig1 - *Intra-lesional injection of steroids is performed in routine by nail doctors. © B. Richert*

Fig2 - *Proximal partial avulsion of the plate shows that some pigmented epithelium on the under surface of the plate. © B. Richert*

Bertrand Richert

MISCELLEANOUS

on the specimen from the matrix, but on the few layers stuck under the plate!! This means that from now on nail surgeons should not replace the nail plate after surgery for longitudinal melanonychia and will need to cover the defect with some sort of nail splint. If they do not want to use the do-it-yourself nail splint out of the suture pack, infusion tubing, surgical glove, syringe cylinder **(Fig3)**... they may order the sterile nail splint that comes in three different sizes in an individual packaging.

References
1- Guéro S, Guichard S, Fraitag SR. Ligamentary structure of the base of the nail. Surg Radiol Anat 1994;16:47-52.

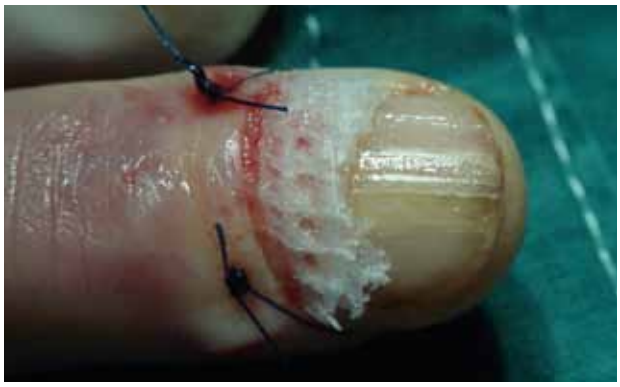


Fig3 - *A vaseline gauze is inserted and secured under the proximal fold to avoid any adherence to the matrix. © B. Richert*

3 The paper on the inhibitory effect of ultraviolet radiation on *Trichophyton rubrum* is extremely interesting for several reasons. It is well known that UV-C radiation kills or inactivates microbes by damaging their deoxyribonucleic acid (DNA) through the absorption of photons. Ultraviolet germicidal irradiation (UVGI) for air disinfection applications has relied on low-pressure mercury vapor lamps for decades.[1] The authors confirm here the efficacy of UVC inhibitory activity on irradiated cultures as already demonstrated previously.[2] But they also showed that UVC do not penetrate the nail plate. We have already learned from Stern et al. that the nail plate is very efficient at blocking UVA and UVB.[3] This means that no UV light is able to get through the nail. They also demonstrate that light emitting diodes (LED), whatever their wavelength, cannot transmit through the nail plate but, however, have a very significant inhibitory effect on *T. rubrum in vitro* at a wavelength of 280 nm.

Onychomycosis is difficult to treat and patients often relapse. It is thought that patients' footwear may act as an important reservoir for reinfection. Up to now, there has been no device for killing the dermatophytes that may have colonized the inner surface of the shoes of those patients. A recent paper from Ghannoum shows that treatment of shoes with a commercial ultraviolet C sanitizing device was effective in reducing the fungal burden in shoes.[4]

Developing LED therapy as an in-shoe device or for decontamination of large reservoirs (pools, lockers, carpets...) might be a cheap, quick and easily feasible option.

References
1- Reed NG. The history of ultraviolet germicidal irradiation for air disinfection. Public Health Rep 2010;125:15-27.
2- Dai T, Tegos GP, Rolz-Cruz G, Cumbie WE, Hamblin MR. Ultraviolet C inactivation of dermatophytes: implications for treatment of onychomycosis. Br J Dermatol 2008;158:1239-46
3- Stern DK, Creasey AA, Quijije J, Lebwohl MG. UV-A and UV-B penetration of normal human cadaveric fingernail plate. Arch Dermatol 2011;147:439-41.
4- Ghannoum MA, Isham N, Long L. Optimization of an infected shoe model for the evaluation of an ultraviolet shoe sanitizer device. J Am Podiatr Med Assoc 2012;102:309-13.

4 Iontophoresis with dexamethasone looked promising at first glance. However the way the study was conducted, without right-left controls, with almost all patients receiving an associated treatment (either topical, intralesional or even systemic such as methotrexate or itraconazole) destroys all hope! And even with this combined treatment, there was only a very slight improvement in the NaPSI, sometimes after more than 50 sessions!

This idea seems attractive and might be an alternative to other treatments, but new studies with a strict protocol should be conducted first.

The nail - What's new ? n°7

Clinical Cases

Robert BARAN

Clinical Case

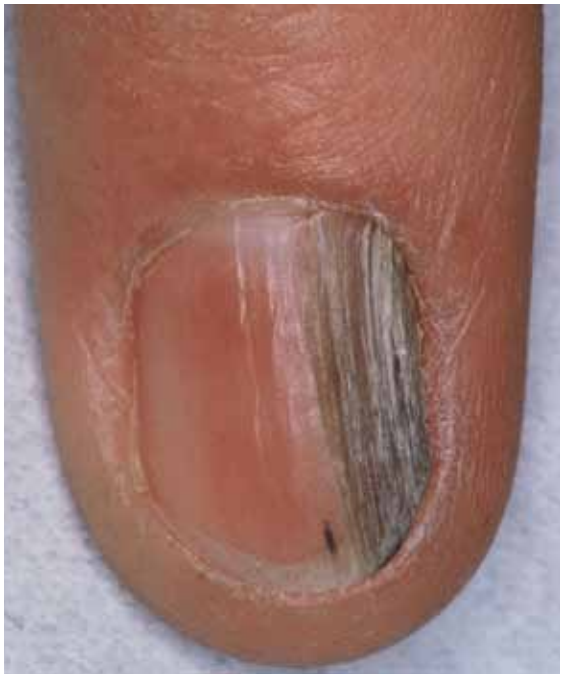


Fig1 - *Longitudinal melanonychia. © R. Baran*

Due to the appearance of a longitudinal melanonychia (LM) on the fourth finger of his right hand **(Fig 1)** a 39-year-old patient was referred to us by his general practitioner. The pigmentation appeared after trauma two years previously and had become progressively more evident. Clinical examination confirmed the presence of an LM that involved the medial quarter of the nail. The affected area was relatively thicker than the rest of the nail. There was an overcurvature and a faint yellowish discoloration that medially bordered the black streak. This was clearly demonstrated by dermatoscopic examination. Because of the strong possibility of an OM, the lesion was treated surgically. Partial avulsion removed the pigmented portion of the nail plate and exposed the underlying tissue. A digitated lesion then because visible at the lateral order of the matrix, and this was excised at its base.

Three biopsy specimens were examined. Two were from the initial excision and included a portion of the avulsed nail and a small ellipse taken from the lateral nailfold bordering the distal matrix. The third specimen was taken from the lateral longitudinal re-excision. The avulsed nail had been cut along its longitudinal axis. The remains of the nail plate and the third specimen were cut transversally into three separate parts: the proximal nail portion, the mid-segment of the nail and the distal edge. The second specimen corresponding to the digitated lesion seen after exposure of the subungual tissue was cut along a longitudinal axis.

What is your clinical diagnosis?

Robert BARAN

Clinical Case

Histologically, there was no connective tissue in the holes of the avulsed nail in the specimen examined after a second, wider excision of the tissues. The underlying matricial and nail bed connective tissue was unchanged. The three zones presented an identical picture of Bowen's disease with multiple foci of clear changes **(Fig 2)**. In contrast to the thin and flat epithelium of the nail bed, the proximal nail portion showed numerous small epithelial digitations perforating the nail plate. These epithelial digitations were covered by a thick keratogenic layer extending into the thickened portion of the nail plate and gave rise to small cavities that appeared either empty or filled with a serous liquid There was no central connective tissue core in these epithelial digitations. The small fragment of the lateral nailfold (second specimen) was hyperplastic with a slight degree of pleomorphism of the cells of the basal layer.

Fontana-Masson stain on the different sections revealed that the pigmentation was due to a simple activation of the matricial melanocytes.

The clinical presentation was that of a pigmented onychomatricoma (OM), an impression confirmed after surgical exposure of the subungual tissue and the proximal portion of the thickened nail plate. Histology, however, revealed an epithelioma in situ with three features that ruled out the possibility of a malignant OM:[1]

1 / lack of stroma and proximal deep invagination;

2/ small, superficial epithelial digitations without a connective tissue core; and

3/ small and numerous cavities in a thickened nail plate (in contrast to the broad cavities of OM).

These three criteria indicate onychogenic Bowen's disease. This case also demonstrates once again the polymorphism of Bowen's disease of the nail and its misleading features compared with Bowen's disease of the skin. Together with its association with LM, the recently described pseudofibrokeratoma, and the erythronychial variant of Bowen's disease, a new pseudo-onychomatricomal type must be added to the patterns of this condition. The histological examination of all types of suspected OM, especially with pigmented bands, is therefore mandatory.[2]

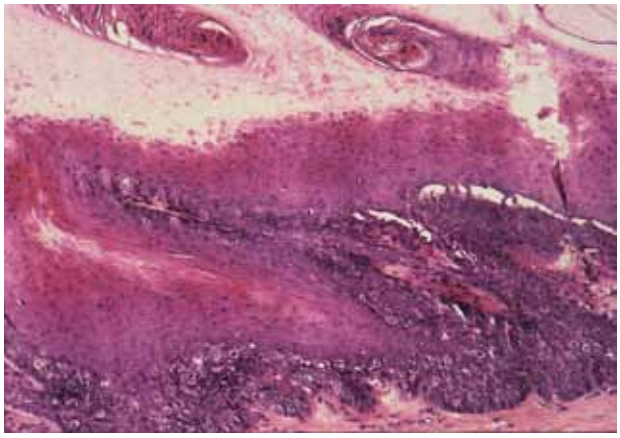


Fig2 - *Multiple foci of Bowen's disease. © R. Baran*

References:

1- Baran R, Perrin Ch. Bowen's disease clinically simulating an onychomatricoma. J. Am Acad Dermatol. 2002; 47:947-9.

2- Fayol J, Baran R, Perrin C, Labrousse F. Onychomatricoma with misleading features. Acta Derm Venereol. 2000; 80:370-2.

Véronique BLATIÈRE

Clinical Case

Fig1 - *Onychodysplasia of the second toe. © V. Blatière*

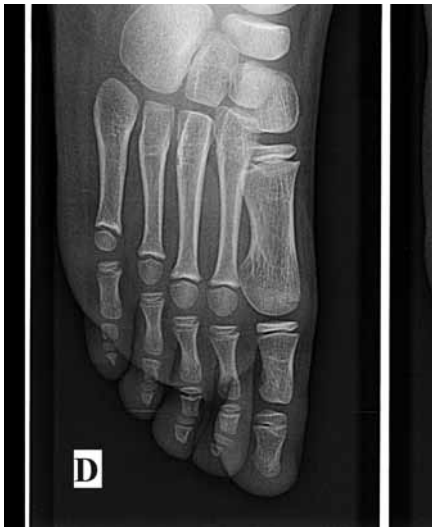


Fig2 - *X-ray: Narrowed phalanx. © Dr Eric Terqueux, Montpellier. France*

Fig3 - *Per-op view: the rudimental nail unit. © V. Blatière*

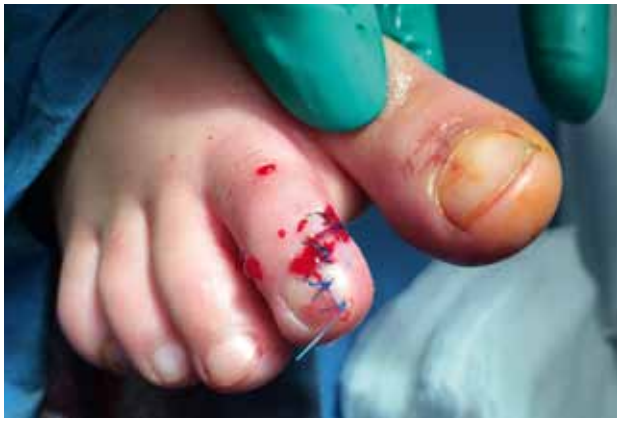


Fig4 - *At the end of the surgery. © V. Blatière*

A 7 year-old girl from the Maghreb consulted because she had pain when her second right toenail was cut. On clinical examination the last phalanx size was normal. A vertical ridge split the nail into two parts, the medial nail being smaller and plicated **(Fig 1)**. She had been suffering for a long time, but as an adopted child, it was difficult to assess a congenital feature, although according to the host family, they had always known of the abnormality, and were not aware of any traumatism. Cutting the child's nail had always been a burden.

