Contact Dermatitis after Calcipotriol and Patch Test Evaluation

Sir,

The vitamin D3 analogue calcipotriol is more and more used topically as replacement of corticosteroids in the treatment of psoriasis. It is usually well tolerated and safe. The adverse events are mainly lesional/perilesional irritations, reported in about 15%, and facial irritations, reported in about 10% of treated patients, mostly mild and in only a few cases the reason for withdrawal of calcipotriol treatment (1-5). The nature of calcipotriol-induced dermatitis is usually considered to be of irritant nature, since it is a general experience that patients may tolerate the drug later if reinstated.

CASE REPORT

In a study of treatment of psoriasis with UVB plus calcipotriol in an ointment formulation, 50 µg/g, compared with UVB plus the ointment base, one patient developed a severe dermatitis causing withdrawal of the treatment.

The patient was a 73-year-old man of good general health with the exception of rheumatic complaints, in particular regarding the back, since many years. He had had psoriasis of limited nummular to plaque type for 13 years. He had used calcipotriol ointment for 4 treatment periods of 4-5 weeks each during the last 2 years without any problems. No additional UVB was given during these periods of calcipotriol treatment. He had previously tolerated sunlight as well as UVB treatment.

At start of the actual treatment he had symmetrical psoriasis plaques on arms and legs. He accepted to participate in a double-blind study of treatment of UVB plus calcipotriol ointment on one side and UVB plus ointment base on the other side. There was a slight but notable improvement after 2 weeks' treatment. Three weeks after start of treatment, the patient noted some itching on one side just after application on the test ointment. A dermatitis involving the lesional as well as the perilesional skin gradually increased in severity, finally causing withdrawal of the topical as well as the UVB treatment. The trial code was broken, revealing that the ointment used on the dermatitis side contained calcipotriol.

An open test was instituted some weeks later on the inner part of the lower arm, on skin not involved by psoriasis or adjacent to psoriatic lesions and previously not treated with calcipotriol. The calcipotriol ointment was applied twice daily within two indicated areas of the skin. After two applications there was an erythema, after four applications a clear dermatitis and after six applications a severe vesicular reaction. No additional UVB was given. The dermatitis at the test areas was treated with corticosteroid cream and healed within a week, but a dark pigmentation remained several weeks after the test.

The patient was then treated with topical betamethasone valerate ointment and cream. He also exposed himself to the sun and suffered no harm.

RESULTS

Three months after the treatment, an open test was performed on the inner part of the lower arm, with application of the same ointment, active and base, used at treatment as well as a patch test including the European standard allergy series used at the clinic, the marketed calcipotriol ointment and cream, the ointment base, and a dilution series of calcipotriol in isopropanol at the concentrations 0.4, 2, 10 and 50 µg/ml. All tests were negative. No additional UVB was given at test areas.

DISCUSSION

The severe dermatitis induced by the calcipotriol ointment application both at treatment and at the first open test indicated that an allergic contact reaction had to be considered. The patient had used calcipotriol ointment during some treatment periods before, without any problems. He had also previously exposed himself to sunlight as well as UVB treatment without any sign of increased light sensitivity. The closed patch tests could not verify any allergic reaction against calcipotriol itself or the formulations used at treatment. Calcipotriol itself has irritating properties (6). The case presented illustrates that in single patients a severe non-allergic contact dermatitis might be provoked with simultaneously strongly positive open application test. The second open test indicated, however, that the lowered threshold was of short duration.

To what extent the UVB irradiation had contributed to the irritancy might be questioned. However, the open test during the active phase of the dermatitis, which turned out to be positive, was not combined with light exposure, and a photosensitivity or phototoxicity or photosensitivity mechanism was, thus, not likely.

In two recent studies of the efficiency of calcipotriol combined with phototherapy, UVB, including 101 and 77 patients, respectively, no increase of lesional/perilesional or facial dermatitis was recorded as compared to calcipotriol alone (unpublished).

Altogether this case illustrates that endogenous variation in the threshold of irritation may render selected patients more vulnerable to irritative events in limited periods of time. To establish a diagnosis of allergic sensation, repetition of testing on some later occasion should therefore be considered mandatory (7, 8). The special risk of false-positive test reading to calcipotriol has been described in recent studies (6, 9). It is likely that some of the previously reported cases of allergy/possible allergy to calcipotriol were not valid, since repeated testing during a non-dermatitis phase was not always performed (10).

REFERENCES

Anaphylactoid Symptoms due to Oral Minocycline

Sir,

Minocycline is a semisynthetic derivative of tetracycline and is bacteriostatic. It has been widely used as an antibiotic drug, with an antimicrobial spectrum of activity against a broad range of gram-positive and gram-negative organisms. There have been several reports of adverse reactions to minocycline, including headache (1) and blurred vision (1) as well as acute renal failure (2), pigmentation of the skin and mucous membranes (3) and serum sickness (4). However, this drug has been generally thought not to cause anaphylactoid reactions. We here report an actual case of anaphylactoid symptoms due to minocycline, which is extremely rare.

A housewife aged 27 years visited us with a 3-day history of lower abdominal pain, which was diagnosed as salpingitis. Minocycline (Minomycin®) and mafenamic acid (Pontalet®) were prescribed. The patient took one 100-mg capsule of Minomycin® and one 250-mg capsule of Pontalet®. Within half an hour she developed dyspnea. After 15 min she started to itch and burn from the cervix, chest and back, and later generalized wheal and erythema developed. She was also distressed because of palpitation and returned to us by ambulance approximately one and a half hours after her intake. On examination, a fall in blood pressure was noted. The symptoms cleared after careful observation, in about 4 h. The patient was not sure if she had received minocycline previously. She did not have a history of sensitivity to aspirin or other nonsteroidal anti-inflammatory drugs. Several days later, a scratch test was performed on her forearm with Minomycin® and Pontalet®. Only Minomycin® revealed a positive reaction, with a large wheal measuring 13 × 16 mm and erythema (40 × 40 mm) in 15 min. Pontalet® showed a negative reaction. Afterwards, a second scratch test was carried out with Minomycin® and its vehicle on her forearm in the same manner. Minomycin® reacted positively and its vehicle gave negative results. A scratch test for a normal control was both negative for Minomycin® and its vehicle. An oral challenge test for Pontalet® was negative. Routine laboratory analyses revealed no apparent abnormal data. It was uncertain whether these symptoms were IgE-dependent or not. A diagnosis of anaphylactoid symptoms due to minocycline was made.

Although anaphylactoid reactions due to penicillins and cephalosporins are well known, those to tetracyclines are uncommon. There have, however, been several papers describing anaphylactoid symptoms to tetracyclines such as tetracycline (5) and doxycycline (6). Since minocycline is one of the tetracyclines, one might expect to find descriptions of the occurrence of anaphylactoid symptoms due to minocycline in the medical literature. However, there appears to have been no report of an actual case of anaphylactoid reactions to minocycline. This is, to our knowledge, the first report describing anaphylactoid symptoms due to minocycline in the English literature.

In view of the world-wide use of this antibiotic and the untoward effects of oral administration in our case, clinicians should be aware of the potential of minocycline to provoke anaphylactoid reactions.

REFERENCES


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