Bullous and Erosive Stomatitis Induced by Nimesulide

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Fixed eruption induced by treatment with drugs is virtually a pathognomonic symptom for drug hypersensitivity [1]. It can be caused by many different agents, but the list of chemical compounds that most frequently induce fixed drug eruption does not include nimesulide. To the best of our knowledge this is the first report of nimesulide as the proven cause of fixed eruption. A girl (M. V.), aged 25 years, presented to our Allergy Unit with red-to-violet lesions surmounted by large bullae and erosions on the oral cavity; in addition she complained of mild pruritus and burning of the lips and oral mucosa, but no skin lesions were present. The patient had taken nimesulide 100 mg twice daily and diclofenac 100 mg during the preceding 5 days as prescribed by her practitioner for a relapsing tendinitis and fever of a seasonal epidemic influenza. There was no history of any other drug intake for the last month nor of atopy or previous drug eruption. There was no history of concomitant or previous serious disease either; she was prescribed systemic steroid and a mouth wash. Erythrocyte sedimentation rate, hemoglobin, platelets, white and red blood cells, alkaline phosphatase, aspartate and alanine amino-transferases, bilirubin, blood urea nitrogen, serum creatinine, blood sugar, total serum protein, immunoglobulins, IgE, complement and antistreptolysin were in the normal range. A month later, when the lesions had subsided, a challenge test with diclofenac 100 mg (this drug has been initially suspected) was performed, but no reaction was observed. Ten days later the patient was orally challenged with nimesulide 100 mg; during the following 12 h a recurrence of the lesions at the same sites was observed: red-violet and edematous lesions with bullae and burning sensation were present.

Nimesulide is a new non-steroidal anti-inflammatory agent, with antipyretic and analgesic activity, given orally or rectally on a twice daily basis in a number of inflammatory and pain states [2]. The chemical formula of nimesulide is 4-nitro-2-phenoxyethanesulphonamide. Bottcher et al. [3] found nimesulide to have an antipyretic activity similar to indomethacin and piroxicam in a yeast fever model in rats, similar analgesic activity in an acetic acid writhing test in rats but far less analgesic activity than these compounds in a benzoquinone writhing test in mice. Nimesulide was found to produce a time-dependent, irreversible inhibition of prostaglandin synthetase, equally inhibiting the formation of prostaglandins E₂ and F_{2α} [4]. There is some evidence to suggest an immunomodulatory action of the drug: in vitro it has been shown to inhibit the 'respiratory burst' of phagocytosing neutrophils (shown by inhibition of chemiluminescence and inhibition of superoxide anion generation) without affecting their phagocytic or chemotactic responsiveness; in vivo nimesulide has been shown to reduce polymorpho-nuclear leucocyte accumulation [5]. Moreover nimesulide has also been observed to

block both classic and alternative complement activation paths by its effect on the C3 component and again to act as a superoxide anion scavenger [6]. The drug is usually well tolerated, but there are no studies in a sufficiently large number of patients to accurately assess the safety profile of nimesulide. The data available suggest that the drug can induce the adverse effects typical of non-steroidal anti-inflammatory drugs, the majority being associated with the gastro-intestinal system [7].

Nimesulide is nowadays widely used and is regarded as a relatively safe drug; despite its widespread usage, cutaneous side effects are not known. Recently a case of thrombo-cytopenic purpura related to nimesulide has been reported [8]. In our patient the causal relationship between fixed eruption and nimesulide seems sure and supported by some evidences: (1) the clinical history of the patient; (2) no lesions were present in the oral cavity before the drug use; (3) the oral challenge test led to a recurrence of the lesions in the same sites; (4) when the drug was withdrawn, the lesions were not observed any more in a 2-month follow-up.

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