

Black Lunula Caused by Tegafur

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Sir,

Tegafur, a fluorinated pyrimidine analogue of 5-Fluorouracil (5-FU), is metabolized *in vivo* with biotransformation to 5-FU (1). It is effective in the treatment of gastrointestinal carcinoma, with the advantages of low myelosuppression and lack of immunosuppression. The cutaneous adverse effects of Tegafur include stomatitis, dry skin, disseminated rash, alopecia, photosensitivity, palmoplantar erythrodysesthesia, palmoplantar keratoderma, acral hyperpigmentation, diffuse or nail-restricted hyperpigmentation, Stevens-Johnson syndrome, sclerodactyly and Raynaud's phenomenon (1, 2). We describe a patient with ascending colon cancer who developed black lunula following chemotherapy with oral Tegafur.

CASE REPORT

A 75-year-old woman, a victim of ascending colon cancer at Duke stage B₂, underwent surgical removal of the tumour in April 2003. Post-operation, adjuvant chemotherapy was given with oral Tegafur (800 mg day⁻¹) and folic acid (5 mg day⁻¹), and after 4 weeks of treatment, black discoloration appeared at the base of all her fingernails (Fig. 1). The toenails were not involved. The nail plates were not thickened or atrophic, and the periungual skin was unremarkable. Microbiological examination of the nails showed no evidence of fungal infection, but several black macules were found on the hands. Laboratory examination, including complete blood count and partial thromboplastin time/prothrombin time, resulted normal. No



Fig. 1. Black discoloration at the base of all the fingernails of the right hand.

history of trauma was known in association with this episode. In June 2003, erythematous itchy hyperkeratotic skin lesions were noticeable on the face, neck, v-chest and upper extremities, without previous history of photosensitivity. Tegafur was then discontinued and the skin lesions gradually resolved under the treatment with systemic prednisolone and topical hydrocortisone ointment. However, the nail discoloration has lasted for 2 months so far.

DISCUSSION

Pigmentation of nail matrix is caused by activation of the melanocytes *in situ*, which, after transfer of the melain to the nail plate, may lead to melanonychia (3). Drug-induced melanonychia usually affects several nails, showing multiple light brown to black longitudinal or transverse bands. Doxorubicin and cyclophosphamide are the antineoplastic drugs most frequently involved in causing melanonychia.

The photodistributed skin eruption in the present case improved with cessation of Tegafur, indicating its association with the drug or its metabolites, fluorouracil. Due to the lagging of 6 weeks between onset of skin rash and initiation of oral Tegafur, the photosensitivity may be a photoallergic rather than a phototoxic reaction. Fluorouracil, by absorbing UV-A, can induce a photoallergic reaction and damage keratinocytes (4). A similar episode may happen to the nail tissue, leading to post-inflammatory hyperpigmentation or activation of the melanocytes in the nail matrix.

Drug-induced haemorrhages range from splinter haemorrhages involving nail bed capillaries to purpura or haematoma of the nail bed due to subungual haemorrhage (5). It can initially present as a black lunula prior to distal migration of the pigment accompanying subsequent growth of the nail plate (6). The signs usually appear in the toenails, which are more readily exposed to frequent minor traumas. Cancer chemotherapeutic agents such as docetaxel have been described as causing subungual haemorrhages and haematomas, probably due to the drug-related thrombocytopenia (5, 7).

Black lunula has been described in 5 patients receiving hydroxyurea (8), and the possible mechanism in our patient was considered to be either direct deposition of Tegafur, probably chelation with iron and/or calcium (9), or involved activation of melanin synthesis. In our case the black discoloration was

localized to lunula without any change of nail plate. This is different from the cases reported by Rios-Buceta et al., in which the nail hyperpigmentation induced by Tegafur manifested as brownish longitudinal bands on the fingernails (1). Since neither thrombocytopenia nor distal migration of the pigment was found, subungual haemorrhage due to minor trauma was less likely. Nail biopsy with histopathological examination, especially with electron microscopy, may lead to a better understanding of the real pathogenesis of lunular dyschromia.

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