

Two Cases of Cefotiam-induced Contact Urticaria Syndrome

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Contact urticaria refers to a wheal-and-flare response after cutaneous exposure to certain chemicals. If contact urticaria is accompanied by systemic symptoms, it is referred to as contact urticaria syndrome. Herein we report two cases of contact urticaria syndrome occurring in nurses due to occupational exposure to cefotiam. (Ann Dermatol 12(2) 119~121, 2000).

Key Words : Contact urticaria syndrome, Cefotiam

Contact urticaria describes a wheal-and-flare response elicited within 30-60 minutes after cutaneous exposure to certain agents¹. Delayed-onset contact urticaria (up to 4-6 hours) could occur and the mechanism for this delay is possibly related to slower percutaneous penetration². Contact urticaria encompasses a number of different clinical manifestations and the symptoms which can vary from the mildest forms of burning, stinging and itching sensation to life-threatening anaphylaxis referred to as contact urticaria syndrome³.

Cefotiam is one of the most popular second generation cephem antibiotics used in Korea. Occupational contact urticaria due to cephalosporins has been reported since 1975⁴, and the cases of contact urticaria due to cefotiam has increased over the last 10 years in Japan⁵. We consider it important for health-care workers to be aware of possible contact urticaria syndrome from cefotiam because cefotiam is used in many hospital settings. Our department reported one case of contact dermatitis due to cephalosporins⁶ and the other case of cefotiam-induced contact urticaria syndrome⁷.

Recently we experienced two nurses showing

contact urticaria syndrome after occupational exposure to cefotiam antibiotics and reviewed the literature concerning this subject.

CASE REPORTS

Case 1

A 25-year-old female patient was presented at our dermatology clinic with generalized pruritic skin eruption and dyspnea. She has been a nurse in our hospital for 3 years and the eczematous lesions on the hands have developed for 2 years. The hand eczema was aggravated during work, but improved after work. One and a half years ago, she developed a generalized pruritic skin eruption, headache, and dyspnea a few minutes after preparing a bottle of cefmetazole and cefotiam. The symptoms disappeared in a few hours. Since then similar episodes including pruritic wheals have occurred several times every year. A few days ago, she handled the same kinds of antibiotics again and developed the same symptoms. She already knew that she had metal allergy and others were nonremarkable.

Case 2

A 26-year-old female nurse in our hospital was presented with generalized pruritic skin eruption over the whole body. She has worked in our hospital for 1 year and 8 months and had developed hand eczema for 6 months. The hand eczema was aggravated during work, but regressed after work.

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Table 1. 14 kinds of antibiotics used in open patch tests

first generation cephalosporins
ceftezole, cefazolin
second generation cephalosporins
cefotiam, cefuroxime, cefmetazole
third generation cephalosporins
cefotaxime, ceftriaxone, ceftazidime
penicillin mixture
sulbenicillin, sulbactam/ampicillin, acid/ticarcillin
other antibiotics
flumoxef, carumonam, aztreonam

Three months ago, she handled cefotiam and then developed a generalized pruritic skin eruption, dyspnea, headache and abdominal pain. After an injection of glucocorticosteroid and antihistamines, the symptoms disappeared. After then, she experienced the same symptoms two times and the eczematous lesions on the hands became aggravated on every attack. Her past medical histories and family histories were noncontributory.

Patch tests

Based on the above histories, we suspected that these two women were suffering from contact urticaria syndrome due to cefotiam. So we performed open patch tests with 14 kinds of antibiotics used in our hospital on their backs (Table 1) and also performed closed patch tests with 23 kinds of the Korean standard series considering the possibility of additional contact dermatitis.

A 20-minute open patch test with 14 kinds of antibiotics showed wheal-and-flare reactions to cefotiam in both patients but not reactive in other kinds of antibiotics (Fig. 1). The results of the closed patch tests with the Korean standard series in patient 1 showed positive responses to cobalt chloride and nickel sulfate on 2-day and weak positive responses on 4-day, weak positive response to mercapto mix on 2-day, but negative on 4-day. The results of patient 2 was weak positive responses to neomycin sulfate, cobalt chloride and balsam of Peru on 2-day, but all negative on 4-day.

