

## Nimesulide-induced, multifocal, urticarial fixed drug eruption confirmed by oral provocation test

Sir,

Fixed drug eruption (FDE) is a common subset of cutaneous reactions that arise due to various drugs. Multifocal FDE (MFDE) is defined by skin eruptions at more than one site. Nimesulide is a cyclooxygenase (COX) inhibitor with a high degree of selectivity to COX-2. Although commonly prescribed, there is only one reported case of nimesulide-induced MFDE in a child.<sup>[1]</sup>

A 41-year-old old female was referred to our clinic because of the sudden appearance of numerous, erythematous, urticarial plaques with slight desquamation on the trunk and extremities over the last 18 hours. According to her history, she usually received paracetamol for her dysmenorrhea; however, over the last eight months, she started using piroxicam or nimesulide over the counter. At the time of the examination, a 3-mm punch biopsy was performed and histological examination confirmed the diagnosis of FDE.

The patient was not able to link the eruption with the intake of any drugs. An oral provocation test was suggested, she consented and an appointment was scheduled a month after the remission of the lesions.

Nimesulide seemed to be the most probable causative agent based on her history. A dose of 25 mg was initially administered and an additional dose of 25 mg was given after an hour as the patient was free of eruptions. Approximately 30 minutes after the 2<sup>nd</sup> dose, we noticed the appearance of a widespread, slightly itching erythema which was localized on the trunk. After an hour, we administered a third dose of 25 mg nimesulide (a total of 75 mg) and multiple, urticarial, erythematous plaques appeared within 15–20 minutes [Figure 1]. Oral provocation tests were also performed with piroxicam and paracetamol and were negative.



**Figure 1: Erythematous, pruritic plaques with slight desquamation after administration of nimesulide**

Nimesulide is a well tolerated, nonsteroidal, anti-inflammatory sulfonamide drug, used with or without medical prescription. The most common reported side effects include nausea, vomiting, and diarrhea while skin rash and pruritus are the most usual cutaneous adverse reactions.

FDE characteristically occurs each time the offending drug is administered, although the number of involved sites may increase. The pathogenesis of the disease is still obscure. It seems that a large homogenous population of CD8 (+) T cells are distributed along the epidermal basal layer in FDE and have the capacity to produce large amounts of IFN-gamma. These cells are likely to play a significant role in FDE lesions.<sup>[2]</sup>

Linking of a drug with FDE may be difficult when the patient is receiving more than one drug. The rechallenge test seems to represent the most reliable method of identifying causative drugs even though it is not 100% reliable and probably hazardous.<sup>[3]</sup> Patch testing at the site of a previous lesion yields a positive response in up to 43% of patients<sup>[4]</sup>, while the reliability of topical provocation on previously involved and uninvolved skin is variable.<sup>[5]</sup>

The early diagnosis of any drug eruption is very important for all patients. Although the most useful tool in the diagnosis of drug reactions, the rechallenge test should be carefully performed when properly after FDE is determined.

**Efstathios Rallis, Evgenia Stavropoulou,  
Ioannis Paraskevopoulos<sup>1</sup>**

Departments of Dermatology and <sup>1</sup>Allergology, Army General Hospital, Athens, Greece

**Address for correspondence:** Dr. Efstathios Rallis, 11 Pafsaniou Str, 11635, Athens, Greece. E-mail: efrall@otenet.gr

## REFERENCES

1. Sarkar R, Kaur C, Kanwar AJ. Extensive fixed drug eruption to nimesulide with cross-sensitivity to sulfonamides in a child. *Pediatr Dermatol* 2002;19:553-4.
2. Shiohara T, Mizukawa Y. Fixed drug eruption: A disease mediated by self-inflicted responses of intraepidermal T cells. *Eur J Dermatol* 2007;17:201-8.
3. Puavilai S, Chunharas A, Kamtavee S. Drug eruptions: The value of oral rechallenge test and patch test. *J Med Assoc Thai* 2002;85:263-9.
4. Barbaud A, Reichert-Penetrat S, Trechot P, Jacquin-Petit MA, Ehlinger A, Noirez V, *et al*. The use of skin testing in the investigation of cutaneous adverse drug reactions. *Br J Dermatol* 1998;139:49-58.
5. Ozkaya-Bayazit E. Topical provocation in fixed drug eruption due to metamizol and naproxen. *Clin Exp Dermatol* 2004;29:419-22.