

LONGITUDINAL MELANONYCHIA CAUSED BY FLUCONAZOLE THERAPY FOR FUNGAL KERATITIS AND ONYCHOMYCOSIS*

FUNGAL KERATİT VE ONİKOMİKÖZÜN FLUKONAZOLLE TEDAVİSİNDEN KAYNAKLANAN LONGİTUDİNAL MELANONİŞİ

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SUMMARY: *Melanonychia striata longitudinalis* or longitudinal melanonychia is a chromonychia usually caused by a pigment-producing focus of melanocytes in the nail matrix. While longitudinal melanonychia is a normal racial variation with increasing frequency in advanced age in dark-skinned persons, it is rarely seen in fair-skinned people. Fluconazole has only once been reported to produce longitudinal pigmentation on the diseased nail by *Trichophyton rubrum* in a dark-skinned patient from India. We report a further case of fluconazole-induced longitudinal melanonychia in a fair skinned patient after long-term and high dose oral fluconazole therapy for fungal keratitis and onychomycosis.

Key Words: : Longitudinal Melanonychia, Fluconazole, Keratomycosis, Onychomycosis.

INTRODUCTION

Melanonychia striata longitudinalis or longitudinal melanonychia (LM) is a chromonychia usually caused by a focal increase of melanin which is produced by nail matrix melanocytes. In blacks and dark-skinned persons, it is a normal racial variation with increasing frequency in advanced age. Pigmented longitudinal nail bands are rarely seen in fair skinned persons (1, 2). They can be idiopathic or produced by repeated trauma, several drugs

OZET : *Melanonişi striata longitudinalis* veya longitudinal melanonişi (tırnakta boyuna çizgilenme), genellikle tırnak matriksindeki melanositlerin oluşturduğu pigment üreten bir odaktan kaynaklanan bir kromonişidir. Siyah ırkta ve koyu derililerde, sıklığı yaşla birlikte artan normal bir varyasyon olmasına karşın beyazlarda nadir görülür. Flukonazole bağlı longitudinal pigmentasyon, daha önce sadece bir kez Hindistan'dan koyu derili bir hastada *Trikofiton nubrum*'la enfekte onikomikozlu tırnakta tanımlanmıştır. Bu bildiriye, fungal kertit ve onikomikoz nedeniyle uzun süreli yüksek doz oral flukonazol tedavisi gören açık tenli bir hastada flukonazolün yol açtığı diğer bir longitudinal melanonişi olgusu sunulmaktadır.

Anahtar Kelimeler: Longitudinal Melanonişi, Flukonazol, Keratomikoz, Onikomikoz.

including chemotherapeutics, zidovudine, hydroxyurea, minocycline, antimalarials and ketoconazole, and by X-ray irradiation. Adrenal insufficiency, malnutrition, vitamine B12 deficiency, AIDS, Peutz-Jegher's syndrome, lichen planus, porphyria, Laugier-Hunziker syndrome and pregnancy are other possible causes (1-4).

To our knowledge, fluconazole has only once been reported to produce LM in a single case from India (5). We present a further case of

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fluconazole-induced LM in a fair skinned patient receiving oral fluconazole therapy for fungal keratitis and onychomycosis.

CASE REPORT

A 44-year-old woman was referred to our clinic for evaluation of nail changes by the Department of Ophthalmology where she had been treated unsuccessfully with topical natamycin for fungal keratitis of her right eye due to *Candida albicans*. Dermatologic examination showed onycholysis and dystrophy of both thumbnails accompanied by chronic paronychia. Nail plates of both great toes and the second toe of the left foot were also thickened and white. KOH examinations of the affected nails were positive for fungal hyphae. Fungal cultures on Sabouraud's dextrose media grew *C. albicans* from the thumbnails and *Trichophyton rubrum* from the toenails. A diagnosis of onychomycosis of fingernails and toenails was made. Because keratomycosis was unresponsive to topical use of natamycin for four weeks and *C. albicans* was identified again from corneal scrapings, oral fluconazole therapy was started in a dose of 150 mg per day. After a four week-treatment period, the dose was reduced to 150 mg once a week. At the end of three months, the patient was referred again to the Dermatology Department, this time with the complaint of nail dyschromia. Examination revealed multiple hyperpigmented longitudinal striae, varying in color and width, ranging from 1 to 6 mm, on the thumbnails. Other fingernails and a total of six toenails were less severely affected. While there was only one stria on each nail involved, multiple and darker striae were present on the thumbnails (Fig. 1). We also observed longitudinal grooves and large lunulae in the middle fingernails, and periungual spread of pigmentation (Hutchinson's sign) in the proximal nail folds of some fingers. There was no mucosal pigmentation.

