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CASE REPORT

Fixed Drug Eruption Due to Allopurinol: Positive Oral Provocation

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A fixed drug eruption (FDE) is characterized by the presence of a solitary or multiple, pruritic, well-circumscribed, erythematous plaques. These lesions have tendency to recur at same sites and heal with residual hyperpigmenation. With repeated attacks, the size and/or number of the lesions may increase. So far, more than 100 drugs have been implicated in causing FDEs, including ibuprofen, sulfonamide, naproxen, and tetracylines. FDE caused by allopurinol has been rarely reported in the literature, but there has been no confirmed case based on oral provocation test. Herein, we report a case of FDE in which the lesions recurred whenever allopurinol was administered for the treatment of gout. A 64-year-old male experienced repeated episodes of well-demarcated dusky erythematous patches on the whole body for 2 months. He took allopurinol intermittently for amelioration of his gout symptom, but denied other medication history. Pruritic erythematous edema developed on the previous lesions 12 hours after oral provocation of 200 mg of allopurinol. **(Ann Dermatol 23(S3) S402～S403, 2011)**

-Keywords-
Allopurinol, Fixed drug eruption, Oral provocation test, Topical provocation test

INTRODUCTION

A fixed drug eruption (FDE) is characterized by a solitary or multiple, pruritic, well circumscribed, erythematous plaques. These lesions have tendency to recur at same sites and heal with residual hyperpigmenation. With repeated attacks, the size and/or number of the lesions may increase. More than 100 drugs have been implicated as causes of FDEs, including ibuprofen, sulfonamide, naproxen, and tetracyclines. FDE caused by allopurinol is a rare occurrence, and no confirmed case has been reported on the basis of oral provocation test. We herein report a case of FDE following the administration of allopurinol for the treatment of gout.

CASE REPORT

A 64-year-old man visited our clinic with complaints of recurrent, dusky, erythematous macules on the hands, elbow, perioral area and right thigh (Fig. 1A). The patient stated that he had a previous history of a similar lesion on several occasions at the same site after consuming alcohol. The patient had occasionally taken allopurinol for treatment of acute gout attack, which was usually followed by drinking. The patient had experienced skin lesions while taking allopurinol, which resolved when drug was withdrawn and recurred in the same location when the drug was re-administered.

The lesions cleared within 7 days of treatment with systemic and topical corticosteroid, leaving slight hyperpigmentation. Topical provocation test was performed 2 weeks after resolution of the skin lesions, in the absence of therapy. Allopurinol, in the crushed and dispersed form for patch testing was applied at a concentration of 10% in petrolatum base at the site of previous lesion. Readings were carried out immediately and 2 days after provoca-

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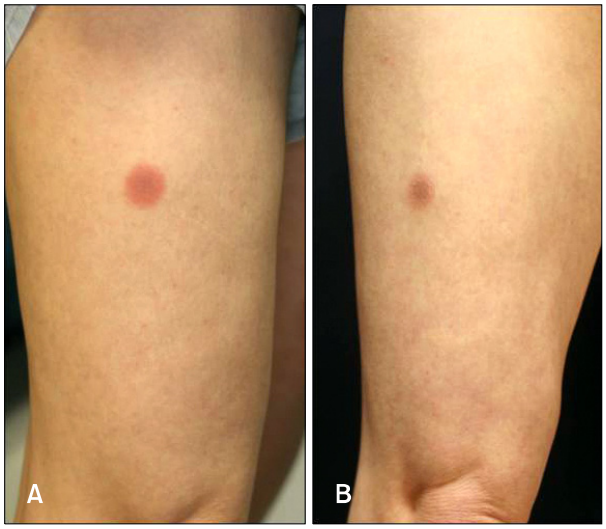

Fig. 1. Clinical appearance of the fixed drug eruption on the patient's trunk (A) at the time of the 1st visit and (B) 12 hours after an oral provocation test with allopurinol.

tion, where the results were negative.

Two weeks after the patch test, we decided to perform an oral provocation with allopurinol. We started to administer a quadrant therapeutic dose of allopurinol (100 mg) with no response. A day afterwards, half the therapeutic dose of allopurinol (200 mg) was administered. Twelve hours after exposure to allopurinol, a flare-up of the FDE occurred, with development of erythema at the previously affected site. Pruritic, erythematous, edematous patches developed on sites of the previous lesion after oral provocation with 200 mg of allopurinol (Fig. 1B). From the findings, we were able to confirm the role of allopurinol as a cause of FDE in our case.

DISCUSSION

FDE can develop from 30 minutes to 8 to 16 hours after ingestion of medications. Lesion may occur on any site on the skin and mucosa. However, preferential sites for involvement in the formation of FDE have been reported for certain drugs.

Allopurinol is rarely a cause of FDE. Dermatologic adverse drug reactions due to allopurinol are usually maculopapular eruptions, but severe cutaneous adverse drug reactions such as drug hypersensitivity syndrome, Stevens-Johnson syndrome and toxic epidermal necrolysis can also occur. In rare instances, allopurinol has been reported to cause eosinophilic pustular folliculitis, toxic pustuloderma, granuloma annulare disseminatum and a pityriasis rosea-like adverse reaction[1].

The pathogenesis of the FDE still remains to be obscure. It seems that a large homogenous population of CD8+ T cells are distributed along the epidermal basal layer in FDE and possess the capacity to produce large amounts of IFN-r. These cells are likely to play a significant role in the formation of FDE lesions. Same-site recurrence may be explained with respect to immunohistochemical findings of prolonged ICAM-1 expression in the lesional keratinocytes, which correlate with the degree of residing epidermal T suppressor/cytotoxic cells[2].

Identification of the causative drugs of FDE is usually established by re-challenge, but patch tests may be a safer alternative[3]. The re-challenge test seems to represent the most reliable method for identifying causative drugs, even though it is not 100% reliable and probably hazardous.

Systemic oral challenge and topical provocation tests are usually performed to identify the drugs responsible for the FDE. Oral challenge tests with a single therapeutic dose of the suspected drug, starting at 1/10～1/2 of the therapeutic dose followed by full therapeutic dose on the subsequent day if there is no reaction to the first dose, is the usually followed protocol[4].

There are several causes for the appearance of false negative results in topical provocation test. First and most importantly, patch test should be done at sites of previous lesions because patch tests at the non-lesional sites usually yield a negative response. Other responsible factors are the timing of patch testing, concentrations and penetration properties of the drug[5].

We performed topical provocation 3 weeks after the last attack. We assumed that this was a refractory period, which resulted in no provocation. Based on our past experience, we recommend topical provocation to be performed at least 2 weeks after resolution of the lesions. Allopurinol is the first-choice drug for maintenance of gout patients and at the same time, the only possible medication. Therefore, we suggest allopurinol desensitization for patients who have FDE to allopurinol.

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