Onychomycosis

19

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(The clinical photographs in this chapter are photographed by Dr Ranthilaka R. Ranawaka, consultant dermatologist, General Hospital Kalutara, Sri Lanka)

(1) A 45-year-old woman complained of easily breakable right toenail for more than 4 months.
   a. What is your diagnosis?
   b. What investigations would you do?
   c. What is the treatment?

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R. R. Ranawaka et al. (eds.), *Atlas of Dermatoses in Pigmented Skin*,
https://doi.org/10.1007/978-981-15-5483-4_19

(2) A 37-year-old housewife came with swelling and burning sensation of her finger nail folds.
   a. What is your diagnosis?
   b. What are the predisposing factors?
   c. What advice would you give the patient?
   d. What is the management?

(3) A 20-year-old girl is worried about her nails.
   a. What is this condition?
   b. What is the differential diagnosis?
   c. What is the non-invasive procedure you can do to differentiate?

(4) What is your diagnosis?
When you do not have facilities for fungal studies how do you assume the pathogens?

Left hand

Right hand

(5) What is your diagnosis?
How do you know whether paronychia is a primary or a secondary problem?

Answers

(1) Onychomycosis

Nail samples for fungal studies (microscopy and culture)

(2) Chronic paronychia

Frequent contact with water or wet environment (e.g., nail biting, finger sucking)

Avoid contact with wet conditions, keep hand dry

(3) Traumatic onycholysis

Onychomycosis

Onychoscopy (shows linear margin at the proximal edge)

(4) Total onychodystrophy

Prevalent fungi are assumed depend on the published studies conducted in that particular environment; e.g. in Sri Lanka it is either NDM or Candida onychomycosis, while in a subtropical country, dermatophyte is most likely.

(5) Proximal subungual onychomycosis with secondary paronychia

In onychomycosis Nail dystrophy is more marked and mostly confined to proximal nail plate. In contrast, in chronic paronychia, nail dystrophy occurs after long-standing paronychial disease (see question 2).

19.1 Introduction

Onychomycosis is fungal infection of the nails.

Causative Organisms

1. Dermatophytes—*T. rubrum*, *T. interdigitale*, and *E. floccosum*
2. Non-dermatophyte molds (NDM)—*Aspergillus* sp., *Fusarium* sp., *Scatilidium* sp., etc.
3. *Candida* sp.—*Candida albicans, Candida* non-albicans

Clinical Manifestations

Onychomycosis is divided into seven main patterns depending on where on the nail apparatus is and how the fungal infection is initiated (de Berker et al. 2016; Hay and Ashbee 2016).

1. Distal and lateral subungual onychomycosis (DLSO)
2. Superficial onychomycosis (SO)—white or black, transverse or patchy
3. Proximal subungual onychomycosis (PSO)—patchy, striate (transverse), longitudinal
4. Endonyx onychomycosis
5. Totally dystrophic onychomycosis (TDO)
6. Mixed onychomycosis; examples include the following on the same nail:
   a. DLSO plus SO
   b. SO plus DLSO
   c. SO plus PSO
   d. DLSO plus PSO
7. Paronychia with onychomycosis (usually DLSO or PSO)

Differential Diagnosis Psoriasis, lichen planus, chronic paronychia, onycholysis

Diagnosis Nail sample for microscopy and culture

Treatments

- Oral terbinafine 250 mg/day for 6 weeks for fingernails, for 12 weeks for toenails.
- Itraconazole 400 mg/day for 1 week per month, 2–3 months for fingernails, and 3–4 months for toenails.
- Topical treatment with amorolfine or ciclopirox olamine can be used in mild infections affecting the distal nail plate only.