An X-ray was performed. There was no traumatic bony lesion; the distal phalanx was narrowed and piriform, but presented no bifurcation **(Fig 2)**.

The diagnosis of onychodysplasia was proposed and surgery was decided to explore and cut the small nail unit out.

A second nail unit, with small cartilage under the nail bed, could be seen per operatively. This was excised « en bloc » after the nail avulsion **(Fig 3)**. The medial periungual skin was sutured to the persistent nail plate to re-create a natural fold **(Fig 4)**.

What is your diagnosis?

Véronique BLATIÈRE

Clinical Case

Most cases described with congenital onychodysplasia have occurred in Japanese children and on the second finger. This entity was first called, COIF (Congenital Onychodysplasia of the Index Finger) and later Iso-Kikuchi syndrome[1, 2, 3] **(Table 1).** Iso-Kikuchi syndrome is mainly described in Japan, but its international incidence is about 4.2 cases/100,000 births.[4] In utero ischemia of the palmar digital artery, and a dysplastic change in the crescent-shaped cap of the distal phalanx, are the two main candidate pathogenetic mechanisms that have been proposed. It could be related to exposure to teratogens during pregnancy (antidepressants, antiepileptic and abortifacient drugs, insulin).[5,6] A recent case was described in an Italian child.[6] This syndrome is often under-diagnosed in Europe.[6]

In our case, the only onychodysplasia, which was probably congenital, presented on the right second toe of a North African girl. There was no other clinical abnormality. Franceschini et al [7] recently described a peculiar facial appearance with congenital onychodysplasia and proposed broadening the spectrum of this syndrome, thus supporting the hypothesis of a basal dysplastic pathogenetic mechanism involving, not only the index fingers, but also perhaps other tissues in different spots. Therefore, we now think it is possible that our case of onychodysplasia of the second toe could be considered as an Iso-Kikuchi syndrome.

References

1- Youn SH, Kwon OS, Park KC, Youn JI, Chung JH. Congenital onychodysplasia of the index fingers Iso-Kikuchi syndrome. A case involving the second toenail. Clin Exp Dermatol. 1996 Nov;21(6):457-8. PubMed PMID: 9167348.

2- Baran R. [Iso Kikuchi syndrome (C.O.I.F. syndrome). A report on 2 cases and a review of 44 cases in the literature (author's transl)]. Ann Dermatol Venereol. 1980 May; 107(5):431-5. French. PubMed PMID: 7224526.

3- Baran R, Stroud JD. Congenital onychodyspasia of the index finger. Iso and Kikuchi syndrome. Arch Dermatol 1984;120:243±244.

4- Raugi GJ. Congenital onychodystrophy of the index fingers. E-Medicine 2009: 1-14.

5- Prais D, Horev G, Merlob P. Prevalence and new phenotypic and radiological findings in congenital onychodysplasia of the index finger. Ped Dermatol 1999; 16: 201-4

6- Pertusi G, Graziola F, Annali G, Giani C, Veronese F, Guala A, Tiberio R, Colombo E. Iso-Kikuchi syndrome in an Italian new-born with Y-shaped bifurcation of the index fingers. Eur J Dermatol. 2011 May-Jun;21(3):423-4. doi: 10.1684/ejd.2011.1297. PubMed PMID: 21515440.

7- Franceschini P, Licata D, Guala A, Di Cara G, Franceschini D. Peculiar facial appearance and generalized brachydactyly in a patient with congenital onychodysplasia of the index fingers (Iso-Kikuchi syndrome). Am J Med Genet. 2001 Feb 1;98(4):330-5. Review. PubMed PMID: 11170077.

Table 1: *Congenital dysplasia or Iso-Kikuchi Syndrome*

<table>
<tr><th colspan="6">Congenital onychodysplasia or Iso-Kikuchi Syndrome criteria revised by Baran and Stroud [3]</th></tr>
<tr><td rowspan="6">Congenital occurence</td><td>Unilateral or bilateral involvement of</td><td>Variability in nail appearance</td><td>Hereditary transmission</td><td colspan="2">Bone malformations</td></tr>
<tr><td rowspan="2">Index Fingers</td><td>Micronychia</td><td rowspan="2">(Family cases) Autosomal dominant mode of inheritance with variable expressivity</td><td colspan="2">Distal phalanx narrowed</td></tr>
<tr><td>Polyonychia</td><td colspan="2">Enlarged with Y shaped bifurcation</td></tr>
<tr><td rowspan="2">Middle fingers</td><td>Anonychia</td><td rowspan="4">Sporadic</td><td colspan="2">Brachymesophalangia of the 5th finger</td></tr>
<tr><td>Hemionychogryphosis</td><td colspan="2" rowspan="2">Cutaneoussyndactyly of an index and middle finger</td></tr>
<tr><td>Thumbs</td><td>Nail malignement</td></tr>
<tr><td></td><td>Deformity of the lunula</td><td colspan="2">Congenital flexion disturbances of the index fingers</td></tr>
</table>

Marie CAUCANAS

Clinical Case

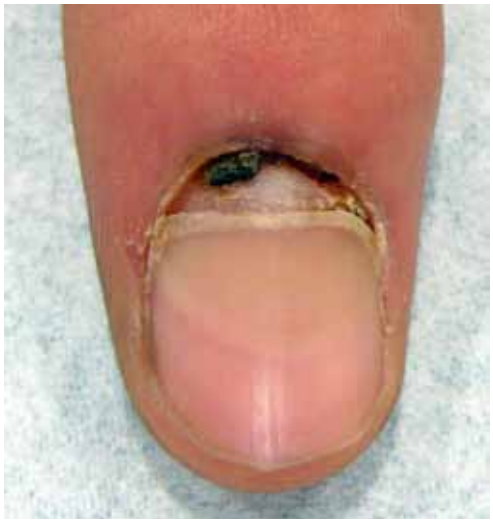


Fig1 - Clinical picture of the left index finger.
© M. Caucanas

Fig2 - Dermoscopic picture of the left index finger.
© M. Caucanas

An 18 year-old man presented for a tender sensation of his left index finger proximal nail fold, associated with a stop in nail growth. Three months before, he had undergone surgery for the removal of wrist pins, inserted after a fracture 6 weeks earlier, wearing brace, but no cast. He did not suffer from any discomfort during immobilization with the braces. His treatment only consisted in mild painkillers. One month after the removal of the wires, the proximal nail fold became tender, swollen and oozing. Crusts started to form in the lunula area after a few weeks and he did not cut his nail anymore **(Fig 1 & 2)**.
3 months later, his mother was afraid of an infection and sought medical advice.

What is your diagnosis?

Marie CAUCANAS

Clinical Case

This case is very much in favour of retronychia, in view of the development of a chronic perionyxis with discontinuation of nail growth and a recent history of traumatism. Crusts in the lunula area were probable remnants of pyogenic granuloma and a second plate was clearly growing under the attached one. Considering the chronology of the events, the surgical removal of the wrist wires might have been the triggering factor, but the exact mechanism remains mysterious.

The main differential diagnosis was onychomadesis and pyogenic granuloma following cast immobilization, described by Tosti et al., in which patients complained about moderate paresthesia and pain of the immobilized hand during cast wearing, followed by the development of painful fingernail inflammatory lesions 7 to 30 days after cast removal. In the present case, it was not a simple onychomadesis and the patient wore braces without pain or paresthesia. Other diagnoses included nails changes reported in reflex sympathetic dystrophy, coccal nail fold angiomatosis and drug-induced pyogenic granuloma, but no consistent context was observed.[1]

Retronychia was first described in 1999 by de Berker et al., 'retro' meaning backwards and 'onychia' meaning nail. It describes a specific type of chronic perionyxis with proximal ingrowing of the nail plate. Mechanical factors, such as traumatisms, are thought to induce a loss of continuity between the nail plate and the nail matrix, preventing the newly formed nail from growing downwards.[2] The plate is then pushed upwards and backwards leading to posterior embedding with two to four superimposed nail plates beneath the nail fold, generating mild to moderate painful paronychia and granulation tissue reaction.[3] Xanthonychia me semble bizarre. N'est-ce pas plutôt: Xanthonychia is also a feature of retronychia, due to the thickening of the plate. Onycholysis is frequent and associated with significant inflammatory exsudate which accumulates beneath the nail.[4] The affection is much more frequent in toes than in fingers. In atypical cases, work-up may include ultrasound examination showing a shorter distance between the origin of the nail plate and the base of the distal phalanx at the distal interphalangeal joint.[3] In the majority of cases, nail avulsion is a diagnostic and a therapeutic procedure.[2] Apart from the rarer fingernail localization, the young age of the patient is also remarkable. Retronychia has been described mainly in adults, but Piraccini et al.[5] reported the same clinical features in young patients aged between 12 and 24 years. It is unclear why the affection is less frequent in this population, given that they are usually prone to more trauma than adults, but it could be due to their faster nail plate growth rate.

References

1- Tosti A, Piraccini BM, Camacho-Martinez F. Onychomadesis and pyogenic granuloma following cast immobilization. Arch Dermatol. 2001;137(2):231-2.
2- Chiheb S, Richert B, Belyamani S, Benchikhi H. Ingrown nail: A new cause of chronic perionyxis. Ann Dermatol Venereol. 2010;137(10):645-7.
3- Wortsman X, Calderon P, Baran R. Finger retronychias detected early by 3D ultrasound examination. J Eur Acad Dermatol Venereol. 2012;26(2):254-6.
4- de Berker DA, Richert B, Duhard E et al. Retronychia: proximal ingrowing of the nail plate. J Am Acad Dermatol. 2008;58(6):978-83.
5- Piraccini BM, Richert B, de Berker DA et al. Retronychia in children, adolescents, and young adults: a case series. J Am Acad Dermatol. 2014;70(2):388-90.

Olivier COGREL

Clinical Case

Fig1a - *Longitudinal erythronychia and tiny keratotic lesion emerging from the hyponychium. © O. Cogrel*

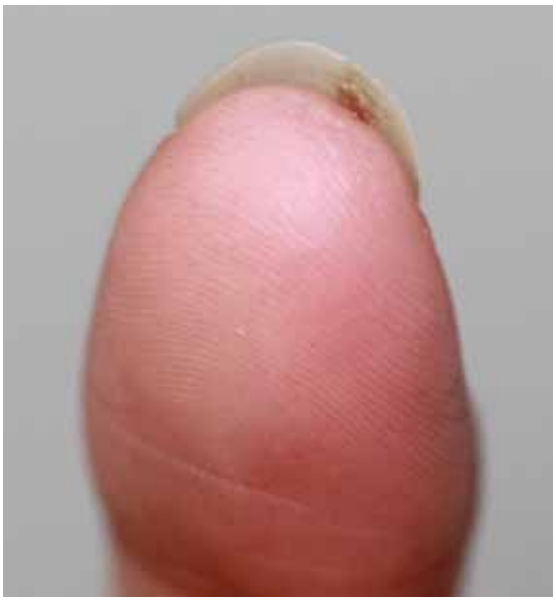


Fig1b - *Tiny brownish keratotic process emerging from under the distal free edge.© O. Cogrel*

A 25 year-old woman presented with a subungual keratotic process on the distal tip of the left thumb, which had been present for several months. She did not recall any trauma to the nails. On physical examination, a very discreet longitudinal erythronychia was seen on the nail **(Fig 1a)**. A tiny, brownish keratotic process emerged from the distal edge beneath the nail plate, in line with the longitudinal red streak **(Fig 1b)**. The other nails were normal and no abnormalities of the skin were noted.

What is your diagnosis?

Olivier COGREL

Clinical Case

The clinical diagnosis for the lesion was onychopapilloma. We performed proximal nail avulsion and saw a keratotic papule on the distal part of the nail matrix **(Fig 2a)**. We performed a very localized tangential excision to shave the distal matrix and to establish a definitive diagnosis **(Fig 2b)**. On histopathological examination, horizontal sections were performed and showed a broad keratogeneous zone with flattened eosinophilic keratinocytes and papillomatosis without any atypic cells **(Fig 3)**. The patient was seen one year later without any remaining lesion.