While onychomycosis and paronychia of both thumbs improved greatly, toenail infection was unresponsive to the therapy and *T. rubrum* was again cultured from the toenails. Keratomycosis also did not resolve completely. In spite of the occurrence of cosmetically undesirable melanonychia, the patient currently continues to intake fluconazole once weekly because of the continuing therapy for keratomycosis.



Fig. 1: Longitudinal melanonychia due to fluconazole that affect most prominently thumbnails but also other fingernails, and median grooving on the middle fingernails with pseudo-Hutchinson's sign.

DISCUSSION

LM is a chromonychia characterized by a tan, brown or black longitudinal nail streak caused by increased melanin deposition which results from activation of normal melanocytes located in the nail matrix (6). Various pharmacologic agents, PUVA, pregnancy, onychotillomania, habitual nail picking and repeated traumas such as friction or pressure from footwear are relatively frequent causes of LM. (2-4, 7) Some chromogenic bacteria and fungi can also cause nail pigmentation. Perrin and Baran (8) have reported two cases of nail pigmentation due to *T. rubrum* clinically resembling LM. Longitudinal nail pigmentation may also result from benign (lentigo or nevus) or malignant hyperplasia (subungual or periungual malignant melanoma) of melanocytes (6). Subungual keratosis, subungual basal cell carcinoma and Bowen disease of the nail bed are other rare causes of melanocyte proliferation (9, 10). Neither the color intensity of pigmented band nor the age of the patient are proof of benignity or malignancy. Baran et al (11) has reported that LM in the nails of Caucasians tends to be malignant rather than benign.

Hutchinson's sign, which is described as the periungual spread of pigmentation into the proximal nail fold, should alert the clinician to

the possibility of subungual malignant melanoma, especially in the presence of following implicating findings; (1) pigmented bands larger than 6 mm and showing variegated discoloration, (2) abrupt onset with blurred edges, (3) history of dysplastic nevus syndrome, (4) the sudden appearance of LM after middle age (5) an association with nail dystrophy (2,10). Subungual melanoma must always be included in the differential diagnosis when the cause of LM is unapparent and such features are present (2, 6). However periungual hyperpigmentation is not always a predictor of malignant melanoma and pseudo-Hutchinson's sign is present in a number of benign disorders such as LM, Laugier-Hunziker syndrome, Peutz-Jeghers syndrome, vitamin B12 deficiency and junctional nevi. Multiple and/or lightly pigmented nail bands are usually not caused by malignancies (2, 10). As our patient had multiple nail involvement, and the condition was closely associated with fluconazole ingestion, we did not consider any melanocyte proliferation and nail biopsy was not performed.

Nail pigmentation secondary to systemic drugs may be due to direct toxicity to the matrix that leads to the stimulation of matrix melanocytes (3). The cause of longitudinal banding pattern is unclear. Stimulation of melanocytes may be regionally different according to the concentration of the drug as a function of local vascular supply, melanin granule density, or the character of the melanocytes themselves (10,11). Fluconazole is a selective inhibitor of fungal cytochrome P450 sterol C-14 alpha-demethylation and is used primarily in systemic therapy of candidiasis and cryptococcosis. In our intensive literature review, we have found only one published case of fluconazole-induced LM in a dark-skinned patient from India. In the mentioned case, pigmentation was limited to the nail infected by *Trichophyton rubrum* (5). To the best of our knowledge, the case described herein is the second case of fluconazole-induced nail pigmentation. Unlike the previous report, we observed pigmented striae both in involved and uninvolved nails by fungal infection. This discrepancy may be due to the ingestion of fluconazole in a much higher total dose compared to the first case, because of the presence of concomitant keratomycosis. We believe that

fluconazole should be added to the list of the drugs which may cause longitudinal nail pigmentation, and this side effect should be kept in mind particularly when it is prescribed in high doses.

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