19.2 Onychomycosis in Sri Lanka

In routine practice we noticed that the prevalence of NDM onychomycosis was much higher in our setting than reported in the literature. Two studies were conducted in 2004 (128 patients, Table 19.1) (Ranawaka et al. 2008, 2012) and in 2012 (178 patients, Table 19.2) (Ranawaka et al. 2015a, b; Ranawaka 2017; Wijesuriya et al. 2015) in patients who came to the skin clinic to assess the prevalence and clinical manifestations of NDM onychomycosis. Patients with nail involvement

Table 19.1 Isolated fungi in 128 patients with onychomycosis in 2004 (Ranawaka et al. 2012)

Species	Total fungal isolates	Both microscopy and culture positive	Microscopy negative, culture positive
Dermatophytes	17	17 (20%)	–
Trichophyton rubrum	11	11 (12.9)	
T. mentagrophytes	6	6 (7)	
Yeasts	31	29 (34.1%)	2
Candida albicans	4	2 (2.35)	
Other Candida sp.	20	20(23.5)	
Other yeasts	7	7 (8.2)	
Non-dermatophyte molds (NDM)	68	39 (45.8%)	29
Aspergillus niger	47	19(22)	18
A. flavus	12	5(6)	4
A. terreus	2	2(2.35)	–
Penicillium sp.	7	3(3.5)	4
Fusarium sp.	8	5(6)	–
Cladosporium sp.	4	3	1
Rhizopus sp.	1	–	1
Acremonium sp.	1	1	–
Paecilomyces sp.	1	1	–
Cylindrocarpon sp.	1	–	1
No growth	8 (6%)		
Mixed infections	4		
Total	128	85 (66.4%)	31(24.2%)

Table 19.2 Isolated fungi in 178 patients with onychomycosis in 2012 (Ranawaka et al. 2015a, b)

Species	Total fungal isolates	Both microscopy and culture positive	Microscopy negative, culture positive
Dermatophytes	15	12 (17.6%)	2
Trichophyton spp.	8	6	1
Mentagrophytes spp.	5	4	–
Epidermophyton spp.	2	2	
Candida species	32	21 (30.9%)	–
Candida albicans	13	13	11
Non-albicans	19	8	
Non-dermatophyte molds	101	35 (51.5%)	66
Aspergillus niger	44	10 (14.7)	34
A. flavus	32	10 (14.7)	22
Aspergillus spp.	4	–	4
Penicillium spp.	5	3 (4.4%)	2
Fusarium spp.	9	8 (11.7)	1
Scopulariopsis brevicaulis	2	1 (1.5)	1
Cladosporium spp.	3	1 (1.5)	2
Paecilomyces spp.	2	2 (2.9)	–
Bacterial growth	7		
No growth	18		
Missing reports	5		
Total	148	68 (45.9%)	80 (54.0%)

with some form of morbidity such as pain, embarrassment over fingernail involvement, foul odor with discharging pus, or limitation in work because of pain and burning sensation were the reasons for seeking treatments.

In both studies' mycology was performed at the Department of Microbiology, Faculty of Medicine Karapitiya, Galle, Sri Lanka.

NDM are filamentous fungi that are commonly found in nature as soil saprophytes and plant pathogens. Nail invasion by NDM was considered uncommon with prevalence rate ranging from 1.45% to 17.6% (Gianni et al. 2000).

In our study population, NDM was the highest (51.5%) followed by *Candida* spp. (30.9%), where dermatophytes comprised only 17.6% (Ramani et al. 1993; Greer 1995). These results enhanced author's findings in 2005 (Ranawaka et al. 2012), where NDM (45.8%) was the most frequently isolated fungi in onychomycosis, followed by yeasts (34.1%); dermatophyte infection made up only 20% and proved that NDM is no longer pure contaminants. High prevalence of NDM onychomycosis had been reported from India (22%) (Ramani et al. 1993), Malaysia (35.5%) (Ng et al. 1999), Thailand (51.6%) (Ungpakorn et al. 2004), and Pakistan (68%) (Farwa et al. 2011), too.

Although NDM and candida can invade healthy nails, secondary colonization of previously damaged nail is common. Barefoot walking and open slippers which are common practices in tropical climate result frequent minor damages to nails, and exposure to contaminated soil predisposes them to pathogenic saprophytic fungi. Frequent contact with water during household work in housewives was the commonest predisposing factor in women. In our case series, except for two patients who had diabetes, all were immunocompetent. Therefore, immune suppression in NDM was disputed in our setting.

