

Multilocular bullous fixed drug eruption elicited by paracetamol and migraine attacks, but not by paracetamol alone

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Fixed drug eruption (FDE) is characterized by cutaneous or mucosal lesions due to drug intake. Re-exposure to the eliciting drug evokes a similar lesion at the same body site, possibly accompanied by additional lesions at other sites.¹ Here, we present the unusual case of a patient with three episodes of FDE following nonsteroidal anti-inflammatory drug (NSAID) taken for treatment of migraine attacks. Of interest, NSAID taken in the absence of migraine continued to be well tolerated.

CASE REPORT

A 30-year-old woman presented with a history of three recurrent episodes of skin lesions that had always developed at the same site on her right forearm (Figure 1). At the last episode, there was also a blister of 5 cm in diameter occurring in the center of one lesion. The lesions persisted for weeks, healing with hyperpigmentation. No other symptoms were reported, namely, no dyspnea and no gastrointestinal symptoms.

Lesions always occurred during severe migraine attacks with concurrent intake of 1 g paracetamol, taken at time intervals of 6 hours (cumulative daily dose of 3 g paracetamol). During the last episode, 600 mg ibuprofen was taken additionally. Notably, occasional intake of paracetamol at lower doses for other conditions was always well tolerated and did not provoke skin lesions.

Based on the history and the typical skin lesions, we diagnosed a FDE. To further define our diagnosis, we performed skin tests with paracetamol and ibuprofen. A patch test in loco with paracetamol and ibuprofen yielded no reaction after 48 and 96 hours, respectively. An intracutaneous test with propacetamol in loco and a scratch test with

ibuprofen were both also negative after 15 minutes and 24 hours, respectively. An oral provocation test with a total dose of 3 g of paracetamol administered on a migraine-free day remained unremarkable without skin lesions.

DISCUSSION

Here, we report a patient with multilocular FDE elicited by paracetamol in combination with severe migraine attacks, but not by paracetamol alone. In loco skin tests and oral provocation test, both representing the gold standard in the diagnostic work-up of FDE,² performed on a migraine-free day, were negative. Although the negative results of the skin tests can be explained by their sensitivity of only up to 40% in the context of FDE, the negative outcome of the oral provocation test was unexpected.^{2,3}

Because the FDE occurred only during migraine attacks, we suggest an altered immune status affecting CD8+ tissue-resident memory T cells in the skin, which have been shown to crucially participate in the pathogenesis of FDE.^{4,5} In fact, migraine has been found to induce proinflammatory cytokines in the serum as well as having a negative impact on the functioning of CD4+ CD25+ regulatory T cells. These alterations, among others, may directly or indirectly lead to enhanced activity of skin-resident memory T cells promoting the FDE.^{6,7}

To our knowledge, this is the first report of an FDE elicited by a drug in combination with migraine, but not by the drug alone. We suggest a migraine-induced activation of resident T cells facilitating occurrence of the FDE as the potential underlying mechanism.



FIGURE 1 Multilocular fixed drug eruption elicited by paracetamol and migraine, but not by paracetamol alone (picture of the third episode, picture taken by the patient, circles around lesions drawn by the patient)

CONFLICT OF INTEREST

All authors confirm they have no conflict of interest.

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