The most common cause of a single longitudinal erythronychia is a nonspecific warty change in the matrix epithelium, extending into a papillomatous ridge of the nail bed and terminating in a multinucleate keratotic nodule beneath a small split in the free edge of the nail. The term of onychopapilloma was coined by Baran and Perrin [1], when a warty nodule at the nail bed end is present. Onychopapilloma is histopathologically characterized by evident acanthosis of the nail bed and marked distal longitudinal papillomatosis, with multinucleated cells and a prominent keratogenous zone in the distal nail bed. This keratogenous zone is identical to that of the nail matrix with associated distal keratin. The most important histological features of onychopapilloma are the metaplasia of 'matrix cells' of the nail bed epidermis, and a nail-like structure protruding from the matrix metaplasia of the distal nail bed. Trap door avulsion, in combination with thin longitudinal excision and repair, may provide diagnosis and cure of the lesion. However in our patient, the shave biopsy of the distal matrix alone, without any excision of the nail bed, was enough to treat the distal keratotic process. This observation pleads for a distal nail bed reactive entity arising secondary to the original matrix pathology [2].

References:
1- Baran R, Perrin C. Longitudinal erythronychia with distal subungual keratosis: onychopapilloma of the nail bed and Bowen's disease. Br J Dermatol 2000;143:132-5.
2- de Berker D. Erythronychia. Dermatol Ther 2012; 25:603-11

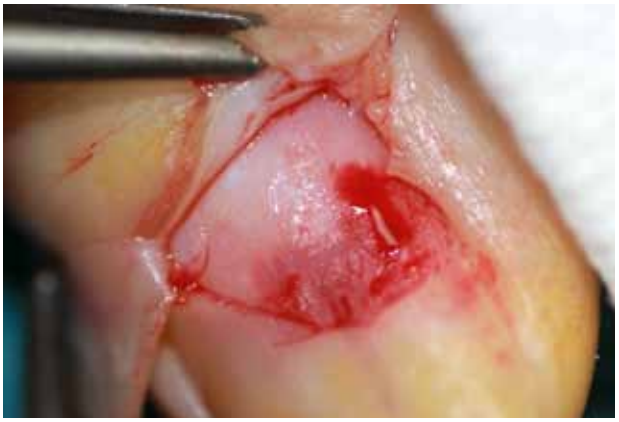


Fig2a - *Keratotic papule on distal matrix before and after shave biopsy. © O. Cogrel*

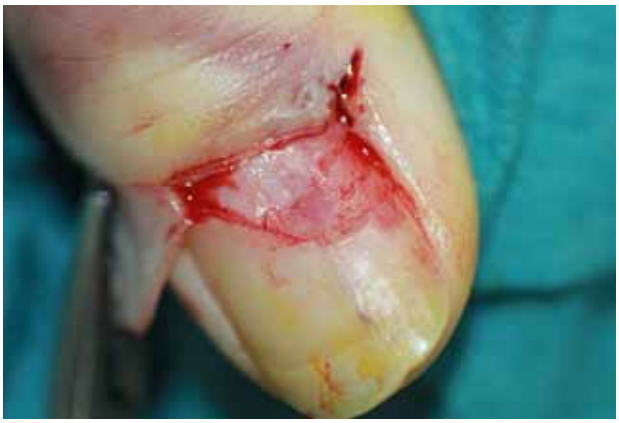


Fig2b - *After shaving of the distal matrix. © O. Cogrel*

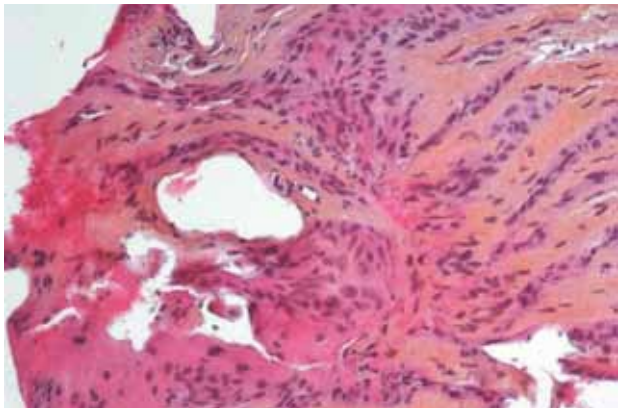


Fig3 - *Keratogeneous zone with flattened eosinophilic keratinocytes and papillomatosis. © O. Cogrel*

Osvaldo CORREIA

Clinical Case

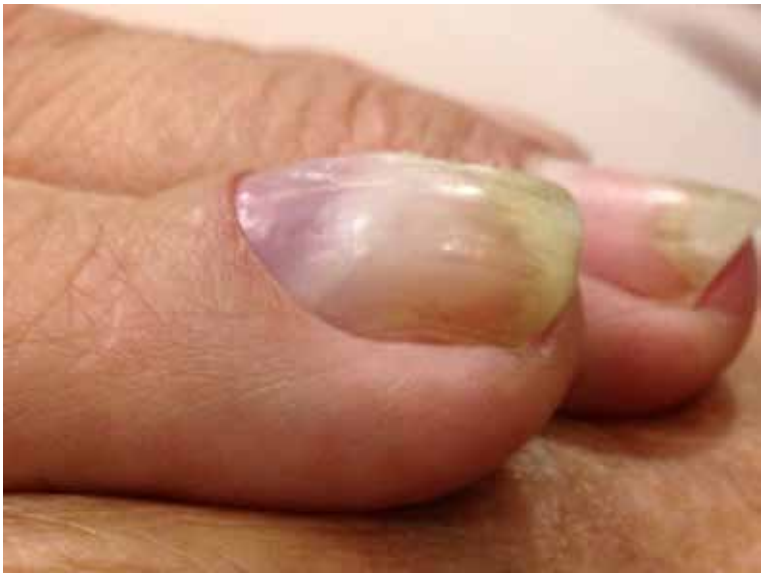


Fig1 - *Painful purple blue tender nodule under the right fourth finger nail plate.*
© O. Correia

A 78-year-old woman presented at our department with a 50-year history of a slow growing, painful, purple-blue, tender nodule under the right fourth finger nail plate **(Fig 1)**. A past nail trauma was revealed by the patient - she accidently sewed her nail with a needle when she was 28 years old. Pain was excruciating at the slightest touch. MRI confirmed the presence of a large subungual tumor and surgical excision was performed after partial nail plate avulsion. Histologic examination revealed a solid tumor composed of branching vascular channels, separated by a myxoid stroma containing glomus cells.

What is your diagnosis?

Osvaldo CORREIA

Clinical Case

History, clinical picture and diagnosis were consistent with a subungual glomus tumor.

Subungual glomus tumors are uncommon tumors that present with a classic triad of temperature sensitivity, paroxysmal pain, and localized tenderness. Most of the time the presenting symptom is a severely painful fingertip, without palpable swelling.[1,2] A glomus tumor is a rare benign vascular tumor, derived from the modified smooth muscle cells of the glomus body. Glomus cell populations are specialized arteriovenous anastomoses, characterized by Sucquet-Hoyer canals, which play an important role in thermoregulation. Up to 90% of cases are reported in women in their forties and it mostly affects the fingernails.[1-3,5] Owing to the small lesions and the absence of specific skin features in the nail bed and nail matrix localizations, glomus tumor may not be considered. In particular, presentation of patients to practitioners of different disciplines for treatment of pain may cause diagnostic delays.[3] As far as our patient was concerned, a progressive, painful, purple-blue, tender nodule appeared under the right fourth finger nail plate after a trauma many years before. Nail dystrophy appears in up to 38% of tumors, most of them presented as subungual nodules.[1] The lesions should be evaluated by X ray, ultrasonography and/or magnetic resonance imaging.[2,4,5] In the treatment of subungual glomus tumor, surgical excision is known to be the only curative method. Different surgical approaches can be performed according to the anatomic location of the tumor.[1,2,5,6] Nail matrix involvement can give complications, such as nail deformity, decreased sensation, and prolonged pain, more than in patients with nail bed lesions.[5] A transungual approach with nail avulsion, and an incision selected according to the tumor location, can produce an excellent outcome with minimal postoperative complications. Dressing with a trimmed nail plate may also be beneficial in managing the wound and preventing postoperative nail deformity.

References

1- Moon SE, Won JH, Kwon OS, Kim JA. Subungual glomus tumor: clinical manifestations and outcome of surgical treatment. J Dermatol. 2004;31:993-7.
2- Song M, Ko HC, Kwon KS, Kim MB. Surgical treatment of subungual glomus tumor: a unique and simple method. Dermatol Surg. 2009;35:786-91.
3- Gencoglan G, Dereli T, Kazandi AC. Subungual glomus tumor: surgical and histopathologic evaluation. Cutan Ocul Toxicol. 2011;30:72-4.
4- Chiang YP, Hsu CY, Lien WC, Chang YJ. Ultrasonographic appearance of subungual glomus tumors. J Clin Ultrasound. 2014 Feb 13. doi: 10.1002/jcu.22138.
5- Lee SH, Roh MR, Chung KY. Subungual glomus tumors: surgical approach and outcome based on tumor location. Dermatol Surg. 2013;39:1017-22.
6- Grover C, Khurana A, Jain R, Rathi V. Transungual surgical excision of subungual glomus tumour. J Cutan Aesthet Surg.2013;6:196-203.

David DE BERKER

Clinical Case

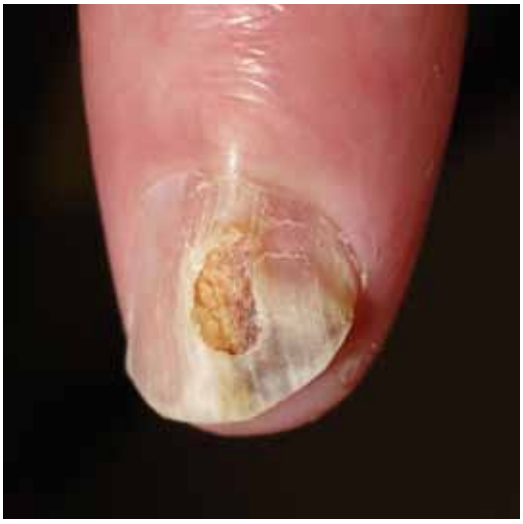


Fig1 - *Tented nail plate with hole centrally and hyperkeratosis beneath with onycholysis.*
© D. De Berker

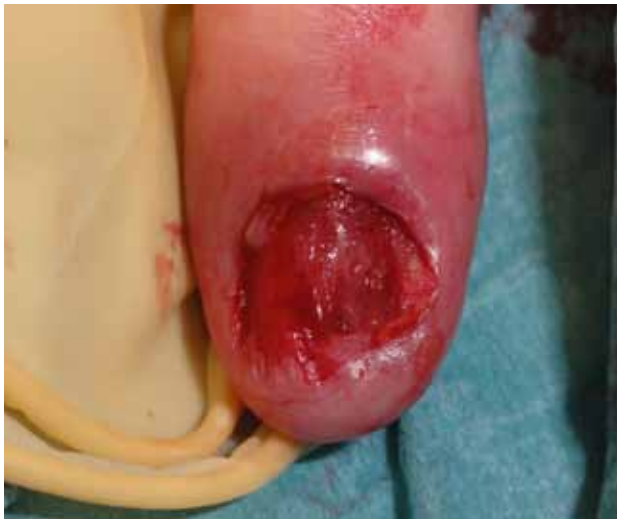


Fig2 - *Fleshy mass in junction of nail bed and matrix revealed by nail avulsion.* © D. De Berker

A 72 year-old man presented to the dermatologist with a dystrophic right little finger nail. He had been treated with topical antifungal and systemic antibiotic by his primary care physician the year before. Clippings for mycology were negative. The GP had curetted the area four months earlier with a clinical diagnosis of pyogenic granuloma. After good healing, the nail did not fully settle and there was continued distortion and a hole within the nail plate **(Fig 1)**. There was no pain. There were no other significant medical or dermatological diagnoses with the patient taking a statin and aspirin. The other nails were all normal. No histology was obtained from the original curettage by the initial clinician.
The clinical differential was broad, but included malignancy, given that this was a single digit dystrophy. Hence a tissue diagnosis was necessary. Avulsion of the nail revealed a fleshy mass in the middle of the nail bed and distal matrix **(Fig 2)**.

What is your diagnosis and treatment?

Histology showed moderately differentiated invasive squamous cell carcinoma. The tumour involved the periosteum, and removal of the distal phalanx was chosen as the definitive treatment. A flap was fashioned from the digit pulp to fold over the stump. There were no problems during the post-operative period and the mobilization was good.

