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, palmo-plantar erythrodysesthesia syndrome, palmo-plantar 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 melanonychia was identified in the 2nd and 3rd fingernails of her right hand (Figure 2B). The skin biopsy revealed mild basal pigmentation. The diagnosis of tegafur-induced hyperpigmentation 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, palmo-plantar erythrodysesthesia syndrome, palmo-plantar keratoderma, sclerodactyly and Raynaud phenomenon. Hyperpigmentation of the skin, mucosa and nails is a side effect associated with various chemotherapy drugs, including 5-FU and its prodrugs. 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. In 1991, Llistosella et al. proposed a mixed mechanism involving melanocyte hyperplasia and a decreased keratinocyte turnover, as basal pigmentation and dermal melanophages were observed histologically.

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

References


Figure 1. Brown macules on the face.

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