Acta Derm Venereol (Stockh) 1993; 73: 210–211

Pemphigus Foliaceus Induced by Nifedipine

SOO-CHAN KIM, JIN HYOUNG WON and SUNG KU AHN

Department of Dermatology, Yonsei University Wonju College of Medicine, Wonju, Korea

We report a case of pemphigus foliaceus caused by nifedipine. In this case casual rechallenge with nefedipine confirmed that this drug was the causative agent. The skin lesions cleared quickly after withdrawal of the drug and treatment with a short course of oral steroids. To our knowledge, this is the first reported patient with nifedipine-induced pemphigus. ***Key word: Drug reaction.***

(Accepted January 11, 1993.)

Acta Derm Venereol (Stockh) 1993; 73: 210–211.

S.-C. Kim, Department of Dermatology, Yonsei University Wonju College of Medicine, 162 Ilsan-dong, Wonju, Korea 220-701.

Nifedipine, a calcium channel blocking agent, widely used for treatment of angina, hypertension and Raynaud's phenomenon, has been reported to have various cutaneous side effects: erythematous edema (1,2), generalized fixed drug eruption (3), photodermatitis (4) and urticarial eruption (5). However, there are no reports in the literature of pemphigus following the use of nifedipine. In this report, we describe a case of pemphigus foliaceus that developed within 3 months after the patient began to take nifedipine for his hypertension.

CASE REPORT

A 48-year-old Korean man with mild hypertension had been taking nifedipine for 3 months. Otherwise, his health was good. One week prior to visiting our department, he developed skin rashes on his trunk and extremities. Examination showed multiple erythematous flaccid bullae and superficial crusted patches on his trunk and both upper and lower extremities (Fig. 1). Oral mucosal lesions were not present. There was no past history of drug hypersensitivity.

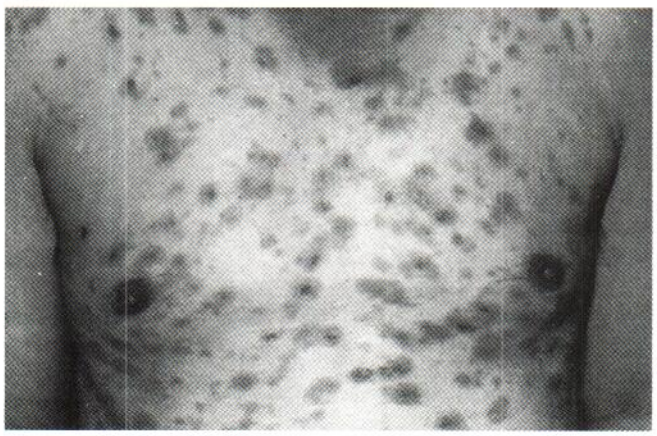

Fig. 1. Flaccid bullae and superficial crusted patches on the patient's chest.

Histologic examination of the skin lesion showed a subcorneal bulla with acantholytic cells. A few eosinophils infiltrated the epidermis. Direct immunofluorescence of a perilesional biopsy specimen and indirect immunofluorescence were negative. Results of a complete blood cell count and 12 factor automated chemical blood analysis (SMA 12) were all within normal limits.

A diagnosis of nifedipine-induced pemphigus foliaceus was strongly suspected, and nifedipine therapy was discontinued. The skin lesions almost resolved within 1 week after treatment with oral and topical corticosteroids. Ten days later, a casual rechallenge with nifedipine (40 mg) was performed by the patient himself due to headache. One day after readministration of the drug, erythematous bullae developed on the trunk and extremities. Again the skin lesions resolved promptly after discontinuation of the drug and treatment with low-dose prednisolone. At a follow-up examination 1 year later, the patient showed complete remission.

DISCUSSION

The most common type of drug-induced pemphigus that has been reported occur in individuals after treatment with a number of drugs with an active sulfhydryl group such as penicillamine and captopril (6,7). In addition, other drugs without a sulfhydryl group such as penicillin (8), rifampicin (9), phenobarbital (10) and piroxicam (11) have also been reported as being responsible for drug-induced pemphigus.