Since NDM is considered common contaminants, both direct microscopy and culture should be positive to diagnose a significant growth. Direct microscopy of nail specimen is an important step in the laboratory diagnosis of NDM onychomycosis. Sensitivity of this test is aided by the collection of good specimens. Collection of samples from dystrophic and hyperkeratotic nail is a tedious task. Conventional methods, that is, nail clipping, have disadvantages, such as it does not give good specimens from hyperkeratotic and very dystrophic nails, those are common in manual laborers and agricultural workers, nail clippers are sometimes not wide enough to encompass the thickness of the nail, clippings take longer time to clarify in KOH, and microscopy is less sensitive if clarification does not provide a single layer of cells to observe fungal elements. To overcome these problems, nail shaving method was developed by Gunasekera et al. (2011). With shaving method, extremely thin shaving samples could be obtained which are clarified in KOH easily. Sensitivity of the shaving method was determined as 96.8%, while sensitivity of the clipping method was 79.5%. We used shaving method in our studies.

Dermatophytic and non-dermatophytic onychomycosis are indistinguishable clinically.

19.3 Clinical Manifestations and Treatment Response in Onychomycosis

19.3.1 Dermatophyte Onychomycosis

Dermatophytes comprise only 17.6 to 20% onychomycosis in Sri Lanka (Ranawaka et al. 2012, 2015a, b) (Figs. 19.1, 19.2, 19.3, 19.4).

Fig. 19.1 (**a**–**f**) Clinical manifestations are common to dermatophytes, non-dermatophyte molds, and Candida onychomycosis. They are clinically indistinguishable

Fig. 19.2 *Trichophyton mentagrophytes* isolated

Fig. 19.3 *Epidermophyton* spp. isolated

19.3.2 Non-dermatophyte Mold Onychomycosis

Non-dermatophytes molds are the highest comprising 35–39% onychomycosis in Sri Lanka. Open slippers and barefoot walking which are common practices in tropical climate result frequent minor damages to nails, and exposure to contaminated soil predisposes them to pathogenic saprophytic fungi. Dermatophyte and non-dermatophyte mold onychomycosis are indistinguishable clinically (Figs. 19.5, 19.6, 19.7, 19.8, 19.9, 19.10, 19.11, 19.12).

19.3.3 Candida Onychomycosis

Candida onychomycosis is found in 29–32% onychomycotic patients present to the hospital skin clinics in Sri Lanka (Jayatilake et al. 2009). This is indistinguishable clinically from dermato-

Fig. 19.4 *Epidermophyton* spp. isolated

Fig. 19.5 *Paecilomyces* sp. was isolated. Greenish pigmentation is due to *Pseudomonas* superinfection

Fig. 19.6 Proximal subungual onychomycosis (PSO) with marked paronychia. *Aspergillus niger* was isolated

Fig. 19.7 Distal subungual onychomycosis with posterior nail fold inflammation. *Penicillium* spp. was isolated

Fig. 19.8 Distal lateral subungual onychomycosis. *Cladosporium* spp. was isolated

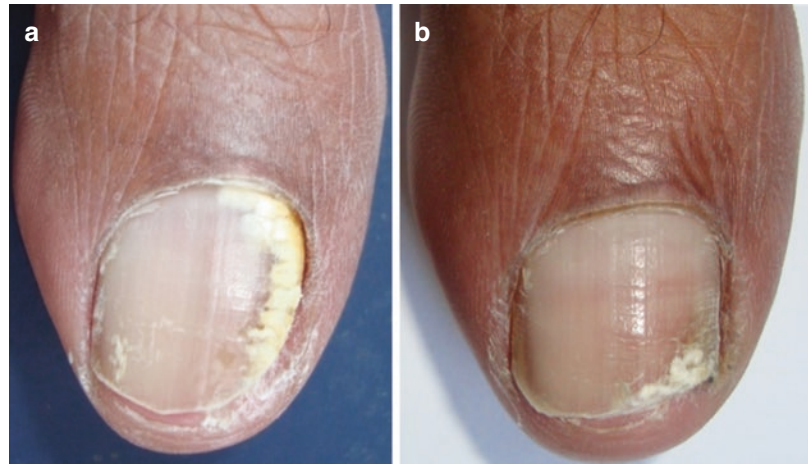

Fig. 19.9 A 45-year-old executive with right toe nail infection (**a**) *Fusarium dimerum* was isolated (**b**) completely cured with three pulses of itraconazole