David DE BERKER

Clinical Case

Five possible diagnoses were considered in this case. The GP mainly considered fungus and pyogenic granuloma. A single digit onychomycosis of the finger can occur, but is uncommon, and would require confirmation by mycology, before assuming it to be the diagnosis. The risk of making a clinical diagnosis of onychomycosis, and treating it in the absence of positive mycology, is that a correct diagnosis may be delayed. The patient is subjected to the risks of taking systemic antifungal without the appropriate diagnosis. The second diagnosis was pyogenic granuloma. This was a reasonable diagnosis to make based on the patient's description, but indicated a substantial change from the initial presentation with onycholysis, and thus a dynamic pathology. Malignancy, such as amelanotic melanoma or squamous cell carcinoma, is always within the differential of pyogenic granuloma at any site and particularly at a subungual location.[1] It is therefore important to obtain histology for all surgical specimens. If pyogenic granuloma had been confirmed, a potent topical steroid might have been a further step in treatment.

At second presentation, the appearance would also have been sufficient for psoriasis. However, with the emphasis being on a single digit with some delay in the provision of a diagnosis, it was necessary to obtain histology. Squamous cell carcinoma of the digit can often be treated locally, without loss of the distal phalanx. Margin controlled excision, or formal Moh's micrographic surgery, is the option of choice.[2] This can require excision of the entire nail unit, due to damage to the central zones of the matrix, which then results in a permanent substantial split in the nail.

A diagnosis of subungual squamous cell carcinoma can correspond to other clinical problems, such as immune impairment or the presence of genital warts. Neither was the case in this instance. Human papilloma virus 16 and 18 is causal and can determine a range of patterns of disease involving other sites. However, in most instances, it is limited to one digit in the immune competent individual.

References

1- Piraccini BM, Bellavista S, Misciali C, Tosti A, de Berker D, Richert B. Periungual and subungual pyogenic granuloma. Br J Dermatol 2010;163:941-53.

2- Lecerf P, Richert B, Theunis A, André J. A retrospective study of squamous cell carcinoma of the nail unit diagnosed in a Belgian general hospital over a 15-year period. J Am Acad Dermatol 2013;69:253-61.

Bruno FOUILLOUX

Clinical Case

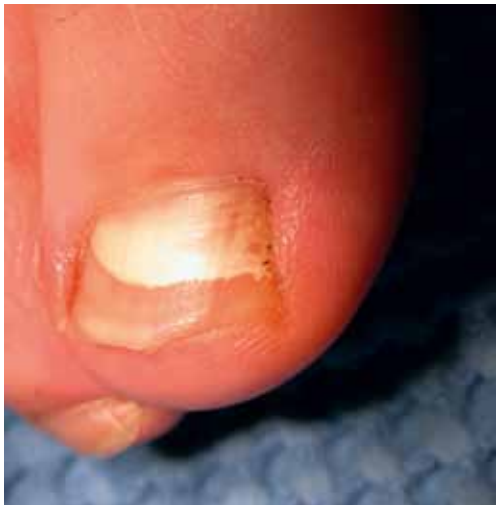


Fig1 - *Proximal white subungual onychomycosis. © B. Fouilloux*

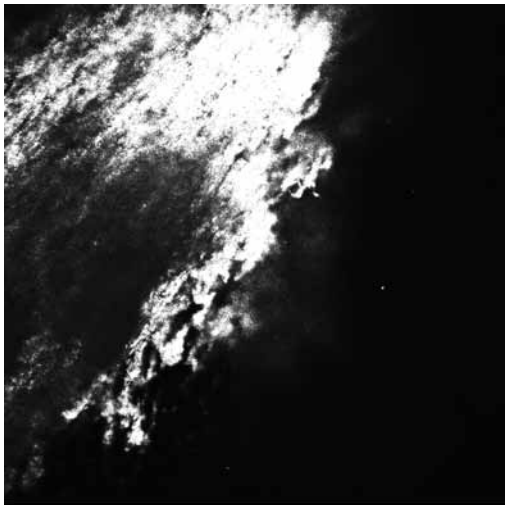


Fig2 - *RCM : spore like aggregates in the nail plate. © B. Fouilloux*

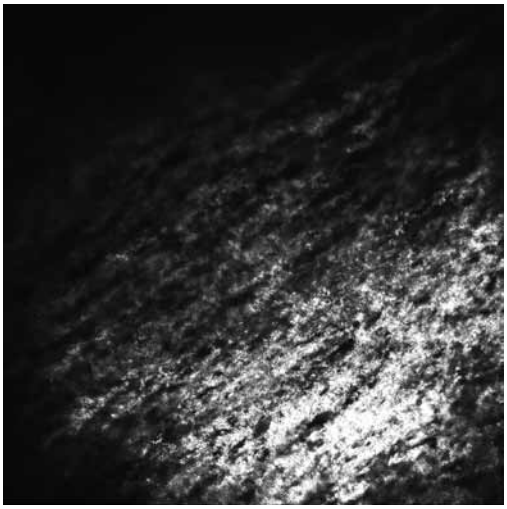


Fig3 - *RCM: thread like structures. © B. Fouilloux*

An 18 year-old woman was referred to our onychology consultation for a proximal leuconychia of the right great toe **(Fig 1)**. In dermatological examination there was no sign of mycotic infection anywhere else.
Eight months before, she had been treated for multifocal dermatophytosis, with positive mycological culture (*T. rubrum*), on the neck and in the toewebs.
This young woman had been followed for a Di George syndrome since her infancy.
Nail examination, using reflectance confocal microscopy (RCM), showed spore-like aggregates with high reflection **(Fig 2)**, and thread-like structures **(Fig 3)** which confirmed diagnosis of onychomycosis, previously suspected.
In contrast, despite curettage of the proximal nail plate, both direct microscopic examination and cultures were negative.

What is your diagnosis ?

Bruno FOUILLOUX

Clinical Case

Onychomycosis in young people is more frequent nowadays than 20 years ago. Practicing sports and tennis footwear are commonly advanced as favouring factors.[1,2] However, proximal onychomycosis is very uncommon in this population. Since the description of Noppakun[3], we know that proximal subungual onychomycosis has been reported as a type more frequently observed in immunodeficiency and especially AIDS. An immunodeficiency must be looked for when facing a proximal onychomycosis. In our case, the Di George syndrome was already known.

It is of great interest to have known that our young patient suffered from previous skin dermatophytosis, and to be aware of the responsible fungus (*T. rubrum*). Indeed, mycological culture is more difficult in proximal subungual onychomycosis, because of the depth and the thinness of the mycosis content at this level. Some studies have suspected a systemic way to explain proximal onychomycosis mechanism.[4]

Nevertheless a recent study in immunosuppressed children showed that onychomycosis is rare and the cases usually observed are white superficial onychomycosis.[5]

RCM appears as a very valuable investigation method. It allows the diagnosis of ony chomycosis in the case where routine mycology tests fail. A previous study has already established the superiority of this investigative imaging method.[6]

The Di George syndrome, so called velocardiofacial syndrome, is due to a deletion of chromosome22q11.2. It is clinically characterized by thymus and parathyroid hypoplasia, cardiac abnormalities, facial dysmorphia and palate cleft.[7] Although a large proportion of patients have an absent or hypoplastic thymus, most seem to have only a minor immune defect. Most studies have reported that patients show a reduction in the mean or median proportion and in the number of CD3 T cells and CD4 T helper cells compared with controls. The function of T cells is generally normal.

For this young woman, as the proximal matrix is infected, the best treatment is terbinafine.

References

1- Rodriguez-Pazos L, Pereiro-Ferreiros MM, Pereiro M Jr, Toribio J. Onychomycosis observed in children over a 20-year period. Mycoses 2011;54:450-3.

2- Leibovici V, Evron R, Dunchin M, Westerman M, Ingber A. A population-based study of toenail onychomycosis in Israeli children. Pediatr Dermatol 2009;26:95-7.

3- Noppakun N, Head ES Proximal white subungual onychomycosis in a patient with acquired immune deficiency syndrome. Int J Dermatol 1986;25:586-7.

4- Baran R, McLoone N, Hay RJ. Could proximal white subungual onychomycosis be a complication of systemic spread? The lessons to be learned from maladie dermatophytique and other deep infections. Br J Dermatol 2005;153:1023-5.

5- Teresa Garcia-Romero M, Lopez-Aguilar E, Arenas R. Onychomycosis in immunosuppressed children receiving chemotherapy.Pediatr Dermatol 2012;29:1-2.

6- Rothmund G, Sattler EC,Kaestle R, Fischer C, Haas CJ, Starz H, Welzel J. Confocal laser scanning microscopy as a new valuable tool in the diagnosis of onychomycosis - comparison of six diagnosis methods. Mycoses 2013;56:47-55.

7- Kobrynski L, Sullivan KE. Velocardiofacial syndrome, DiGeorge syndrome: the chromosome 22q11.2 deletion syndromes Lancet 2007;370:1443-52.

With many thanks to Dr Elisa Cinotti and Dr Dominique Serre.

Eckart HANEKE

Clinical Case

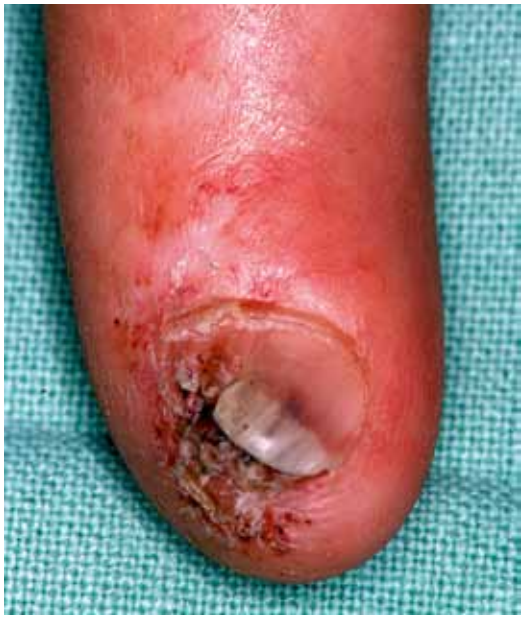


Fig1 - *Dystrophic nail plate partially deviated with an abnormal nail bed.* © E. Haneke

A 16-year-old girl presented with her parents for a severe onychodystrophy of her left index and middle finger **(Fig 1)**. The nail was small, radially deviated and partly onycholytic. The nail field was very small. The immediate periungual skin appeared smooth and shiny, the distal dorsal joint creases had disappeared and there were desquamation and rhagades covering more than half of the fingertip. The girl complained of dysaesthesia and cold sensitivity. No explanation for the condition could be given.

What is your diagnosis?

Insistence and re-questioning finally revealed that the girl had had ungual warts at the age of 9 years. These were first treated, in vain, by a dermatologist and the parents then consulted a paediatrician, who supposedly tried a number of remedies including suggestive treatment. As none were of help, she was finally referred to an elderly radiologist who was known for "healing everything" without side effects. Approximately 3 sessions were performed. No data were available as to the dose and voltage applied. The clinical diagnosis of radiation-induced permanent nail dystrophy and radiodermatitis was made. A plastic surgery repair was rejected by the parents.

Common warts are banal infections often seen in children and adolescents, but they may occur at any age. Ungual warts are mainly due to human papillomavirus types 1, 2, 4 and 7. It is generally said that a viral wart has a life-span of approximately 2 years with a period extending from 1 to 5 years. However, during this period, a wart may give rise to new daughter warts, thus a wait-and-see policy is usually not accepted by the patients and their parents.

As warts are self-limited benign lesions any therapy which is too aggressive and has a risk of life-long scarring, is contraindicated. Thus conservative treatments are commonly prescribed. Even though there are hundreds of therapeutic recommendations, hardly any give a guarantee of cure.

Eckart HANEKE

Clinical Case

In the past, ionizing radiation was used for many conditions and thus also for warts. The partisans of wart radiotherapy claimed that this was a short, effective and clean treatment without serious adverse effects.

