

diaper dermatitis, it was isolated from the lesions in 77.1% of the infants. The clinical types of diaper dermatitis in that study included symmetrical intertrigo, dermatitis erosiva, eczematous dermatitis, napkin psoriasis and papular dermatitis. If *Candida albicans* is the primary cause or should be considered a secondary invader was not possible to evaluate in our study.

Around one third of our patients developed skin disorders later on. Two developed psoriasis and two atopic dermatitis. This is not consistent with Andersen & Thomsen's (1) finding, where only 10% developed a skin disease in later life, two out of sixty developed psoriasis, none developed atopic dermatitis.

In a study of HLA-antigens Skoven & Hjortshøj (4) found that a diagnosis of psoriasisiform napkin dermatitis is not associated with the common HLA types B13, B17 and Bw37, which are often associated with psoriasis.

Our results lead to the conclusion that infants, suffering from psoriasisiform napkin dermatitis may run a greater risk of developing skin diseases, not especially psoriasis however, later in life.

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Diltiazem-Associated Exfoliative Dermatitis in a Patient with Psoriasis

A. P. M. LAVRIJSEN,¹ CORNELIS VAN DIJKE² and BERT-JAN VERMEER¹

¹Department of Dermatology, University Hospital, Leiden, and ²Netherland's Centre for Monitoring of Adverse Reactions to Drugs, Leidschendam, The Netherlands

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We present a patient with psoriasis who developed exfoliative dermatitis with concomitant fever, malaise and liver enzyme elevations, two days after the introduction of the new calcium antagonist diltiazem. The symptoms rapidly resolved after discontinuation of diltiazem and treatment with prednisone. Three years previously, this patient developed a similar reaction after 12 days of treatment with chloroquine. Diltiazem and chloroquine have a structural resemblance, which suggests that cross-reactions between these drugs may occur. *Key words:* Calcium antagonist; Chloroquine; Adverse drug reaction. (Received April 22, 1986.)

A. P. M. Lavrijsen, Department of Dermatology, University Hospital, Rijnsburgerweg 10, 2333 AA Leiden, The Netherlands.

Diltiazem (Tildiem) is a new calcium antagonist, in use for various forms of angina pectoris. The literature on its possible dermatological side effects is still sparse. Several patients with exanthema have been mentioned in clinical reports and the incidence of this side effect has varied in large series between 0.1 and 1.2% of treated patients (1). A patient with a photosensitivity reaction has been reported from Japan (2).

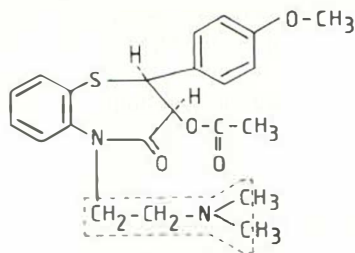
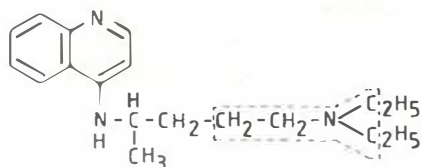
DILTIAZEMCHLOROQUINE

Fig. 1. Structural formula of diltiazem and chloroquine.

We here present a case of exfoliative dermatitis shortly after introduction of diltiazem, in a patient with psoriasis, who previously had a similar reaction to chloroquine.

CASE REPORT

The patient, a woman born in 1913, had a history of psoriasis vulgaris, seronegative polyarthritis, diabetes mellitus, hypertension, angina pectoris and myocardial infarctions. In 1981 exfoliative dermatitis developed 12 days after she had started with chloroquine as an anti-arthritis drug. This was accompanied by malaise, a temperature rise up to 38.5°C and liver enzyme elevations. After discontinuation of chloroquine the symptoms disappeared spontaneously within a few days.