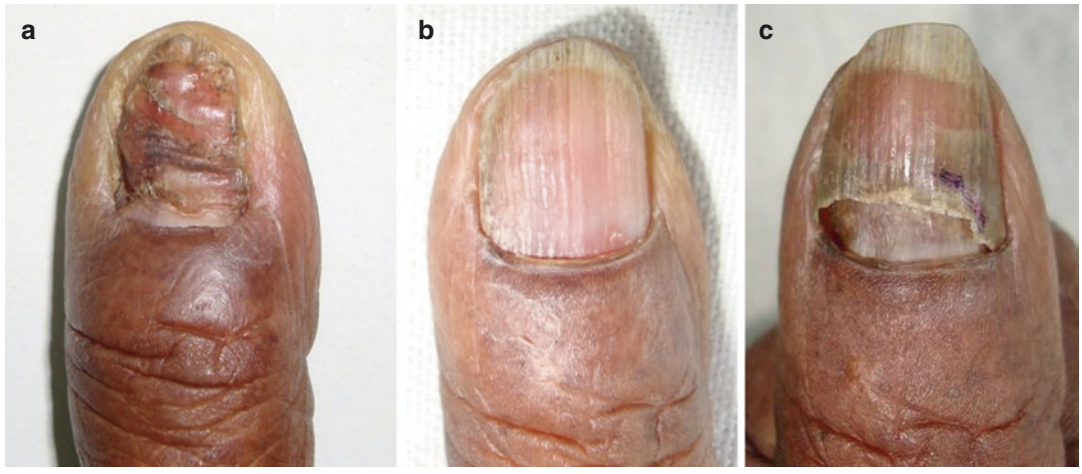

Fig. 19.10 A 68-year-old woman with left thumb nail dystrophy for 4 years. *Fusarium dimerum* was isolated. (**a**) Before treatments. (**b**) This was cured completely with two pulses of terbinafine. (**c**) Recurrence of nail destruction 19 months later. Terbinafine additional pulse was given and continued topical 3% thymol local application

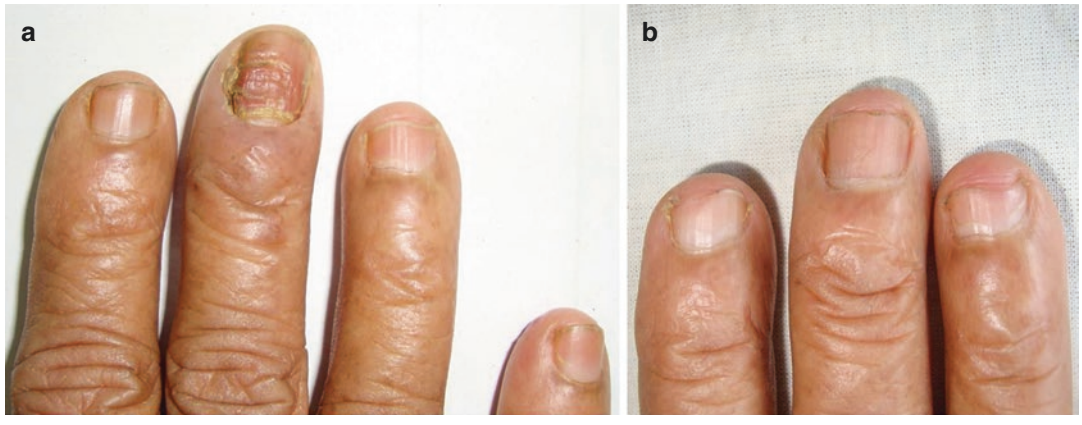

Fig. 19.11 A 73-year-old housewife, (**a**) R/middle finger dystrophy for 1 year; *Aspergillus niger* was isolated. (**b**) Completely cured with itraconazole three pulses

phyte or non-dermatophyte mold onychomycosis. More than one third of Candida onychomycosis are associated with paronychia (Ranawaka et al. 2012, 2015a, b).

Differential Diagnosis Dermatophyte onychomycosis, NDM onychomycosis, chronic paronychia

Treatment of *Candida* onychomycosis Itraconazole 200 mg b.i.d. for 1 week per month, 2–3 pulses for fingernails and 3–4 pulses for toenails (Figs. 19.13, 19.14, 19.15).

19.4 Diagnosis of Onychomycosis

19.4.1 Collection of Nail Samples for Microscopy and Culture

Shaving sample shows 96.8% microscopy positivity, while the conventional method (nail clipping) is 48.4% (Gunasekera et al. 2011).