Common warts are often notoriously resistant to treatment. Many physicians have their own treatment approaches according to their own, and sometimes even family, experience. Keratolytics such as solutions, creams, ointments or varnishes are the most commonly prescribed. Others use cytotoxic drugs hoping to have a virustatic effect and others use lasers or cold-steel surgery. Immunostimulation with purified protein derivative or other substances has been tried. Interferons were injected.[1] Local immunotherapy with sensitizing chemicals, such as dinitrochlorobenzene – no longer used because of potential mutagenic effects – squaric acid dibutyl esther or diphenylcyclopropenone[2] were reported to have been effective in a number of cases. Recently, topical immunotherapy with imiquimod, after aggressive keratolysis, was advocated. Intralesional bleomycin is judged to be the most effective treatment for periungual warts by other groups,[3] but the treatment is very painful and risks permanent nail dystrophy when not performed with the utmost care. Cidofudir topically was reported to be highly active [4], but the price of a compounded cidofudir preparation is virtually prohibitive. Sinecatechins from plants were recently approved for wart and condyloma treatment.[5]

Histopathology of radiodermatitis depends on the duration and stage of the disease. There is a sclerosis of the dermis and epidermal atrophy, sometimes with areas of hypertrophy. Cellular atypia and inflammation may also be seen **(Fig 2)**.

Although radiotherapy rules have dramatically changed in the last 50 years, and X-rays are fortunately no longer the treatment of choice for a variety of benign lesions, the physician has to be aware that, even now, radiotherapy may be used as a magic bullet for wart treatment, particularly by elderly colleagues, who still have a radiotherapy machine in their practice. As long as Grenz rays were applied – either as a physical treatment or as a placebo method – the long-term sequels went mostly unnoticed by the medical community. However, in case of a treatment, as in our patient, the consequences are catastrophic, and physicians should be conscious of the fact that malignant degeneration may occur years or even decades later.

Recently imiquimod was used to successfully treat radiodermatitis of the hands and nails.[6]

References

1- Al-Zahrani D, Raddadi A, Massaad M, Keles S, Jabara HH, Chatila TA, Geha R. Successful interferon-alpha 2b therapy for unremitting warts in a patient with DOCK8 deficiency. Clin Immunol. 2014 Apr 15. pii: S1521-6616(14)00090-4. doi: 10.1016/j.clim.2014.04.005.

2- Choi Y, Kim do H, Jin SY, Lee AY, Lee SH. Topical immunotherapy with diphenylcyclopropenone is effective and preferred in the treatment of periungual warts. Ann Dermatol 2013;25:434-439

3- Herschthal J, McLeod MP, Zaiac M. Management of ungual warts. Dermatol Ther 2012;25:545-550

4- Cleary A, Watson R, McMahon CJ. Successful treatment of refractory cutaneous warts using topical 3% cidofovir in a child after heart transplant. J Heart Lung Transplant 2014 Feb 14. pii: S1053-2498(14)00974-7

5- Stockfleth E1, Meyer T. Sinecatechins (Polyphenon E) ointment for treatment of external genital warts and possible future indications. Expert Opin Biol Ther 2014 Apr 28. [Epub ahead of print]

6- López V, Alonso V, Jordá E. Efficacy of topical imiquimod 5% in a patient with chronic radiodermatitis on the hands. Actas Dermosifiliogr 2012;103:441-442

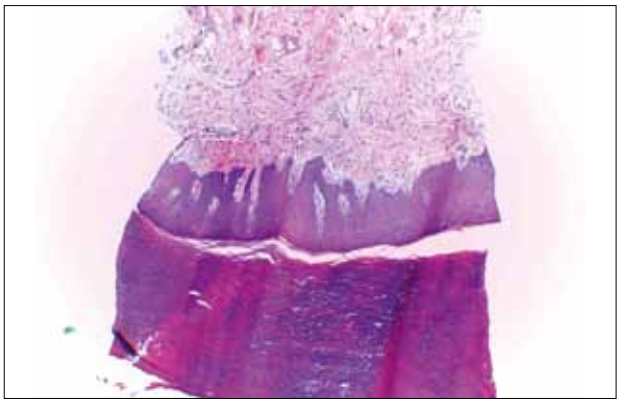


Fig2 - *Scanning view of a biopsy from the radial aspect of the proximal nail fold of the left index finger. There is considerably hyperkeratosis and acanthosis of the epidermis as well as telangiectasiae. © E. Haneke*

Jose Maria MASCARO

Clinical Case

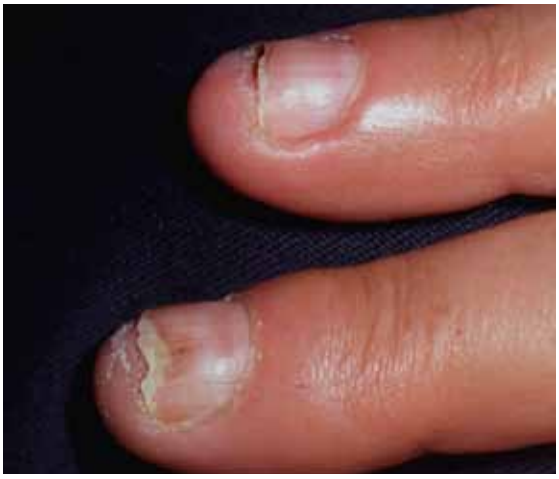


Fig 1 - *Painful keratotic growth under the median nail plate. © JM. Mascaro*

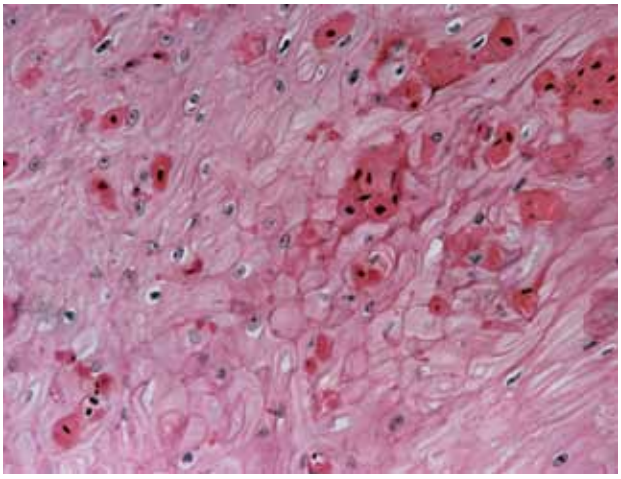


Fig 2 - *Epithelial squamous proliferation with conspicuous dyskeratosis. © JM. Mascaro*

A 47 year-old woman, with a history of many self regressive subungueal "warts" on her fingers nails, presented with a six month painful keratotic growth, which had recently decreased, under the left median nail plate **(Fig 1)**. X ray examination showed a scalloped osteolytic lesion of the underlying phalanx. A biopsy revealed the presence of an epithelial squamous proliferation with conspicuous dyskeratosis **(Fig 2)**.

What is your diagnosis?

Jose Maria MASCARO

Clinical Case

Taking into consideration the antecedent of previous multiple lesions, diverse diagnoses could be taken into consideration, particularly: viral wart (VW), squamous cell carcinoma (SCC) and keratoacantoma (KA).
VW do not usually produce underlying osseous lesions with the exception of the rare *carcinoma cuniculatum* of the sole in the spectrum of HPV-induced carcinoma. SCC is usually a single tumor and multiple cases are not limited to the subungueal area. On the other hand subungueal KA is usually painful and may produce osseous invasion. Multiple painful KA-like tumors have been associated with *incontinentia pigmenti* (STIP) and therefore this was the presumed clinico-pathological diagnosis.
In fact, the patient's daughter had had a blistering disease in babyhood, identified as IP, and she still had typical pigmentary vestiges of that disorder. Moreover the patient's mother, as well as her daughter, had suffered from partial hypodontia.
Clinical examination of the patient revealed severe nail fingers dystrophies from past keratoacantomas **(Fig 3)** and hypochromic sequellae of her own IP rash on the left lower limb.

Comment and follow up of the patient

Incontinentia pigmenti is a well-known X-linked disease associated with a NEMO gene mutation presenting multisystemic manifestations. Additionally to the early typical outbreak of linear vesiculobullous lesions, that later mutate to verrucous and dyschromic changes, patients may present with other manifestations: ocular (retinal pseudoglioma, cataract, optic atrophy), neurologic (mental retardation, seizures, spastic di or tetraplegia), squelettal (scoliosis, skull anomalies). Partial anodontia is common and could be the clue to recognizing affected women, who carry the syndrome in a family with IP cases.
In 1966 Hartman et al [1] reported the development of painful self-healing subungueal keratotic tumors associated with IP (STIP). Other reports [2-7] confirmed this association and some authors categorized these lesions as KA.
In our case, etretinate 25mg / day was prescribed, based on the long term efficacy of systemic retinoids in patients who develop multiple squamous cell carcinoma (as in xeroderma pigmentosum and epidermodysplasia verruciformis). The treatment was well tolerated with no significant side effects (only moderate cholesterol increase and cutaneous and labial dryness were noted and easily controlled). Eighteen months later no new STIP had appeared.
This case illustrates how a nail alteration could be linked to a genetic multisystemic disorder. On the other hand, subungueal KA (or KA-like STIP) must be taken into consideration and treated because, in spite of their self-healing tendency, they are able to produce not only pain, but underlying bone alterations and cause a significant decrease in a patient's quality of life. Systemic retinoids could be useful in controlling these neoplasms.

References
1- Hartman DL. Incontinentia pigmenti associated with subungual tumors. Arch Dermatol 1966;94:632-635.
2- Piñol J, Mascaro JM, Herrero C et al. Tumeurs sous unguéales dyskératosiques douloureuses spontanément résolutives. Ses rapports avec l'incontinentia pigmenti. Ann Derm Syphil 1973;100:159-168.
3- Mascaro JM, Palou J, Vives P. Painful subungual keratotic tumors in incontinentia pigmentil. J Am Acad Dermatol 1985;13: 913-918.
4- Malvehy J, Palou J, Mascaro JM. Painful subungual tumors in incontinentia pigmenti, Response to treatment with etretinate. Brit J Dermatol 1998;138:554-555.
5- Montes CM, Maize JC, Guerry-Force ML. Incontinentia pigmenti with painful subungual tumors. J Am Acad Dermatol 2004;50:S45-52.
6- Young A, Manolson P, Cohen B et al. Painful subungal dyskeratotic tumors in incontinentia pigmenti, J Am Acad Dermatol 2005;52:726-729.
7- Donati P, Muscardin L, Amantea A et al. Detection of HPV-15 in painful subungual tumors of incontinenhtia pigmenti: successful topical therapy with topical therapy with retinoic acid. Eur J Dermatol 2009;19:243-247.

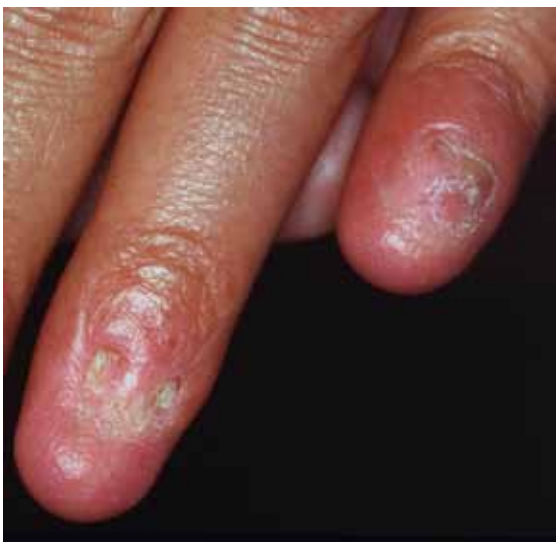


Fig 3 - *Nail fingers dystrophies from past similar lesions.*
© JM. Mascaro

Marcel PASCH

Clinical Case

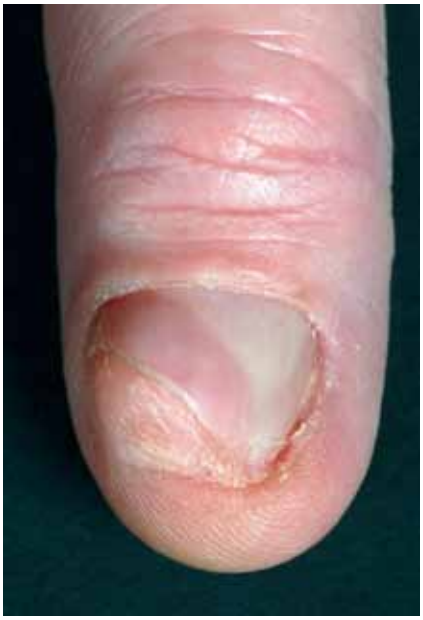


Fig1 - *A solitary erythematous elastic tumour under the lateral side of the left thumb nail. © M. Pasch*

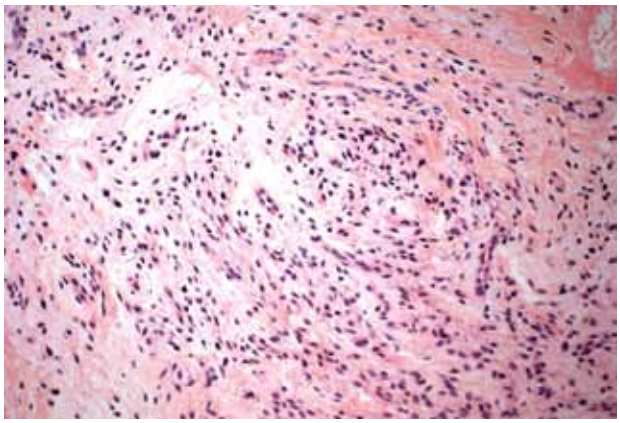


Fig2 - *A partly fibrous dermis with a deep uncapsulated proliferation of short fusiform and spindle-shaped cells in a myxoid stroma. © M. Pasch*

A 39-year-old female visited our out-patient clinic with a slowly growing tumour under her left thumb nail. There was no history of trauma or any other provoking factor. Her dermatological and general medical history did not give any additional clues. Examination revealed a solitary erythematous elastic tumour under the lateral side of her left thumb nail **(Fig 1)**. Our differential diagnoses were a subungual exostosis, a subungual fibroma, or a primary or metastatic malignant disease. X-ray examination ruled out an exostosis, but revealed a partly sclerotic and poorly demarcated irregularity of the corona ungualis.