DISCUSSION

Most patients with contact urticaria due to cefo-

Fig. 1. A wheal-and-flare reaction to cefotiam but not reactive to the other antibiotics in case 2.

tiam are nurses. The reasons for the high incidence of contact urticaria syndrome in the nurses may be that cefotiam is one of the most potent sensitizers through contact with the skin, high consumption of cefotiam and may be related to the vacuum vials⁵. Intermittent epidermal or mucosal exposure is by far the best way to sensitize. In some cases, hand eczema and tiny dyshidrotic vesicles frequently appeared on the fingers. Hand eczema was thought to be induced secondarily to contact urticaria, as the condition improved after these patients had stopped handling these antibiotics. However, it is also suspected that the nurses could have been sensitized through damaged skin, for most of them had hand eczema. All kinds of cephalosporin antibiotics have in common the cephalosporinic acid, so these could be crossreacted theoretically, but their radicals are different, presenting some changes in activity and pharmacokinetics.

In our two cases, their urticarial reactions appeared immediately after the patients handling of the antibiotics including cefotiam and they might be sensitized during repeated occupational exposure, suggesting immunologic mechanism involved, but we could not perform passive cutaneous transfer testing and prick testing. In addition, open patch tests with the constituents of cefotiam, cefotiam dihydrochloride and sodium carbonate anhydride were not done. Although the hand eczema had been resistant to local steroid therapy, it disappeared (or was relieved) after the avoidance of exposure to cefotiam, suggesting that cefotiam was at least one of the causative agents inducing and/or exacerbating

hand dermatitis. Also, skin irritability of cefotiam might have some relevance to the occurrence of hand dermatitis and the resultant easy penetration of cefotiam and sensitization against it.

Occupational contact urticaria from foods⁸, rubber gloves⁹, chlorhexidine¹⁰ and certain drugs¹¹⁻¹³ has been reported. But contact urticaria from antibiotics, especially cephalosporin, is uncommon and only a few cases of contact allergy due to cephalosporin compounds have been reported^{2,4}. As shown in our cases, we consider it important to be aware of possible contact urticaria syndrome in nurses with cefotiam exposure.

REFERENCES

1. Krogh G, Maibach HI : The contact urticaria syndrome-An update review. *J Am Acad Dermatol* 5:328-342, 1981
2. Calnan C : Delayed onset contact urticaria. In Fisher AA : *Contact Dermatitis*, 4th ed. Philadelphia, Lea & Febiger, 778-807, 1995
3. Harvell J, Bason M, Maibach HI : Contact urticaria and its mechanisms. *Fd Chem Toxic* 32:103-112, 1994
4. Tuft L : Contact urticaria from cephalosporins. *Arch Dermatol* 111:1609, 1975
5. Shimizu S, Chen KR, Miyakawa S : Cefotiam-induced contact urticaria syndrome: An occupational condition in Japanese nurses. *Dermatology* 192:174-176, 1996
6. Woo JH, Shin KY, Park CW, Lee CH : A case of allergic contact dermatitis due to cephalosporins. *Kor J Dermatol* 36:1125-1127, 1998
7. Shin KY, Lee JY, Park CW, Lee CH : A case of cefotiam-induced contact urticaria syndrome. *Kor J Dermatol* 36:1092-1095, 1998
8. Hjorth N, Reed-Peterson J : Occupational protein contact dermatitis in food handlers. *Contact Dermatitis* 2:28-42, 1976
9. Lahti A, Turjanmaa K : Prick and use tests with 6 glove brands in patients with immediate allergy to rubber proteins. *Contact Dermatitis* 26:259-262, 1992
10. Fisher AA : Contact urticaria from chlorhexidine. *Cutis* 43:17-18, 1989
11. Mancuso G : Contact urticaria and severe anaphylaxis from fifamycin SV. *Contact Dermatitis* 27:124-125, 1992
12. Keller K, Schwanitz HJ : Combined immediate and delayed hypersensitivity to mezlocillin. *Contact Dermatitis* 27:348, 1992
13. Rudzki E, Rebandel P : Occupational contact urticaria from penicillin. *Contact Dermatitis* 13:192, 1985