Fig. 19.12 A 62-year-old retired clerk, who did gardening on bare hand, had this nail destruction for more than 6 years. (**a**) *Aspergillus niger* was isolated. (**b**) Completely cured with three pulses of Itraconazole

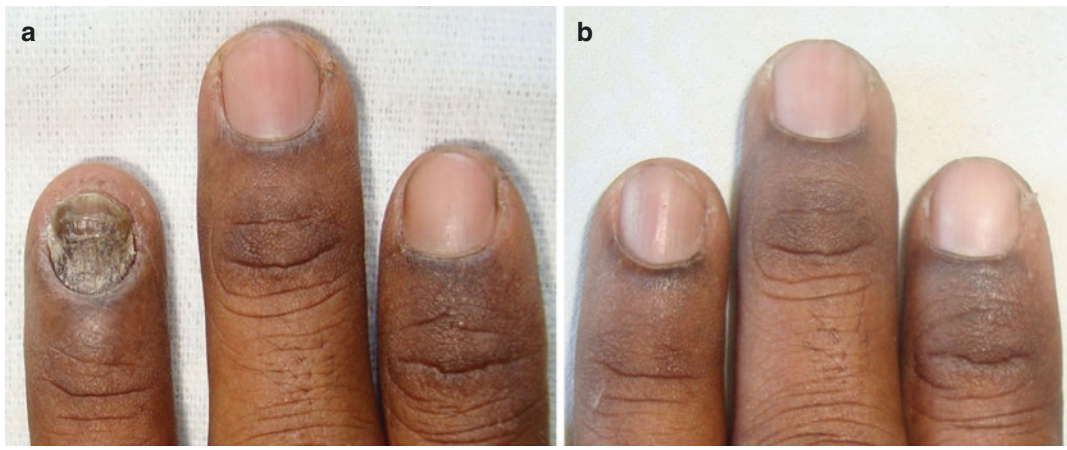

Fig. 19.13 Candida onychomycosis (**a**) before therapy (**b**) complete clinical cure after itraconazole three pulses and topical antifungal lotions for 12 months. This is clinically indistinguishable from dermatophyte or NDM onychomycosis

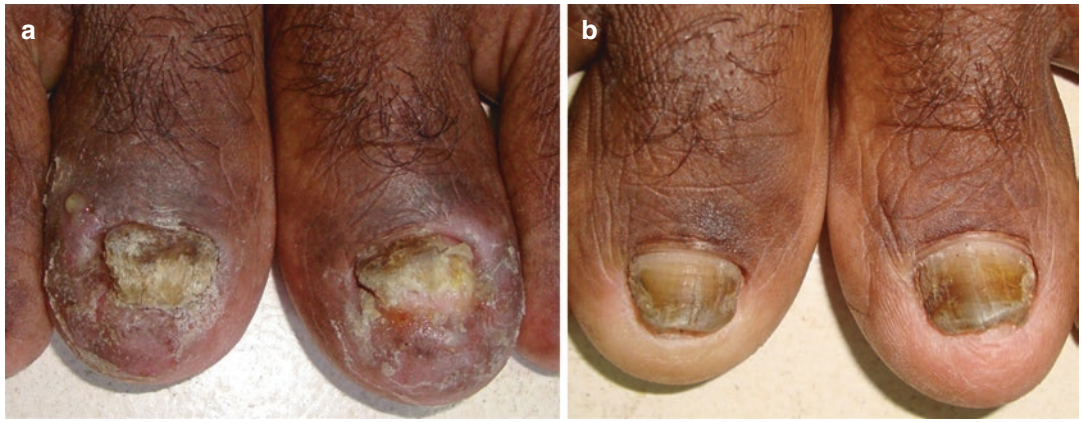

Fig. 19.14 (**a**) Above patient with toenails before treatments. *Candida albicans* was isolated. He was treated with itraconazole three pulses and 3% thymol in spirit local application continued for 12 months. (**b**) Toenails showed marked improvement. He was prescribed additional itraconazole pulse

Fig. 19.15 A 73-year-old housewife who looked after her bed-ridden husband came with (**a**) bilateral thumb nail dystrophy for 3 months. Candida non-albicans was isolated. She was treated with itraconazole two pulses and 3% thymol in spirit local application continued for 12 months. (**b**) At 12 months both thumb nails showed marked improvement. Additional itraconazole pulse was prescribed.

