

## Dark fingernails

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Visuvanathan VV, Koh KC. Dark fingernails. *Malays Fam Physician*. 2015;10(3):40-42.

### Keywords:

melanonychia, longitudinal melanonychia, Zidovudine

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### Case summary

Madam S, a 40-year-old woman of South Asian origin was diagnosed with HIV infection through spousal contact tracing. Her husband, who had a history of intravenous drug use, was diagnosed with HIV infection while incarcerated in a prison. She was asymptomatic and had no clinical evidence of opportunistic infections. Her CD4 cell count was 180 cells/mm<sup>3</sup>. Based on the Malaysian national guidelines for the treatment of adults with HIV-infection, Madam S was commenced on cotrimoxazole (Bactrim) tablets for prophylaxis against *Pneumocystis jiroveci* infection and a combination of antiretroviral (ARV) agents consisting of zidovudine (AZT), lamivudine (3TC) and efavirenz (EFV) to treat her HIV infection.

After 3 months, Madam S returned for the follow-up at the infectious diseases clinic. She was tolerating her ARV regime well with minimal side effects. She complained of fingernail colour changes (Figures 1 and 2), which were aesthetically distressing to her. Almost all her fingernails were noted to have longitudinal bands of hyperpigmentation. However, her toenails were spared and there was no hyperpigmentation of mucosa membranes and palmar creases.



Figure 1. Hands of the patient



Figure 2. Pigmentation on fingernails of right index, middle and ring finger of the patient

### Questions

1. What is the most likely diagnosis of changes in the colour of her fingernails?
2. What is the most probable cause?

### Answers

1. This woman has acquired longitudinal melanonychia. Melanonychia is a common condition characterised by melanin-derived light brown to black pigmentation of the nails. The three common presentations of melanonychia are (i) longitudinal melanonychia (LM) (ii) transverse melanonychia and (iii) complete melanonychia. Melanin within the

nail plate (nail) is produced by melanocytes in the nail matrix, a majority of that are normally dormant.<sup>2</sup> Activation of these dormant melanocytes or hyperplasia of melanocytes result in increased melanin deposition within the nail plate.

2. Being of South Asian origin with Fitzpatrick Skin type V, LM may be physiological in this woman. Melanonychia has been reported to be more prevalent in darkly pigmented individuals, where the number and width of bands increases with age.<sup>2,3</sup>

However, the abrupt onset of LM involving numerous digits and temporal relation with initiation of ARV therapy suggests the possibility of drug-induced melanonychia. Zidovudine, a thymidine analogue, has frequently been implicated in the development of acquired LM.<sup>3</sup> Examples of other drugs associated with melanocytic

activation are hydroxyurea, methotrexate, phenytoin, chloroquine, bleomycin and infliximab.<sup>2</sup> Cotrimoxazole, Lamivudine and Efavirenz have not been reported to cause LM.

HIV-1 infection itself may be responsible for melanonychia. Several reports have been published regarding nail colour changes in patients infected with HIV-1 who were ARV therapy naive. In these patients, LM has been associated with mucocutaneous hyperpigmentation that was attributed to increased melanin production by melanocytes due to over-expression of melanocyte-stimulating hormone.<sup>4,5</sup>

Other common causes of LM include pregnancy, repeated trauma, nail biting, chronic paronychia, onychomycosis, melanoma and Addison's disease.<sup>2</sup> A complete list of causes of melanonychia is depicted in Table 1.<sup>6</sup>

