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LETTERS TO THE EDITOR

Chemotherapy-induced Acral Erythema due to Tegafur

Sir,

Tegafur is a tetrahydrofuranyl derivative of 5-fluorouracil, used in the treatment of advanced gastrointestinal neoplasms (1). It is considered as an alternative oral therapy to intravenous 5-fluorouracil. In this report, we describe the occurrence of chemotherapy-induced acral erythema following Tegafur intake.

CASE REPORT

A 69-year-old woman underwent a right hemicolectomy for a colonic mucosecretor adenocarcinoma (Duke's classification C2). One month later, she started treatment with Tegafur orally (400 mg twice daily). After 1 month she complained of a slight burning sensation of palms and soles that progressed in 2 weeks to painful erythema. The patient continued taking Tegafur and the lesions worsened. Five months after starting Tegafur therapy she was sent for dermatological evaluation. No systemic symptoms were appreciated. Exploration showed palmoplantar erythematous plaques with a violaceous hue and sharp margins. No hyperkeratosis was noted. Central aspects of palms and soles were spared (Fig. 1). On the dorsa of fingers and toes the erythema affected periungual and interphalangeal skin. No mucosal lesions were appreciated. Analytical blood tests were normal or negative. The patient discontinued Tegafur therapy and the lesions faded in 4 weeks.

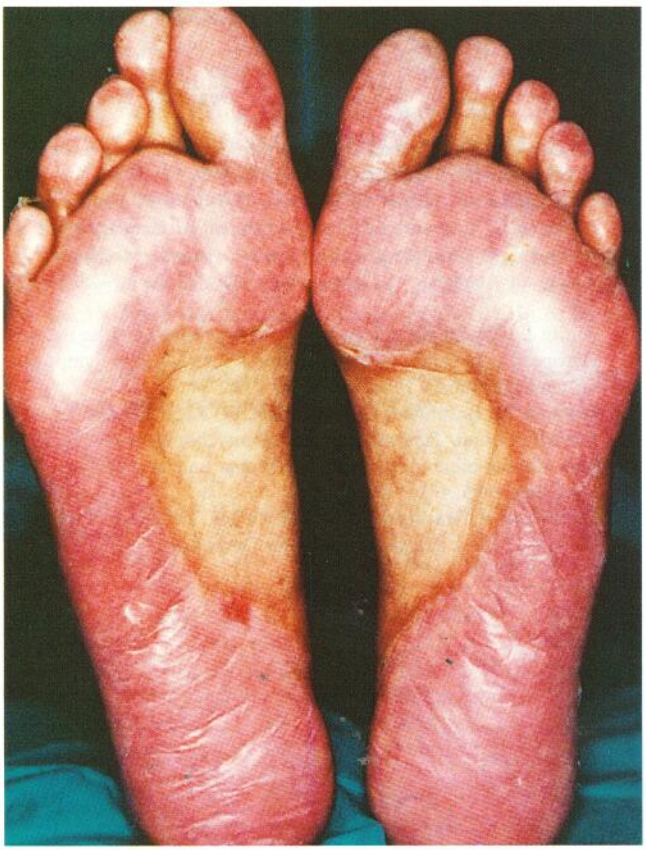

Fig. 1. Plantar erythema with sharp margins.

No recurrence has been observed after 5 months. A skin biopsy from the dorsal aspect of the finger performed 1 week after withdrawal of therapy showed features of residual lichen planus-like drug eruption. The patient refused drug rechallenge.

DISCUSSION

Cutaneous side-effects of Tegafur are frequent events. Skin lesions such as rashes and pigmentation occur in up to a third of patients treated (1). However, only 3 cases of chemotherapy-induced acral erythema in such patients have been reported (2–4). It has been suggested that chemotherapy-induced acral erythema in patients taking Tegafur could be a 5-fluorouracil dependent reaction (4), since Tegafur is metabolized to 5-fluorouracil and cases of chemotherapy-induced acral erythema in patients treated with intravenous 5-fluorouracil have been reported (5).

However, other mechanisms should also be considered. Chemotherapy-induced acral erythema is a frequent cutaneous side-effect of therapy with parenteral 5-fluorouracil and is related to high plasmatic levels of this drug (5). However, blood levels of 5-fluorouracil in patients taking Tegafur orally are lower than 1% of blood levels of Tegafur in the same patients, equivalent to intravenous infusion of very low doses of 5-fluorouracil (1). In addition, cutaneous adverse reactions appear to be more frequent with Tegafur than with 5-fluorouracil. In a previously reported series, cutaneous side-effects occurred in 31% of patients treated with Tegafur in contrast with 10% of patients treated with 5-fluorouracil (6). A possible explanation is that Tegafur is metabolized not only to 5-fluorouracil, but also to dehydro-tegafur and other hydroxilated metabolites (1), which may be pharmacologically active and may be responsible for these unexpected reactions. This is supported by a previously reported case of chemotherapy-induced acral erythema due to Tegafur, in which discontinuation of the therapy caused resolution of lesions and the subsequent instauration of intravenous 5-fluorouracil was free of recurrences (3).

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