- **DLSO**—most proximal portion of the affected nail bed. Nail plate material should contain as much subungual debris as possible.
- **SWO**—layer of the dorsal surface of the nail plate may be cut tangentially from the nail using #23 or #15 scalpel.
- **PSO**—punch biopsy from the nail plate.
- **Endonyx**—nail plate is shaved/clipped as much as possible without hurting the patient too much.
- **TDO—**cut away large chunk of infected nail.

19.4.2 Collection of Nail Sample for Histopathology

The hyphae are usually found in the keratinized part of the nail bed (subungual debris) or in the deepest part of the nail plate. A superficial biopsy of the nail plate may therefore give a false negative result (Baran et al. 2006) (Figs. 19.16, 19.17, 19.18, 19.19).

Fig. 19.16 Shaving sample for microscopy and culture

Fig. 19.17 Nail clipping with subungual debris for histopathology

19.4.3 Onychoscopy

Piraccini et al. (2013, 2018) described dermoscopic signs specific for distal subungual onychomycosis (DLSO) that could facilitate its diagnosis and differentiation from traumatic onycholysis. Dermoscopic digital images of 57 consecutive patients who had onycholysis of a single toenail were studied. They identified three recurring peculiar dermoscopic features, two of which were present only in DLSO.

1. Jagged proximal edge with spikes of the onycholytic area
2. Longitudinal striae

The other feature was seen only in traumatic onycholysis.

3. Linear edge—without spikes—of the onycholytic area

Detection of these signs is simple and can, in selected cases, help to avoid mycology. Piraccini et al. conducted the studies on onychomycosis caused by dermatophytes (Piraccini et al. 2013, Piraccini et al. 2018, Romaszkiewicz et al. 2018) Following onychoscopy pictures are from NDM onychomycosis (photographed by Dr Ranthilaka R. Ranawaka) (Figs. 19.20, 19.21, 19.22, 19.23, 19.24, 19.25, 19.26, 19.27).

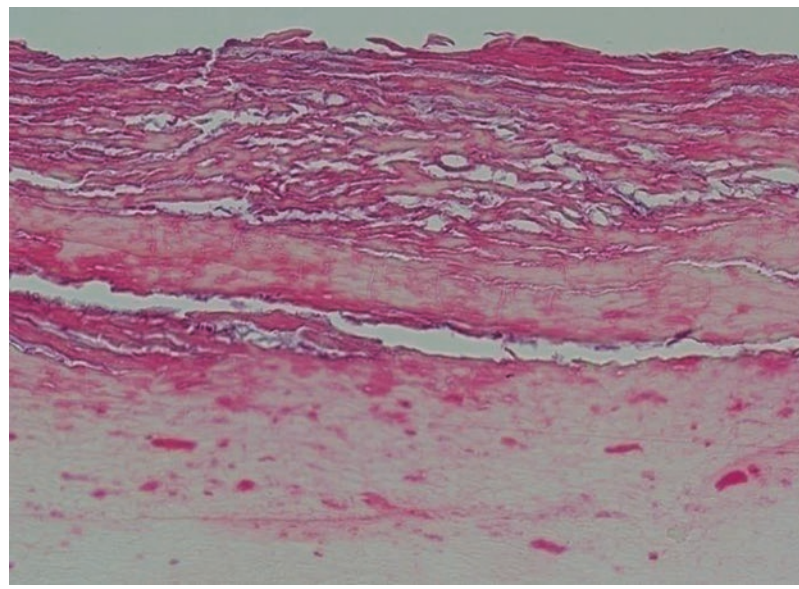

Fig. 19.18 Histopathology of *Fusarium* onychomycosis from the nail sample Hematoxylin & Eosin stain (picture courtesy Prof Eckart Haneke, Dept Dermatol, Inselspital, Freiburgstrasse 14, Ch—3010 Bern, Switzerland)