**Table 1.** Conditions associated with longitudinal melanonychia.<sup>6</sup>

Melanocytic activation	
<p><b>1. Physiologic causes</b></p> <ul style="list-style-type: none"> <li>• Racial melanonychia</li> <li>• Pregnancy</li> </ul> <p><b>2. Local and regional causes</b></p> <ul style="list-style-type: none"> <li>• Repeated local trauma from poor footwear or overriding toes</li> <li>• Onychotillomania</li> <li>• Nail biting</li> <li>• Occupational trauma</li> <li>• Carpal tunnel syndrome</li> </ul> <p><b>3. Dermatologic causes</b></p> <ul style="list-style-type: none"> <li>• Onychomycosis</li> <li>• Chronic paronychia</li> <li>• Psoriasis</li> <li>• Lichen planus</li> <li>• Amyloidosis</li> <li>• Chronic radiation dermatitis</li> <li>• Systemic lupus erythematosus</li> <li>• Localised scleroderma</li> <li>• Onychomatricoma</li> <li>• Bowen's disease</li> <li>• Myxoid pseudocyst</li> <li>• Basal cell carcinoma</li> <li>• Subungual fibrous histiocytoma</li> <li>• Verruca vulgaris</li> <li>• Subungual linear keratosis</li> </ul>	<p><b>4. Systemic causes</b></p> <ul style="list-style-type: none"> <li>• Endocrine disorders (Addison's disease, Cushing's syndrome)</li> <li>• Nelson's syndrome, hyperthyroidism, and acromegaly</li> <li>• Alcaptonuria</li> <li>• Nutritional disorders</li> <li>• Haemosiderosis</li> <li>• Hyperbilirubinemia</li> <li>• Porphyria</li> <li>• Graft versus host disease (lichen planus-type changes accompanied by longitudinal melanonychia)</li> <li>• AIDS</li> </ul> <p><b>5. Iatrogenic causes</b></p> <ul style="list-style-type: none"> <li>• Phototherapy</li> <li>• X-ray exposure</li> <li>• Electron beam therapy</li> <li>• Drug intake</li> </ul> <p><b>6. Syndromes</b></p> <ul style="list-style-type: none"> <li>• Laugier-Hunziker syndrome</li> <li>• Peutz-Jegher syndrome</li> <li>• Touraine syndrome</li> </ul>

**Table 1.** Classification of conditions associated with longitudinal melanonychia (adapted from J. Andre, N. Lateur. Pigmented nail disorders) (Continue)

Melanocytic hyperplasia
1. Lentigo
2. Naevus <ul style="list-style-type: none"> <li>• Congenital naevi</li> <li>• Acquired naevi</li> </ul>
2. Nail apparatus in situ and invasive melanoma

**Discussion**

Nail and mucocutaneous hyperpigmentation can cause significant distress to patients. Benign, pigmented nails and mucous membranes are perceived to be aesthetically unacceptable by many patients.

Other than being unsightly, the presence of dark nails may be perceived as stigmata of HIV infection similar to the role of Kaposi sarcoma in the pre-ARV era and lipodystrophy in the early years of Highly Active Antiretroviral Therapy (HAART) when stavudine was commonly used. Patients on zidovudine who develop melanonychia may decide to default their ARV therapy leading to non-adherence and subsequently drug resistance. It may be wise for the physician initiating a patient on ARV therapy to consider this consequence and decide on an appropriate alternative medication for zidovudine, for example, tenofovir.

The presence of LM, when other common causes have been ruled out, should prompt the

clinician to consider offering HIV-screening test to the patients who may not be aware that they are infected with HIV.

Patients who develop melanonychia should be informed that the condition is benign in nature. However, the clinician should rule out more serious conditions, for example, malignant melanoma by obtaining history and looking for physical signs suggestive of melanoma, such as: (1) discoloration bands in the nails that are wider than 3 mm and have irregular borders, (2) extension of the band into the proximal and/or lateral nail fold (Hutchinson’s sign), (3) a lesion with a triangular shape, (4) nails that are split or have fissures, and (5) if the pigmentation is not homogenous.<sup>3</sup> In the absence of these features and other common causes, the patient should be reassured and perhaps offered an alternative regime that does not cause melanonychia. The reversal of melanonychia may take a long time and during this period usage of nail polish as camouflage may be suggested.

**References**

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