Palmar-plantar Erythrodysaesthesia Syndrome and Other Cutaneous Side-effects after Treatment with Tegafur

Sir,

Tegafur is a fluorinated pyrimidine analogous to 5-fluorouracil, used in the treatment of digestive neoplasms with low myelosuppression and absence of immunosuppression. Neurologic, gastrointestinal and mucocutaneous side-effects are common (up to 2–8% of cases). Lesions are usually shown by slight stomatitis, skin dryness, disseminated rash, alopecia, diffuse or nail-restricted hyperpigmentation (1), Stevens-Johnson syndrome (2) and rarely palmar-plantar erythrodysaesthesia syndrome (PPES) (3) or palmoplantar keratoderma secondary to acral erythema (4).

PPES is characterized by a burning-dysaesthetic erythema and oedema of palms and soles followed by desquamation. This syndrome has been described after usage of several chemotherapy drugs but until now we have found only one report of palmoplantar keratoderma secondary to acral erythema related with Tegafur in the English literature (4).

We present 2 patients with digestive neoplasia and hepatic metastasis who developed a typical PPES (case 1) and with palmoplantar keratoderma secondary to PPES associated with cutaneous diffuse, tongue and nails hyperpigmentation (case 2) after treatment with Tegafur.

CASE REPORTS

Case 1

A 57-year-old woman underwent a subtotal gastrectomy in 1990 for an adenocarcinoma. In March 1992, hepatic metastasis was detected and treatment with Tegafur 500 mg/day and Folinic acid 120 mg/day was started. Three months later, she developed a burning disaesthetic erythema and oedema of palms and soles (Fig. 1a), followed by fissuration and desquamation. On cutaneous biopsy, oedema, vascular proliferation and a discrete lymphohistiocytic infiltrate were seen in the dermis. In the epidermis, scattered necrotic keratinocytes, mild vacuolar degeneration of the basal layer and mild spongiosis were found. No changes were seen at the eccrine sweat glands. With the diagnosis of drug reaction, Tegafur was stopped and the lesions disappeared in 10 days. No other drugs were involved.

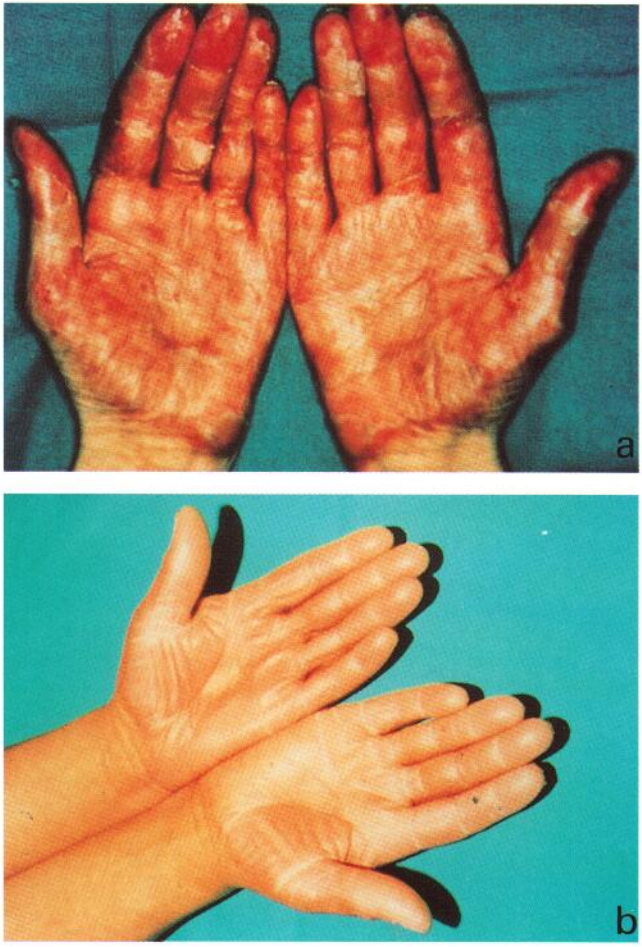

Fig. 1. (*a*) Case 1. Symmetric, well-defined swelling and erythema of palms. (*b*) Case 2. Palmoplantar keratoderma secondary to PPES.