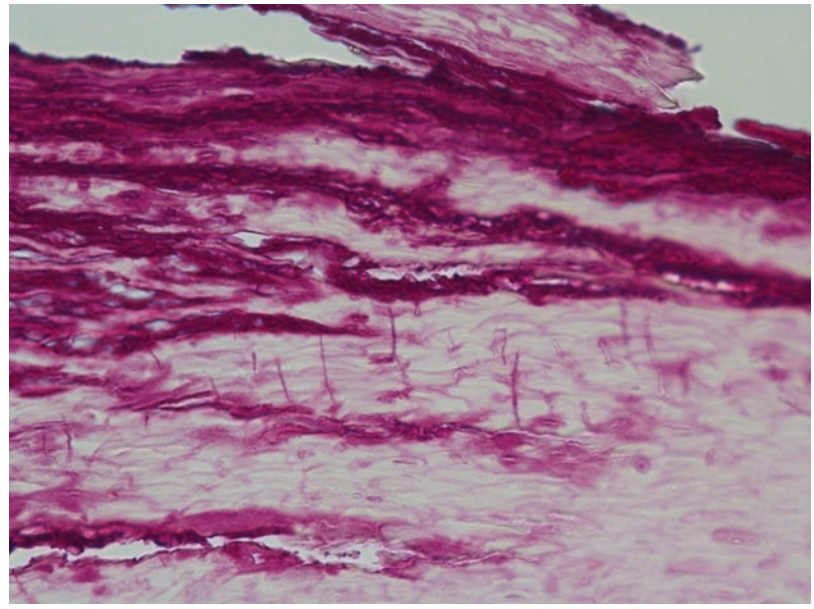

Fig. 19.19 Histopathology of *Fusarium* onychomycosis from the nail sample Periodic Acid Schiff (PAS) stain. Vertically penetrating very fine filaments on the nail surface—an extremely rare phenomenon in onychomycosis histopathology (picture courtesy Prof Eckart Haneke, Dept Dermatol, Inselspital, Freiburgstrasse 14, Ch—3010 Bern, Switzerland)

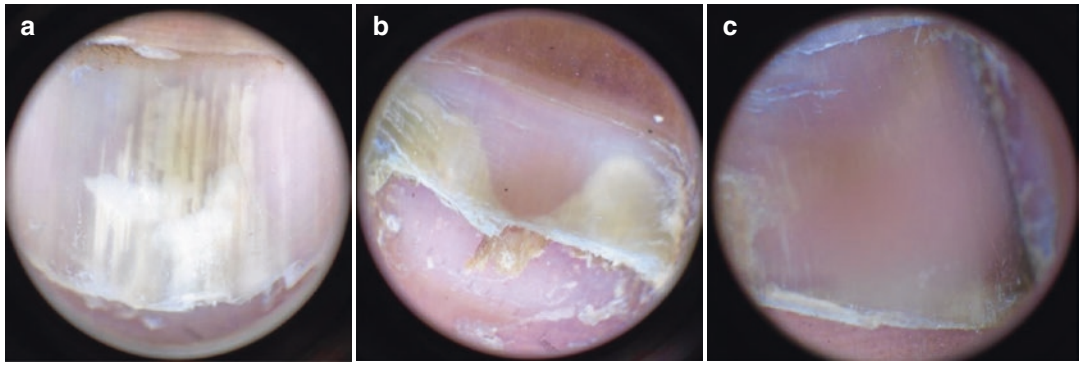

Fig. 19.20 (**a**–**c**) These onychoscopy pictures are from NDM onychomycosis. These pictures also show two dermoscopic features seen in dermatophyte onychomycosis; jagged proximal edge with spikes of the onycholytic area and longitudinal striae

Fig. 19.21 *Fusarium dimerum* was isolated from this nail sample. Onychoscopy shows jagged proximal edge with spikes of the onycholytic area, and fluffy cloudy appearance