A diagnostic biopsy was performed and histopathology showed an uncapsulated dermal proliferation of spindled cells without mitoses or any relevant cytonuclear atypia, immersed in a myxoid stroma. A CD34 staining was inconclusive. The spindled cells were negative for actin, desmin, MART, pan-keratines and factor 13A. MIB-1 revealed a low proliferation index. No certain diagnosis was made, - possibly a reactive fusiform lesion.

At that time Professor Eckart Haneke was my teacher in nail surgery and we decided to excise the complete lesion. The tumour was dissected and excised after lateral reflection of the nail plate. Histopathology showed a partly fibrous dermis with a deep uncapsulated, but sharply demarcated, proliferation of short fusiform and spindle-shaped cells in a myxoid stroma. The stroma contained many capillaries, but no inflammatory infiltrate. The lesion did not show pleiomorphism, mitotic activity or necrosis **(Fig 2)**. The tumour cells were positive for vimentin and CD34. Actin was only present in the vessels, and the pankeratin staining was negative, as well as S100 and EMA (epithelial membrane antigen). The MIB-1 staining revealed a low proliferative activity.

What is your diagnosis?

Marcel PASCH

Clinical Case

The soft tissue tumour in our patient was first described by Fetsch in 2001: a superficial acral fibromyxoma, also known as acral (or digital) fibromyxoma. This benign neoplasm has a predilection for the subungual or periungual region of the hands and feet. However, the heel, palm, and ankle can also be affected. The clinical characteristics have been described in a case-series of 124 patients (Hollmann et al, 2012)[3] and has shown a slight male predominance (1.3:1; 70 males, and 54 female). The age at diagnosis ranged from 4 to 86 years, with a mean of 48 years and a median of 49 years. Each patient presented with a solitary mass, often slowly growing over many months or years. Presentation can be variable; 41% of these patients presented with a painful mass, 39% with an asymptomatic mass, 9% with bleeding and 2% with infection. Nail deformity, as in our patient, occurred in a small minority of patients - 9%. The vast majority of the tumours arose on the hands (52%) or feet (45%), with most arising on the digits (94% of hand lesions and 82% of foot lesions). Of the digital tumours with specific localization, 97% of finger tumours and 96% of toe tumours occurred near the nail apparatus.

Complete surgical excision is the treatment of choice. Local recurrence rates are high with incomplete excision (up to 24%). No malignant transformation has been reported (Hollmann et al 2012).[3]

The tumours pose a diagnostic problem for pathologists, resulting in misclassification and overtreatment (Hollmann et al 2012).[3] Histologically a proliferation of CD34-positive spindle-shaped or stellate-shaped fibroblast-like cells with pale eosinophilic cytoplasm and a random or loosely fascicular growth pattern may be found. Most tumours (80%) are poorly marginated. The overlying epidermis may be hyperkeratotic (Ashby-Richardson H et al, 2011).[1] The majority of tumours show alternating areas of fibrous and myxoid stroma, with a minority showing predominantly fibrous or myxoid features. An increase in mast cells or the presence of prominent capillaries may be seen. Because the myxoid areas of digital fibromyxoma are more cellular than myxoma, and the remarkable capillary proliferation is uncommon in myxoma, the term "myxoma" should be avoided. It should be used only in the very hypocellular, myxoid morphology common to solitary cutaneous myxoma, dermal mucinosis, or intramuscular myxoma. Immunoflouresence reveals immunoreactivity for CD34 (most with strong, diffuse expression) in 70%. All digital fibromyxomas seem to be negative for S100.

The differential diagnosis mainly comprises neurofibroma, acquired digital fibrokeratoma, periungual/subungual fibroma, and dermatofibroma, but also myxoid tumours like low-grade fibromyxoid sarcoma, myxofibrosarcoma, dermatofibrosarcoma protuberans, synovial sarcoma, myxoid neurofibroma, perineurioma and superficial angiomyxoma. The distinction between digital fibromyxoma and malignant myxoid tumours is important, since the latter often have a protracted clinical course characterized by multiple recurrences and metastasis (Hollmann, 2012).[3]

To summarize, digital fibromyxoma is a distinct, cutaneous spindle cell neoplasm with a striking predilection for the subungual or periungual region of the hands and feet. Complete excision is mandatory in order to prevent local recurrences.

References

1- Ashby-Richardson H, Rogers GS, Stadecker MJ. Superficial acral fibromyxoma: an overview. Arch Pathol Lab Med. 2011;135(8):1064-6.

2- Fetsch JF, Laskin WB, Miettinen M. Superficial acral fibromyxoma: a clinicopathologic and immunohistochemical analysis of 37 cases of a distinctive soft tissue tumor with a predilection for the fingers and toes. Hum Pathol. 2001;32(7):704-14.

3- Hollmann TJ, Bovée JV, Fletcher CD. Digital fibromyxoma (superficial acral fibromyxoma): a detailed characterization of 124 cases. Am J Surg Pathol. 2012;36(6):789-98.

(This case partly has been presented at the Scientific Meeting of the Dutch Society for Dermatology and Venereology, 2007: [A rare subungual tumour]; Kroft EBM, Haneke E, Pruszczynski M, Blokx WAM, Pasch MC)

Bianca Maria PIRACCINI

Clinical Case

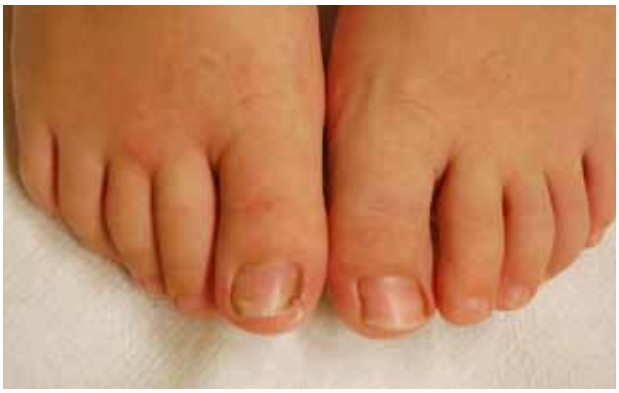


Fig1 - *Mild distolateral nail ingrowing of the 1st toenails in a 4 year- old girl. © BM. Piraccini*

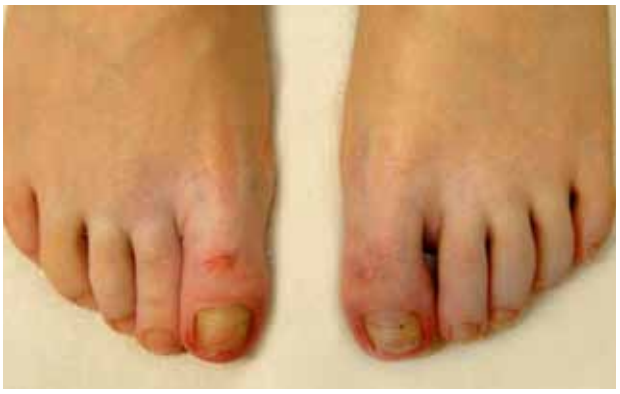


Fig2 - *Same patient as Fig1, showing diffuse skin hypopigmentation involving the dorsum of the feet and the digits after a 4-months application of high potency topical glucocorticosteroids. Note the presence of Beau's lines due to shoe trauma to the distal nail. © BM. Piraccini*

A 4 year-old Caucasian girl was referred to us for impaired deambulation caused by a 3 month inflammation of both the great toenails. Clinical examination revealed mild inflammation of the nail folds and a malalignment of the nail plates, that the mother confirmed as having been present since birth **(Fig 1)**. We made a diagnosis of mild nail ingrowth due to congenital malalignment of the great toenails and hypertrophy of the lateral folds.
Treatment consisted in daily warm soakings, followed by a downward massage of the lateral fold with high potency topical glococorticosteroids (clobetasol propionate ointment). After 4 months of treatment, the inflammation of the nail folds was resolved, but the child had developed a diffuse, not defined, skin hypopigmentation of the nail folds and toes **(Fig 2)**. The mother had noticed the gradual appearance of this hypopigmentation after the second month of topical glococorticosteroid application. When asked, she stated that sometimes she was not so precise in the application of the cream, which was often used in high quantity and applied extensively over the toes. Clobetasol propionate cream was discontinued and local treatment with vitamin E was started. Skin hypopigmentation resolved 6 weeks later without any other local complications.

What is your diagnosis?

Bianca Maria PIRACCINI

Clinical Case

Reversible skin hypopigmentation after topical application of high potency glucocorticosteroids.

Topical glucocorticosteroids are currently the most frequently prescribed topical treatment in the management of inflammatory skin disorders. Hydrocortisone was the first molecule successfully used in 1952 by Sulzberger.[1] During the following decades, research on these drugs allowed the introduction of new molecules, where modifications of the basic chemical structure led to an increase in potency. Therefore topical glucocorticosteroids have been divided into various classes, depending on their potency, and evaluated on the basis of vasoconstrictor assay and comparative clinical trials. Topical glucocorticosteroids act with multiple mechanisms of action including anti-inflammatory, immunosuppressive, antiproliferative and vasoconstrictive effects, responsible for the improvement of skin disorders associated with inflammatory signs. However, the same properties can lead to an adverse effect.

In the literature, both local and systemic side effects have been documented with the use of topical glucocorticosteroids, even if local complications are more prevalent than systemic reactions. Hypopigmentation is a common side effect, but it is often not noticed.[2-3]

In the child described here, reversible skin hypopigmentation appeared on the treated skin and it was due to the fact that the patient's mother had applied clobetasol propionate ointment inaccurately, not only in the nail folds, but also on the toes. In this case, high potency topical glucocorticosteroids were prescribed to decrease inflammation and also to induce some skin atrophy of the inflamed hypertrophic lateral folds. Topical glucocorticosteroid-induced hypopigmentation of the periungual tissues can however, also occur in patients who use their hands to apply high potency steroids for treating other body areas **(Fig 3)**. This side effect is rarely described in literature, which contains many case reports about cutaneous hypopigmentation after intralesional injections of corticosteroids.[3-6]

Hypopigmentation due to topical glucocorticosteroids occurs more commonly in dark-skinned people. It has been hypothesized that the drugs act directly on the synthesis of melanin by smaller melanocytes.

In order to avoid this side effect, patients should be instructed to use the exact prescribed amount of the drug, treating only the diseased skin. When the hands are used to apply topical glucocorticosteroids on other body areas, the use of protective gloves should be advised or, alternatively, hands should be carefully washed after the procedure.