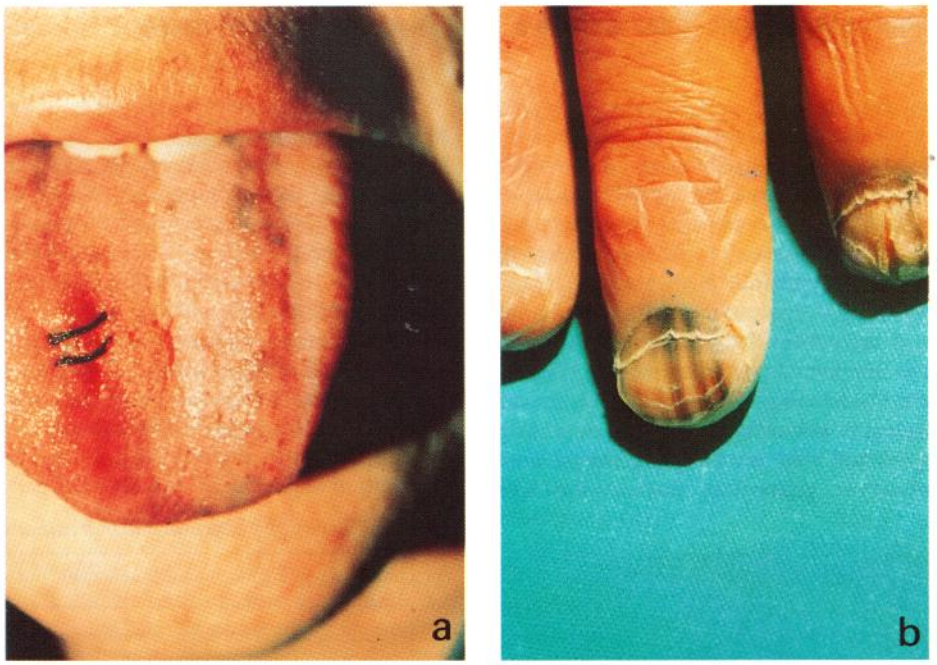

Fig. 2. (*a*) Case 2. Tongue hyperpigmentation. (*b*) Case 2. Brownish longitudinal grooves on the hand nails.

Case 2

A 58-year-old woman had a partial colectomy for a colonic adenocarcinoma detected in 1982. In 1984 hepatic metastasis was detected and treatment with Tegafur 1,600 mg/day, 21 days per month, was started. Two months later she noticed diffuse and tongue hyperpigmentation (Fig. 2a) with dysgeusia. Simultaneously, brownish longitudinal grooves appeared on the hand nails (Fig. 2b) with burning erythema and fissuration, with the subsequent development of a diffuse hyperkeratosis on palms and soles (Fig.1b). These last described lesions disappeared when she finished the cycle to start again with every new cycle. When Tegafur was stopped all the lesions disappeared without recurrence. A cutaneous biopsy of the sole was performed, with histological features similar to those in case 1. No other drugs were involved.

DISCUSSION

PPES was first described by W. Burdorf in 1982. Since then, several terms have been used to describe this disorder: acral erythema, palmoplantar erythema, hand-foot syndrome, peculiar acral erythema, Burdorf reaction and PPES. A recent review of chemotherapy-induced acral erythema includes several drugs as the cause of PPES (5-fluorouracil, cytosine arabinoside, doxorubicin, cyclophosphamide, hydroxyurea, mercaptopurine, methotrexate and mitotane) (5) but not Tegafur. Regimens with either bolus or continuous low-dose infusions can cause the reaction by a dose-dependent mechanism. Usually it appears 1 to 300 days after the beginning of the treatment, and in most cases when hepatic metastasis occurs. Cutaneous lesions are often preceded by a prodrome of dysaesthesia, which is followed by painful, symmetric, well-defined swelling and erythema. Sometimes similar lesions may appear in periungual areas, knuckles, scalp, neck and chest. Palmoplantar keratoderma can appear after cronical PPES (4). The course of PPES is self-limited and pyridoxine appears to decrease the intensity and pain of the lesions.

Our patients also presented cutaneous nails and mucous hyperpigmentation which are unusual side-effects of Tegafur (1).

Because of the increasing use of Tegafur, we believe that these cases are of interest as examples of the different side-effects of this drug.

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