Fig. 19.22 Onychoscopy of superficial white onychomycosis

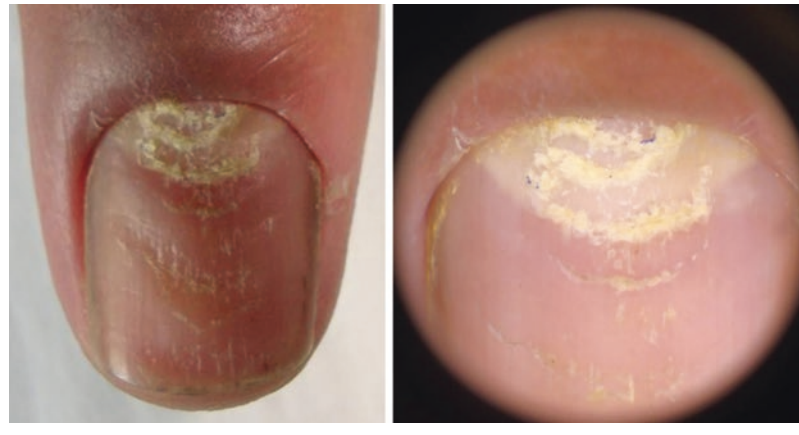

Fig. 19.23 Onychoscopy of proximal subungual onychomycosis

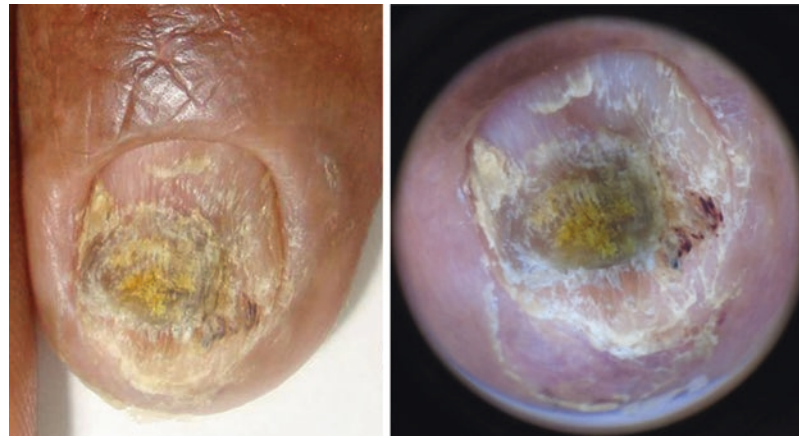

Fig. 19.24 Onychoscopy of total onychodystrophy

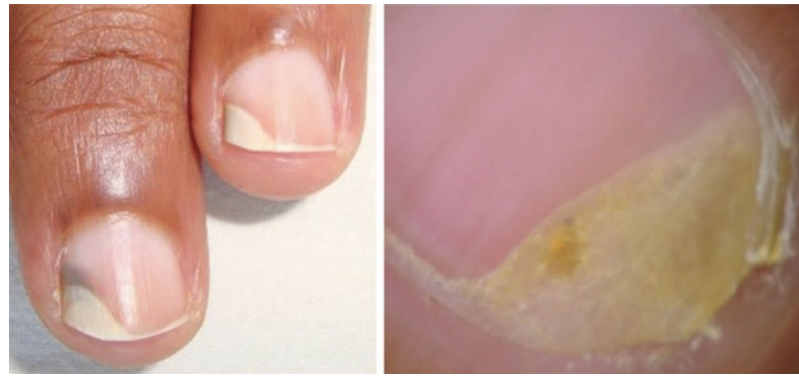

Fig. 19.25 Traumatic onycholysis. Note the linear shape of the proximal border

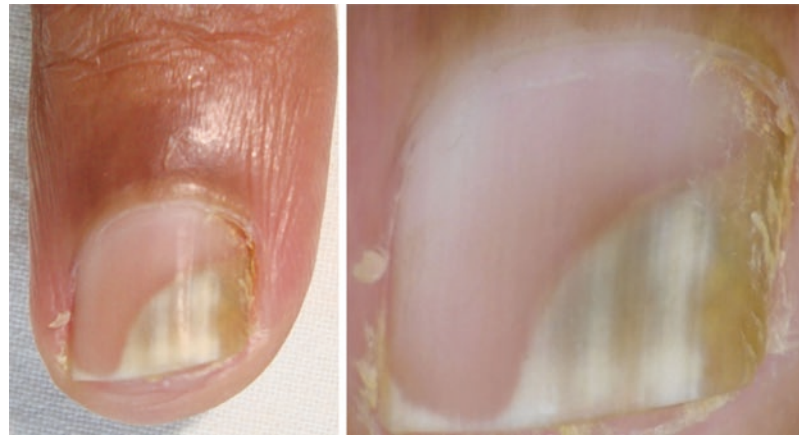

Fig. 19.26 Traumatic onycholysis. Note the linear shape of the proximal border

Fig. 19.27 Stain on the nail plate

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