

Itraconazole-induced Drug Eruption Confirmed by Challenge Test

Sir,

Drug eruptions are rarely induced by itraconazole (1–4). Acute generalized exanthematic pustulosis (AGEP) (1, 2) and purpuric eruption (3) induced by itraconazole have been reported, however, no case of itraconazole-induced drug eruption has been confirmed by challenge test. We present here a case of itraconazole-induced eruption confirmed by challenge test, which is thought to be the first case ever presented.

CASE REPORT

A 29-year-old man had a past history of infantile asthma and atopic dermatitis. Since he was found to have tinea superficialis on the trunk, itraconazole (Itrizole[®], Janssen Pharmaceutica, Belgium) (100 mg twice a day) was administered by his physician. One week after initiation of itraconazole, erythematous infiltrative papules and macules developed on the face, extremities and trunk where no skin lesion had existed previously. He was then referred to our clinic. His eruptions were different from tinea lesions, and fungi were not found in the lesions microscopically. The new lesions were infiltrative papules and macules. Given the possibility of drug eruption, itraconazole was stopped. Seven days after discontinuation of itraconazole, the eruptions cleared. He had no history of taking 5-FC or any other oral antifungal drug. Scratch test, patch test, scratch patch test (10% and 30% pet.) and drug-induced lymphocyte stimulation test for itraconazole (content of Itrizole[®] and itraconazole powder kindly provided by Janssen-Kyowa Co. Ltd, Tokyo, Japan) were all negative. On the other hand, a challenge test for Itrizole[®] (50 mg, single dose) induced pruritic erythema on the face 3 h later. Six hours after the test, pruritic erythematous papules and macules developed on the hands and dorsa of the feet. The eruptions cleared within 2 days. The Itrizole[®] capsule without contents had no allergic effect. This case was therefore diagnosed as maculopapular-type drug eruption caused by itraconazole.

DISCUSSION

Itraconazole is reported to have gastrointestinal disturbance (4%) and headache (1%) as its most common side-effects (5). Adverse cutaneous reactions to itraconazole are known to be quite rare. Heymann & Manders (1) and Park et al. (2) reported itraconazole-induced AGEP. Kramer et al. presented a case of itraconazole-induced purpuric eruption (3). Those authors presented not only clinical descriptions but also findings of histology. However, confirmation of the eruptions with challenge tests has not been performed.

Our patient exhibited infiltrative erythematous papules and macules in response to itraconazole administration, which cleared with discontinuation of the drug. The erythematous macules were reproduced by challenge test with a single dose

of itraconazole, suggesting allergic reaction. He had not previously taken any oral antifungal drug. Since patch test, scratch patch test and drug-induced lymphocyte stimulation test were all negative, metabolite of itraconazole possibly induced allergic reaction.

Itraconazole has been used widely for onychomycosis and dermatomycosis, especially as "pulse therapy" (6). Recently, the effectiveness of antifungal drugs for seborrhoeic dermatitis and atopic dermatitis has been suggested (7). The opportunities for administration of itraconazole will increase in the future. Itraconazole-induced drug eruptions should be considered by dermatologists when treating patients with this drug, even though it is a rare complication.

ACKNOWLEDGEMENT

The authors thank Dr Michael Connolly (Translation Co. Ltd, Osaka, Japan) for critical reading of the manuscript and the medical representative and information staff of Janssen-Kyowa Co. Ltd (Tokyo, Japan) for their technical assistance.

REFERENCES

1. Heymann WR, Manders SM. Itraconazole-induced acute generalized exanthematic pustulosis. *J Am Acad Dermatol* 1995; 33: 130–131.
2. Park YM, Kim JW, Kim CW. Acute generalized exanthematous pustulosis induced by itraconazole. *J Am Acad Dermatol* 1997; 36: 794–795.
3. Kramer KE, Yaar M, Anderson W. Purpuric drug eruption secondary to itraconazole. *J Am Acad Dermatol* 1997; 37: 994–995.
4. Plotnick AN, Boshoven EW, Rosychuk RA. Primary cutaneous coccidioidomycosis and subsequent drug eruption to itraconazole in a dog. *J Am Anim Hosp Assoc* 1997; 33: 139–143.
5. Pierard GE, Arrese-Estrada J, Pierard-Franchimont C. Treatment of onychomycosis: traditional approaches. *J Am Acad Dermatol* 1993; 29 Suppl: S41–S5.
6. Doncker PD, Gupta AK, Marynissen G, Stoffels P, Heremans A. Itraconazole pulse therapy for onychomycosis and dermatomycosis: an overview. *J Am Acad Dermatol* 1997; 36: 969–974.
7. Faergemann J. *Pityrosporum ovale* – what's new? *Mycoses* 1997; 40 Suppl 1: 29–32.

Accepted August 23, 1999.

Yasushi Goto, Takeshi Kono*, Kayoko Teramae and Masamitsu Ishii

Department of Dermatology, Osaka City University Medical School, 1-4-7 Asahimachi, Abeno-ku, Osaka, 545-8585, Japan

*Address for offprints