Tegafur-induced acral hyperpigmentation

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Abstract

Tegafur is a prodrug of 5-fluorouracil (5-FU) with a similar spectrum of antitumor activity. It is used in the treatment of advanced gastrointestinal neoplasms. Over 5-FU, tegafur has the advantage of oral administration and less hematologic toxicity. Gastrointestinal toxicity is its main dose-limiting factor. The cutaneous adverse effects of tegafur include mucositis, photosensitivity, diffuse or nail-restricted hyperpigmentation, palmoplantar erythrodysesthesia syndrome, palmoplantar keratoderma, sclerodactyly and Raynaud phenomenon. We report here the case of a patient who developed acral hyperpigmentation during treatment with tegafur.

Case Report

A 48-year-old woman, phototype V, with an advanced rectal adenocarcinoma stage C (Duke's classification) diagnosed in December 2009, who developed acral hyperpigmentation during tegafur intake. Radio-therapy and chemotherapy (including tegafur) were initiated as neoadjuvant agents followed by rectal anterior resection. Tegafur (500 mg/d) was reintroduced one month after surgery. Four months later, the patient appeared with multiple 2-10 mm round and oval-shaped brown macules on the face (Figure 1), tongue (Figure 2A), hands, soles and nails. Almost all nails were involved, and longitudinal melano-nychia was identified in the 2nd e 3rd fingernails of her right hand (Figure 2B). The skin biopsy revealed mild basal pigmentation. The diagnosis of tegafur-induced hiperpigmentation was made. One month after discontinuation of tegafur, the hyperpigmented acral lesions began to clear.

Discussion

The cutaneous adverse effects of tegafur include mucositis, photosensitivity, diffuse or nail-restricted hyperpigmentation, palmoplantar erythrodysesthesia syndrome, palmoplantar keratoderma, sclerodactyly and Raynaud phenomenon[1-4]. Hyperpigmentation of the skin, mucosa and nails is a side effect associated with various chemotherapy drugs, including 5-FU and its prodrugs.[5] The time course of tegafur therapy, the cutaneous reaction and its clearance after discontinuing the treatment suggest a causal relationship based on chronological criteria. The cause of such pigmentation is unknown, although there may be a mechanism common to other chemotherapy drugs. These substances may increase pigmentation by direct or MSH-mediated stimulation of melanocytes.[6] In 1991, *Llistosella et col.* proposed a mixed mechanism involving melanocyte hyperplasia and a decreased keratinocyte turnover, as basal pigmentation and dermal melanophages were observed histologically.[1]

Clinicians should be aware of this side effect of tegafur, since it is being increasingly used in patients with advanced colon cancer.

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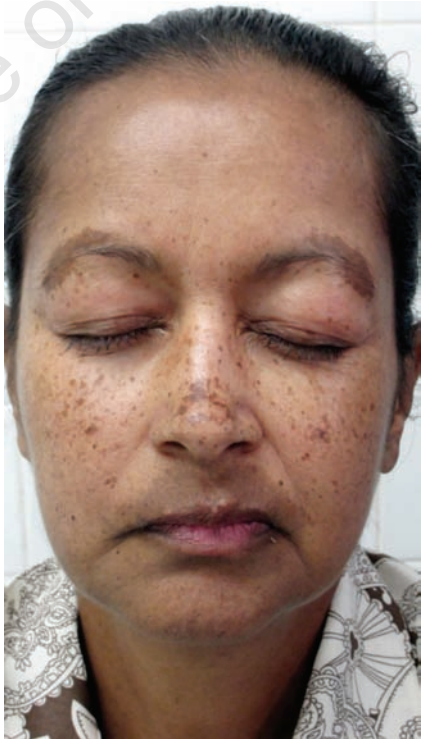

Figure 1. Brown macules on the face.

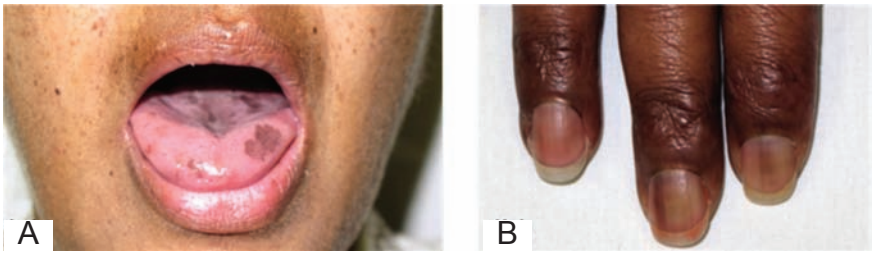

Figure 2. Hyperpigmentation on the tongue (A) and longitudinal melanonychia in the 2nd e 3rd fingernails (B).