In 1984 she was maintained on the following medication: methyl dopa, isosorbide dinitrate, dipyridamol, nitroglycerin, indomethacin, nitrazepam, metoprolol and nifedipine. On November 19, 1984, nifedipine was replaced by diltiazem. Two days later a pruritic rash appeared on her trunk, which spread to her arms and face and was accompanied by malaise and fever (38.4°C).

On admission on December 1, the whole skin was involved with slightly infiltrated erythematous plaques which were demarcated and had some scaling. On the lower legs small purpuric lesions were present. In several erythematous areas psoriatic lesions were visible. No evidence for infections was found and no enlarged lymph nodes were palpable.

Laboratory investigations showed an elevated white cell count of $16.6 \times 10^9/l$ with 1% basophils, 2% eosinophils, 30% bandforms, 57% neutrophils, 7% lymphocytes and 3% monocytes and an erythrocyte sedimentation rate of 72 mm in the first hour. Bilirubin and liver enzymes in the serum were also elevated: total bilirubin 20 $\mu\text{mol/l}$ (normal <17), conjugated bilirubin 10 $\mu\text{mol/l}$ ($n < 4.3$), aspartate aminotransferase 27 IU/l ($n < 15$), alanine aminotransferase 112 IU/l ($n < 15$), alkaline phosphatase 118 IU/l ($n < 60$), lactate dehydrogenase 183 IU/l ($n < 160$). Urea nitrogen, creatinine, total serum proteins, albumin and urinalysis were normal. Urinary cultures for bacteria and serological tests for syphilis were negative. A radiography of the chest was normal. Histological investigation of the affected skin showed an acute dermatitis with edema, many neutrophilic granulocytes in the epidermis and slight erythrocyte extravasation in the stratum papillare.

On admission diltiazem was stopped but the other medications were continued. Because of a temperature rise up to 39°C on the second day and increasing malaise, the patient was treated with prednisone, initially 30 mg daily and thereafter in declining dosage during a period of 14 days. Within 24 hours after treatment with prednisone had begun the temperature normalized. The skin rash resolved within 10 days with extensive scaling. The blood and liver enzyme abnormalities disappeared also within this period.

DISCUSSION

Exfoliative dermatitis is most commonly caused by drugs or an underlying disease such as psoriasis (3). In our patient, the recent episode of exfoliative dermatitis occurred shortly after the introduction of diltiazem. A number of other drugs were also taken, but they were in use for a long time and were continued without problems. No evidence for infections was detected and the psoriasis was in a stable phase. Also the appearance of liver enzyme elevations is more compatible with a drug-induced exfoliative dermatitis than with an exacerbation of the psoriasis.

As far as we are aware, diltiazem-associated exfoliative dermatitis has not been described in the literature before. There are some similarities between our case and a patient described by Scolnick & Brinberg (4) who used diltiazem and experienced lymphadenopathy, fever, liver enzyme elevations and exanthema, followed by peeling of the skin of the palms and soles (3).

It may be of significance that our patient previously experienced a similar reaction to chloroquine. Although this may have been a coincidence, the possibility of a cross-reaction between these drugs should be considered. The structural formula shows that both molecules indeed have a similarity, in that they both contain a

$-\text{CH}_2-\text{CH}_2-\text{N}<\text{C}-\text{N}-\text{C}$ group (Fig. 1).

It is well known and illustrated by our patient, that antimalaria drugs such as chloroquine and hydroxychloroquine possess a special risk for patients with psoriasis (5). On the basis of one case it is of course not possible to predict whether the same holds true for diltiazem. However, it is very interesting that of the 7 patients, reported to the Food and Drug Administration of the United States of America with exfoliative dermatitis associated with the use of diltiazem, one also had psoriasis (W. Turner, personal communication).

In summary, the exfoliative dermatitis in the described case was most probably caused by diltiazem. The history of our patient suggests that it is possible that cross-reactions may occur between diltiazem and chloroquine. Furthermore, patients with psoriasis may be at special risk for this side effect and physicians should be aware of this possibility. Further studies on this issue are necessary.

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