Fixed Drug Eruption Caused by Tolphenamic Acid

Sir,

Fixed drug eruption (FDE) is a common cutaneous reaction caused by various drugs (1–3). In most cases the agent causing FDE is obvious from the patient's history. However, oral or topical challenge is often needed in uncertain cases to confirm the suspected causative agent. Topical challenge is especially useful with phenazone derivatives (4).

Tolphenamic acid (Clotam, GEA) is a widely used anti-inflammatory drug especially in Scandinavia. Mephenamic acid, another common anti-inflammatory drug, is structurally closely related to tolphenamic acid and has been reported to cause FDE (5). However, to our knowledge FDE caused by tolphenamic acid has not been previously reported.

CASE REPORT

A 51-year-old man had since 1979 suffered from transient prostatic pains. In order to relieve the pains he had used acetylsalicylic acid and tolphenamic acid. Since 1990, after taking tolphenamic acid, he had experienced itching. After a few hours erythematous, violaceous-turning patches, 2–5 cm in diameter, developed on his wrists, back and genitals, always exactly on the same sites. At first the patches had been light red and had vanished in two days. Later the skin macules had begun to leave hyperpigmented scars after the patch had vanished, and in the middle of some patches a small blister had been noticed. The patient had not used any other drugs except acetylsalicylic acid, which had never caused any skin rashes. He had had no symptoms in his mouth. During the last year our patient had had the macules up to twice a month; however during the last six months he had not had any symptoms.

The patient was referred to the Department of Dermatology, Helsinki University Central Hospital (Finland) in October 1992. At that time he had approximately ten hyperpigmented macules on his wrists, back and genitals, round or oval in shape and 2–4 cm in diameteer, the clinical picture being suggestive of FDE (Fig. 1).

In November 1992 the patient was taken inpatient for provocations. Because phenazone group is by far the most common cause of FDE in Finland, a local provocation with 10% phenazone salicylate in petrolatum was performed on one FDE patch. The provocation result was negative.

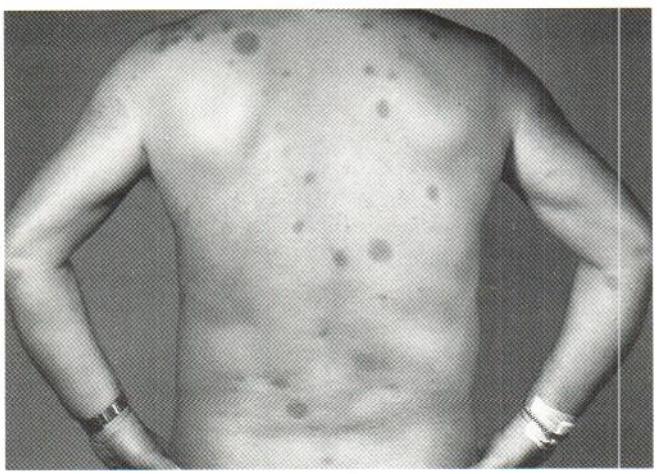

Fig. 1. Hyperpigmented macules on the patient's back.

Thereafter oral provocation with 30 mg tolphenamic acid was performed. One hour after the provocation the sites of the previous patches became itchy and erythematous. Some new patches also developed but no blisters were seen. The clinical picture was typical of FDE.

A biopsy specimen was taken from an erythematous patch of a wrist 1 1/2 h after drug intake. The histological picture was typical of FDE, with an accumulation of pigment in the dermis and in the basal cell zone of the epidermis.

In December 1992 a topical provocation with 10% tolphenamic acid and 10% mephenamic acid in ethanol and petrolatum on the old patches was performed. The test sites were followed up to 12 h and they remained negative.

DISCUSSION

Fixed drug eruption is one of the most common drug-induced eruptions. In a series of 446 reactions from 1971 to 1980, fixed drug eruption comprised 20% of the cutaneous reactions (6). The most common agents causing FDE are phenazones, barbiturates, sulfonamides and tetracyclines (1, 2, 6, 7). There is, however, variation depending on which drug is commonly used in each country. Tolphenamic acid has for many years been widely used in Scandinavia. However, no report of FDE caused by tolphenamic acid has previously been published. Our patient had used tolphenamic acid and other anti-inflammatory agents several years before the typical lesions of FDE developed. Because phenazone derivates are widely used in combination analgetics, we performed a topical provocation with phenazone salicylate according to Alanko et al. (4). When it proved negative oral provocation with tolphenamic acid was made with a positive result.

Because mephenamic acid and tolphenamic acid are structurally closely related, we performed a topical provocation with both agents (4). Both topical tests remained negative. As far as we know our case is the first FDE caused by tolphenamic acid and confirmed with oral challenge.

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