References

1- Sulzberger Mb, Witten Vh. The effect of topically applied compound F in selected dermatoses. J Invest Dermatol. 1952;19:101-2.
2- Hengge UR, Ruzicka T, Schwartz RA, Cork MJ. Adverse effects of topical glucocorticosteroids. J Am Acad Dermatol. 2006; 54:1-15.
3- Say EA, Shields CL, Bianciotto C, Shields JA. Perilymphatic subcutaneous fat atrophy and cutaneous depigmentation after periocular triamcinolone acetonide injection in a child. JAAPOS. 2011;15:107-8.
4- Saour S, Dhillon BS, Ho-Asjoe M, Mohanna PN. Ascending hypopigmentation of the forearm following injection of triamcinolone. J Plast Reconstr Aesthet Surg. 2009; 62: 597-8.
5- Nanda V, Parwaz MA, Handa S. Linear hypopigmentation after triamcinolone injection: a rare complication of a common procedure. Aesthetic Plast Surg. 2006; 30: 118-9.
6- Evans AV, McGibbon DH. Symmetrical hypopigmentation following triamcinolone injection for de Quervain's tenosynovitis. Clin Exp Dermatol. 2002; 27: 247-51.

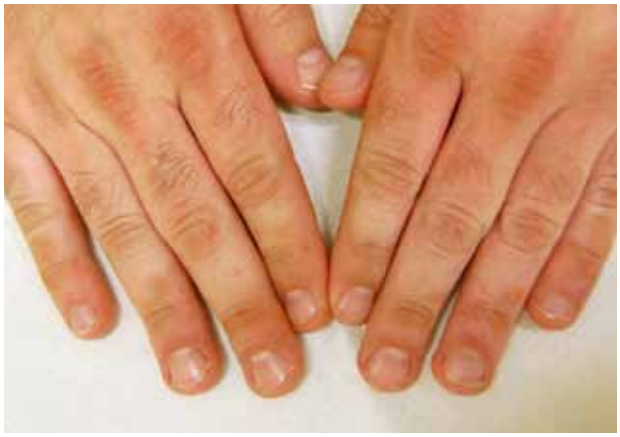


Fig3 - *Irregularly distributed skin hypopigmentation of the dorsum of the hands of a 30 year-old man, who for 3 months had been applying daily high potency topical glucocorticosteroids in scalp areas affected by alopecia areata. © BM. Piraccini*

Bertrand RICHERT

Clinical Case

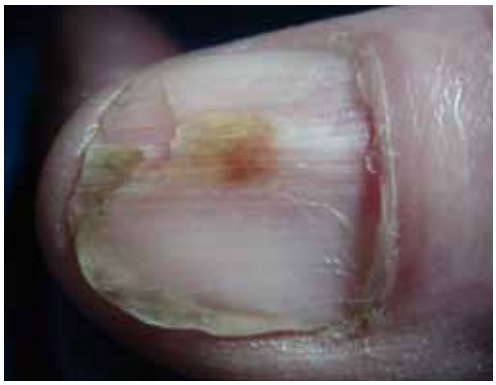


Fig1 - *Distal lamellar splitting and proximal brown notch. Note the discrete longitudinal ridge emerging from under the proximal fold. © B. Richert*

This 58 year-old man was referred to our nail consultation for a problem on his right thumb, which had been present for several years. He had visited several dermatologists and no diagnosis had ever been made. The last one he had seen thought it may be a subungual tumour and asked for an X-ray. This was normal with discrete joint alteration evoking osteoarthritis.
Clinically, the thumbnail showed a severe lamellar splitting at the distal edge, with a brown notch at its most proximal part. The discoloured patch was located in the midline and was overlying a discrete longitudinal ridge emerging from under the proximal fold **(Fig 1)**.

What is your diagnosis and management?

The clinical picture evoked a submatricial myxoid pseudocyst (also called type C). Avulsion confirmed the diagnosis **(Fig 2)**.
Myxoid pseudocysts (MPC) are common nail tumours and it is now believed that they occur from a leakage of synovial fluid through a breach in the joint capsule of the distal interphalangeal joint.[1] This phenomenon is promoted by osteoarthritis and radiologic evidence of primary interphalangeal osteoarthritis is noted in about three quarter of the cases.[2]
Fingernails are mainly affected, but involvement of toenails is possible. Their clinical features depend upon their location at the nail apparatus. De Berker classified them in three subtypes:[3]
• **Type A:** in this most common presentation, the MPC presents as a translucent, dome-shaped, smooth-surfaced, asymptomatic nodule arising on the dorsum of the digit, located laterally to the midline, between the crease of the distal interphalangeal joint and the proximal nail fold [4] **(Fig 3)**.
• **Type B:** the MPC is located under the proximal nail fold. Longitudinal grooving of the nail plate facing the MPC results from pressure on the underlying matrix. The groove often varies in depth according to the fluctuant volume of the cyst **(Fig 4)**. A small keratotic tip protruding from under the proximal nail fold may be observed.
• **Type C:** in some rare instances, the MPC may extend beneath the matrix and is more difficult to recognize. The findings of a red lunula, an isolated pincer fingernail, and a variable destruction of the proximal part of the nail plate should suggest the diagnosis. Distal splitting is not a common finding - as in our case. The longitudinal ridge is a more evocative feature.
MPC are usually solitary, but multiple MPC may occur in the same individual.[2] It is the unsightly aspect that bothers the patient more than the pain. Diagnosis is clinical in types A and B. In case of doubt, a puncture with a 16G needle will allow some translucent jelly to pop out **(Fig 5)**. MRI is a useful tool in this condition for several reasons: it allows accurate diagnosis, especially in the submatricial form and demonstrates the existence of a peduncle between the cyst and the distal joint in about 85 % of cases.[5] The main differential diagnosis is fibrokeratoma in subtype B.
Numerous treatments have been recommended for this affection. Their aim is to obliterate the leakage from the joint, by inducing a fibrosis around the capsule. For the fearful and the elderly, a non aggressive approach should be proposed: repeated drainage associated with compressive dressings for several months were shown to have a cure rate of 72% [6] and after drainage, 2 cycles of 20 seconds of cryotherapy followed by compressive

Bertrand RICHERT

Clinical Case

dressings resulted in a cure rate of 56 to 86%.[7] Audebert proposed a treatment with injection of sclerosants.[8] Even if successful in a large number of cases, its use should be avoided due to severe unexpected side effects (permanent nail dystrophy, joint stiffness). CO2 laser was tried in a small series and more recently infrared coagulation was proposed. None of these techniques has been able to reach the high rate of success (over 95 %) achieved with surgery. Methylene-blue guided surgery for ligature of the leak of joint fluid is a very elegant, quick and effective technique, as it provides a very high success rate on the fingers (94 %). On the toes, the technique reaches only 57 %, probably because, in this location, the pressure of fluid escaping from the joint is increased by the weight of the standing position.[9] This procedure is also very comfortable for the patient. For submatricial location (type C) repeated drainages with firm dressings should be tried first for several weeks. Otherwise the methyl blue procedure is indicated.

References
1- de Berker D, Lawrence C. Ganglion of the distal interphalangeal joint (myxoid cyst): therapy by identification and repair of the leak of joint fluid. Arch Dermatol 2001;137:607-10.
2- Lin Y-C, Wu Y-H, Scher RK. Nail changes and association of osteoarthritis in digital myxoid cyst. Dermatol Surg 2008;34:364-9.
3- de Berker D, Goettman S, Baran R. Subungual myxoid cysts: clinical manifestations and response to therapy. J Am Acad Dermatol 2002;46:394-8.
4- Mani-Sundaram D. Surgical correction of mucous cysts of the nail unit. Dermatol Surg 2001;27:267-8.
5- Drapé JL, Idy-Peretti I, Goettmann S, Salon A, Abimelec P, Guérin-Surville H, et al. MR imaging of digital mucoid cysts. Radiology 1996;200:531-6.
6- Epstein E. A simple technique for managing digital mucous cysts. Arch Dermatol 1979;115:1315-6.
7- Böhler-Sommeregger K, Kutschera-Hienert G. Cryosurgical management of myxoid cysts. J Dermatol Surg Oncol 1988;14:1405-8.
8- Audebert C. Treatment of mucoid cysts of fingers and toes by injection of sclerosant. Dermatol Clin 1989;7:179-81.
9- de Berker D, Lawrence C. Ganglion of the distal interphalangeal joint (myxoid cyst): therapy by identification and repair of the leak of joint fluid. Arch Dermatol. 2001;137:607-10.

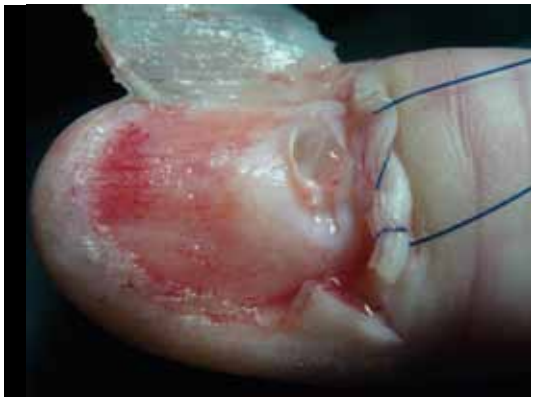


Fig2 - *Avulsion and incision of the distal matrix confirms the diagnosis. © B. Richert*

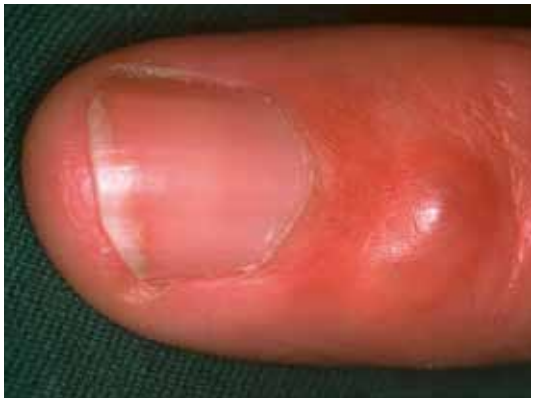


Fig3 - *Myxoid Pseudocyst type A. © B. Richert*

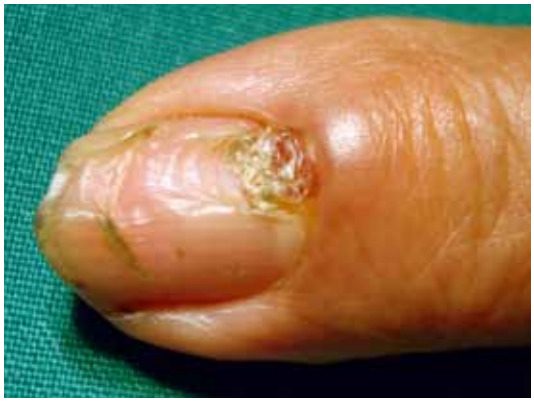


Fig4 - *Myxoid Pseudocyst type B. © B. Richert*

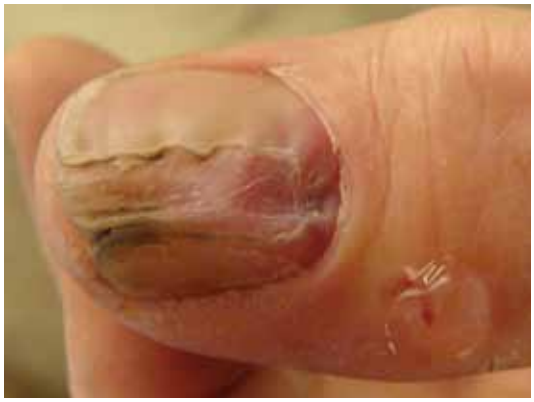


Fig5 - *Translucent jelly pops out when pricking the pseudomyxoid cyst. © B. Richert*

The nail - What's new ? n°7

Continuing Medical Education

David DE BERKER

PARONYCHIA

Paronychia means inflammation of the soft tissues surrounding the nail. Historically this meant the lateral and proximal nail folds, but some interpretations would extend this to the distal pulp and nail bed. The inflammation can arise through four pathological processes, which often overlap so that one or more may be present in a clinical presentation. The four are: inflammatory, infective, traumatic and neoplastic. The primary diagnostic entities are usually eczema or psoriasis, staphylococcus aureus, ingrowing, nail biting or nail fold biting and squamous cell carcinoma (usually in situ). The disease can be chronic or acute, with the aetiology often being the main determinant. If we take four scenarios and examine the factors involved we can provide an overview of the topic.