It has been proposed that the pemphigus foliaceus antigen is a desmosomal core protein, desmoglein 1 (12), and that the pemphigus vulgaris antigen is a 130 KD cadherin cell adhesion molecule (13). Both pemphigus antigen molecules form a complex with plakoglobin via disulfide bonding (14). Sulfhydryl-containing drugs, therefore, can bind to these pemphigus antigen molecules and may produce acantholysis by at least two mechanisms. First, the drug binding may alter the molecule to produce a neoantigen and result in autoantibodies (15). Second, binding of the drug to the antigen may directly interfere with its normal function, which is presumed to be cell-cell adhesion (16). In this case, acantholysis can occur in the absence of autoantibodies.

However, reasonable explanations for the mechanism of pemphigus induced by drugs without a sulfhydryl group are lacking at the present time. It is most likely that nifedipine directly produced acantholysis in this patient. Several factors support this hypothesis. First, the tissue-bound and circulating autoantibodies were absent in this patient. Second, the skin lesions promptly resolved after discontinuation of nifedipine. Third, on rechallenge the skin eruption recurred quickly within 1 day. But, we cannot exclude the possibility that the antibody production in this patient was too weak to be detected with laboratory tools.

In conclusion, we emphasize the fact that nifedipine should be included in the list of drugs that can induce pemphigus foliaceus. Further studies are needed to elucidate the pathomechanism of nifedipine-induced pemphigus.

REFERENCES

1. Bridgman JF. Erythematous edema of the leg due to nifedipine. Br Med J 1978; 276: 578.
2. Tordjman K, Rosenthal T, Burstyn M. Nifedipine induced periorbital edema. Am J Cardiol 1985; 55: 1445.
3. Alcalay J, David M, Sandbank M. Cutaneous reactions to nifedipine. Dermatologica 1987; 175: 191–193.
4. Zenarola P, Gatti S, Lomuto M. Photodermatitis due to nifedipine: report of 2 case. Dermatologica 1991; 182: 196–198.
5. Toner M, White A, Moriarty J, Clancy L. Allergic urticarial eruption, leukocytosis and abnormal liver function tests following nifedipine administration. Chest 1988; 93: 1320–1321.
6. From E, Frederiksen P. Pemphigus vulgaris following D-penicillamine. Dermatologica 1976; 152: 358–362.
7. Katz RA, Hood AF, Anhalt GJ. Pemphigus-like eruption from captopril. Arch Dermatol 1987; 123: 20–21.
8. Fellner MJ, Mark AS. Penicillin- and ampicillin-induced pemphigus vulgaris. Int J Dermatol 1980; 19: 392–393.
9. Lee CW, Lim JH. Kang HJ. Pemphigus foliaceus induced by rifampicin. Br J Dermatol 1984; 111: 619–622.
10. Dourmishev AL, Rahman MA. Phenobarbital-induced pemphigus vulgaris. Dermatologica 1986; 173: 256–258.
11. Martin RL, McSweeney GW, Schneider J. Fatal pemphigus vulgaris in a patient taking piroxicam. N Engl J Med 1983; 309: 795–796.
12. Eyre RW, Stanley JR. Human autoantibodies against a desmosomal protein complex with a calcium-sensitive epitope are characteristic of pemphigus foliaceus patients. J Exp Med 1987; 165: 1719–1724.
13. Amagai M, Klaus-Kovtum V, Stanley JR. Autoantibodies against a novel epithelia cadherin in pemphigus vulgaris, a disease of cell adhesion. Cell 1991; 67: 869–877.
14. Korman NJ, Eyre RW, Klaus-Kovtum V, Stanley JR. Demonstration of an adhering-junction molecule (plakoglobin) in the autoantigens of pemphigus foliaceus and pemphigus vulgaris. N Engl J Med 1989; 321: 631–635.
15. Korman NJ, Eyre RW, Zone J, Stanley JR. Drug-induced pemphigus: autoantibodies directed against the pemphigus antigen complexes are present in penicillamine and captopril-induced pemphigus. J Invest Dermatol 1991; 96: 273–276.
16. Yokel BK, Hood AF, Anhalt GJ. Induction of acantholysis in organ explant culture by penicillamine and captopril. Arch Dermatol 1989; 125: 1367–1370.