CASE 1: [1]

A 33-year-old hairdresser presents with ridging of the nails and soreness of the proximal nail fold. He has recently changed jobs from computer help desk to hairdresser. His hobby is gardening. After six months in his new work, he has problems with sore hands and in particular the nail folds and nails. He does not use gloves when working, but does use emollient on his hands at night. There are no skin problems elsewhere, although he had eczema as a child and he has asthma. The patient is not aware of any allergies to products used in the work place.
On examination, the 5 nails of his dominant hand have transverse ridges and he has redness of the proximal nail fold with loss of cuticle. The thumb and index finger are affected on the non-dominant hand. The nail fold is "bolstered", which means that it is swollen with a heaped up quality and slightly retracted away from the nail. A gap can be seen between the nail fold and the dorsum of the nail. The skin on his hands is a little red with some cracking of the digit pulps, but otherwise normal **(Fig 1).**

The background here is of someone with a low threshold for eczema, given the atopic background, and who recently started work with a high level

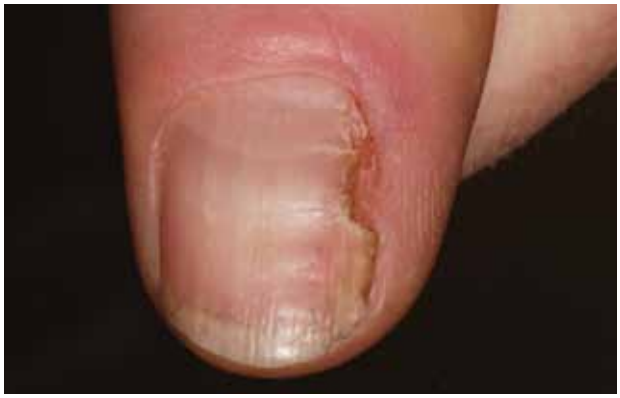


Fig1 - *Chronic paronychia of the proximal nail fold with loss of cuticle. © D. De Berker*

of exposure to irritants. Hairdressers have many hand problems and this often manifests around the nails. Many of them are also keen to have their nails manicured, as it is part of the "hair and beauty" culture. Manicure may entail manipulation of the cuticles and excavation of material from beneath the nail. In addition, hair cutting results in small spicules of cut hair that can be an additional irritant. There is a documented record of these creating foreign body reactions beneath and around the nail. A further potential hazard is allergic contact sensitivity to one of the products used in hair care. Although it is possible for such a presentation to be complicated by infection, it is rarely a major factor. Management entails adaptation of work to minimize exposure to wet materials and cleansing materials, wearing of gloves when undertaking any direct wet or hair work and good hand care with emollient, soap substitutes for washing and targeted steroid ointment. The emollient needs to be thick and should be applied frequently, particularly at night when it is supplemented with a potent steroid, such as clobetasol propionate ointment. It is rare for any antimicrobial therapy to be needed.
However, if there is concern about low grade infection, a short initial course of antibiotics, with or without a daily 5 minute antiseptic soak, can be helpful. Review at one month is needed to make sure that the use of the super potent steroid is effective and a plan is established to reduce it, but at the same time the hand care and emollient therapy practices are reinforced. In the longer term, he will need to

David DE BERKER

PARONYCHIA

recognize that, unless he is able to control this disease in ways other than by using a potent steroid, he will not be able to continue this job. If there is little or no progress with the above, treatment patch testing may be indicated and in some instances could be part of the initial work up.

Variants of this presentation include people with frequently wet hands, typically as part of domestic or food preparation work. In this setting Candida is sometimes implicated, and although it can be relevant as an exacerbating factor, the management plan above will usually work, without recourse to specific anticandidal therapy.

CASE 2:

Infective paronychia is uncommon, usually acute and associated with a precipitating activity or event. It can be a complication of one of the other variants of paronychia and in particular associated with nail biting.

A 12-year old boy presents with a three day history of a sore inflamed index finger. He is a nail biter and this includes biting the lateral nail folds and cuticles. His general health is good and he takes no medication.

On examination, there is redness involving one lateral nail fold and the proximal nail fold. The finger is slightly swollen in comparison with the contralateral digit. There is a small yellow focus pointing at the surface. The subungual space is not involved.
Management entails the option of drainage, coupled with systemic antibiotics. Flucloxacillin, or similar, for 7 days is usually adequate, but if the pus is not drained it may be necessary to extend the course. Drainage is medically preferred, but not every 12-year-old boy will tolerate it. A quick lancing of the surface, after alcohol wipe, usually works and is relatively painless, leading to relief with decompression. Either EMLA or ethyl alcohol spray can help give confidence to the boy or the use of a small local proximal block, which could be to just one of the 4 longitudinal nerves of the digit, dorsally on the affected side. Pus should be cultured for sensitivities. It is then possible to use salt water baths, at least once a day, to ensure that there is no further collection of pus. The wound should be dressed daily and reviewed at 1 week.

If the subungual space is involved, there is more pain. If it is proximal and not draining, there is a risk of damage to the matrix, which could result in scarring. In that situation, the case for a proximal block and drainage is stronger, particularly if there is inadequate progress after 48 hours with antibiotics alone. This may be the right time to address the background issue of nail biting!

CASE 3: [2]

Trauma from ingrowing or picking of the nail fold can be inflammatory and painful with no frank infection. Ingrowing is generally seen in young adults or the elderly, but rarely those in between. The former in association with turgid digits, sharp nails and trauma associated with sport or footwear. The latter are usually associated with misshapen nails acquired over the years and sometimes complicated by peripheral œdema, which may precipitate a specific event.

A 22-year-old woman presents with a sore big toe. She is in good health, has tried wearing flat footwear and also daily salt water soaks, but it does not calm. Her brother had problems of ingrowing nails in the past and her father had his big toenails removed. She is keen on hockey, but due to this problem has not played for 6 months. The GP has tried 3 courses of oral antibiotics with no benefit. Most recently potent topical steroid was tried, but did not solve the problem.

On examination, there is ingrowing of the lateral nail with a sharp serrated nail embedding in a zone of increased granulation **(Fig 2)**. The toe is not inflamed, other than at this focus. The big toenail

David DE BERKER

PARONYCHIA

on the other foot is short and the edge is close to embedding.
There are multiple treatment options, including conservative management with cotton wool pledgets, plastic gutters and metal braces, which can be applied to the top of the nail in an attempt to eventually pull it out from the embedded tissue. However, this is a student, who is at home for 3 weeks and wants to return to sport quickly. She does not want anything that might fail. The most definite success comes from a lateral nail margin ablation with phenol and she has seen how this has worked for her brother. This

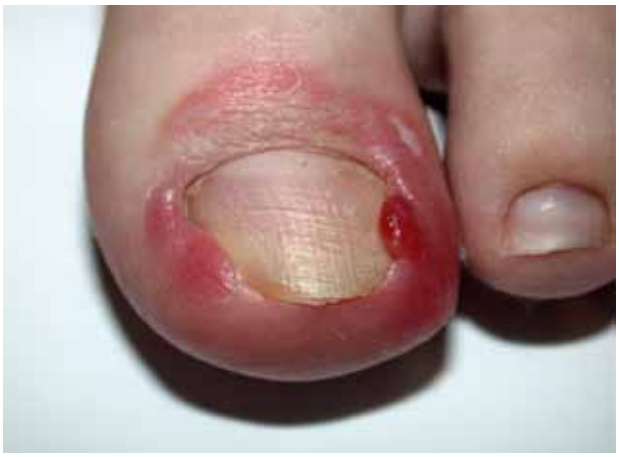


Fig 2 - *Lateral ingrowing, most marked on one side with inflammation and granulation tissue. Treatment on one side with lateral ablation will enable the other side to settle. © D. De Berker*

is what she chooses.
All conservative measures for managing ingrowing nails are effective to a degree, but if the prevailing anatomy and forces do not change, then the likelihood of relapse will be high. A family history is quite common and possibly reflects an inherited anatomical basis. The main drawback to surgery is that the phenol creates a burn that oozes for several weeks and sometimes even longer. This can be minimized by scrupulous cleaning of the surgical site each day to remove exudate and avoid trauma. Success rates are very high, typically > 95%. Advice on nail cutting to avoid a sharp corner near the lateral nail fold, may help prevent other nails from developing the same problem.

CASE 4: [3]

Bowen's disease of the nail fold can be misdiagnosed as paronychia, as it presents with the classic combination of redness, slight swelling, cracked skin, tenderness and sometimes oozes, especially if the disease extends beneath the nail. However, the distinguishing features are that it is truly chronic – usually having been present for more than 5 years. It is likely to have a clear margin detected on dermoscopy and it almost always only involves one digit in a middle-aged person.

A 64-year-old man presents with a sore right thumb, where the skin splits intermittently on the proximal nail fold. He has noted this for 4 years and there was an initial diagnosis of fungus, then paronychia, but with no response to topical therapies. He is well and works as a piano teacher.

On examination there is a zone of confluent red altered texture on the proximal nail fold and extending up one lateral nail fold. The cuticle is lost. The nail is slightly altered in line with the changes and there is a loss of nail production at the lateral edge **(Fig 3)**. Other nails and nail folds are normal. On dermoscopy, the redness is well demarcated. He has not suffered any oral or genital diseases and

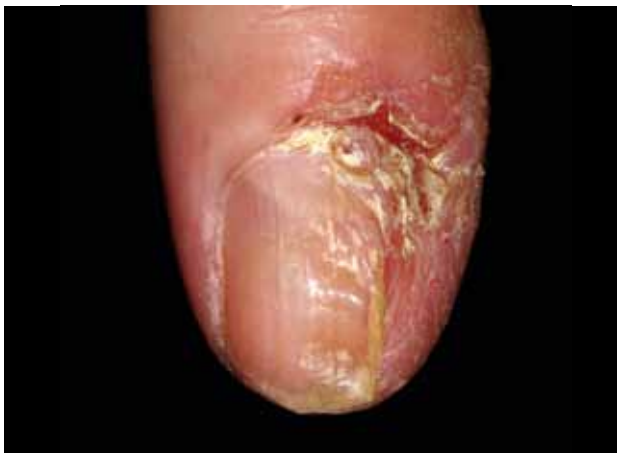


Fig3 - *Periungual Bowen's disease with cracking and loss of nail production on the margin where the matrix will be altered by in situ squamous cell carcinoma. © D. De Berker*

David DE BERKER

PARONYCHIA

denies having genital warts.
The expert opinion is that this is not a classic chronic inflammatory paronychia and requires a diagnostic biopsy. This can be done with a thin ellipse radiating from the nail fold and closed with 6.0 nylon suture. Histology confirms *in situ* squamous-cell carcinoma and the patient opts for surgical excision.

This requires management by someone experienced in the excision of periungual squamous cell carcinoma, because the mapping of the involved tissue often demonstrates disease that is more extensive than anticipated. It is common to lose part, or all, of the nail unit to achieve definitive treatment. Treatments, such as PDT or imiquimod or 5-fluorouracil, have a high chance of relapse and may ultimately commit the patient to more surgery, than if they had been surgically treated from the beginning. Both Mohs' and traditional serial excision with margin control can be used and repair can be by a full thickness graft or secondary intention. The former heals much more rapidly, but is best carried out when clearance is confirmed histologically, as excision may be in stages, according to the histological clearance. If histology suggests there is a deep component, either through invasion or hypertrophic Bowen's at the deep aspect and a clear margin cannot be demonstrated, removal of the distal phalanx will be necessary.

References
1- Montgomery BD. Chronic paronychia: putting a finger on the evidence. Aust Fam Physician 2006;35:811, 813.
2- Haneke E. Nail surgery. Clin Dermatol 2013;31:516-25.
3- Lecerf P, Richert B, Theunis A, André J. A retrospective study of squamous cell carcinoma of the nail unit diagnosed in a Belgian general hospital over a 15-year period. J Am Acad Dermatol 2013;69:253-61.

notes

Chief Editor Dr Christine CAZEAU
Published and distributed in 2014 by Pierre Fabre Dermatologie
Registration of copyright : September 2014

Composition Florence Richert - graphic designer - www.florencerichert.book.fr
Printed by Art & Caractère - Z.A. des Cauquillous - 87 rue Gutenberg - BP 80073 - 81502 LAVAUR cedex - France

Pierre Fabre
DERMATOLOGIE

Pierre Fabre
DERMATOLOGIE

ENS
European Nail Society

RICHERT*graphisme* 09/14 - 498158