

Ocular involvement in generalized fixed drug eruption from nimesulide

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Fixed drug eruption (FDE) is a drug-induced reaction that typically recurs at the same cutaneous and/or mucosal site, with singular or multiple lesions. FDE usually presents with round, sharply margined, erythematous to violaceous macules, evolving into oedematous plaques and healing with residual pigmentation.^{1,4} Less common presentations include eczematous, hyperpigmented, papular, targetoid, purpuric,¹ psoriasiform,² urticarial,³ nodular⁴ or bullous⁵ lesions. The lips, the extremities and genitalia are frequently involved.¹ Sulfonamides are the most commonly implicated drugs, followed by tetracyclines, azoles and nonsteroidal anti-inflammatory drugs (NSAIDs).¹

A 59-years-old woman presented with irritation and foreign body sensation in the left eye. On clinical observation, mild injection and edema of conjunctiva was noted, along with an erythematous plaque with moderate scaling on the lower eyelid (**Fig.1a**). Ophthalmological evaluation revealed a best-corrected visual acuity of 20/20 in both eyes, no corneal abnormalities, intraocular pressure, fundus examination and Schirmer test within normal limits. Six hours after ocular symptoms development, skin rash occurred, with circular erythematous maculae spreading on the trunk, arms and legs (**Fig.1b**). The patient reported having ocular symptoms about 12 hours after the ingestion of a 100 mg Nimesulide sachet: she had assumed that drug as a self-prescription for a low back pain. Detailed clinical history did not reveal any significant medical disease nor allergies or previous drug reactions. We suggested her to discontinue the drug and to use preservative free tear substitutes and topical corticosteroids treatment in the left eye for 2 weeks. A skin biopsy of the leg was carried out, demonstrating an inflammatory pattern with lymphocytic infiltrate at the dermoepidermal junction and superficial derma, vacuolar degeneration of the basal layer and focal dermal edema. These histological findings were consistent with FDE. Laboratory routine tests including blood cell count, protidogram and liver enzymes were normal, except for a mildly elevated erythrocyte sedimentation rate. Serological examination was negative for HSV-1, HSV-2, EBV, Coxsackie A and B, Mycoplasma pneumoniae and Borrelia burgdorferi infections.

On 3-weeks control, lesions have healed with moderate residual pigmentation on the trunk and the eyelid (**Fig.2**), and neither conjunctival nor corneal alterations were noted. Patch testing was performed on 4-weeks control: nimesulide powder has been diluted in petrolatum to the final concentration of 10%,⁶ and prepared with Chemotechnique Diagnostics Finn Chambers ® (Vellinge, Sweden). As this drug was strongly suspected to be the cause of the

ocular and cutaneous manifestation, patch tests were applied on residual pigmented lesional skin on the back of the patient,⁶ and removed after 48h. Positive reactions were observed on day 2 (+) and 4 (++) and negative on day 6 reading. The patient refused to perform prick tests and oral challenge test with nimesulide, given the low risk-to-benefit ratio, and the possibility of hypersensitivity reactions development. On 3 and 6 months follow-up controls, she had not experienced any skin reaction, without Nimesulide drug assumption.

The clinical history, the allergological and histopathological findings and the follow-up evaluation demonstrated that nimesulide powder had been the triggering agent of our patient FDE. Few cases of FDE elicited by nimesulide ingestion have been reported to date, with a spectrum of different skin manifestations.²⁻⁵ Nevertheless, the eyelid involvement is quite rare in FDE spectrum of manifestations.¹ To our knowledge, this is the first case of nimesulide-induced FDE presenting with both ocular and cutaneous involvement. In particular, it is not common that ocular signs develop before skin rash spreading. Hence, this report stresses the importance of collaboration between dermatologists and ophthalmologists for a more rapid diagnosis and an appropriate management.

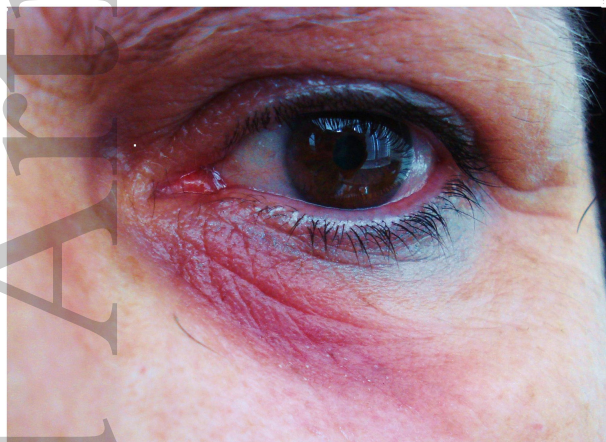
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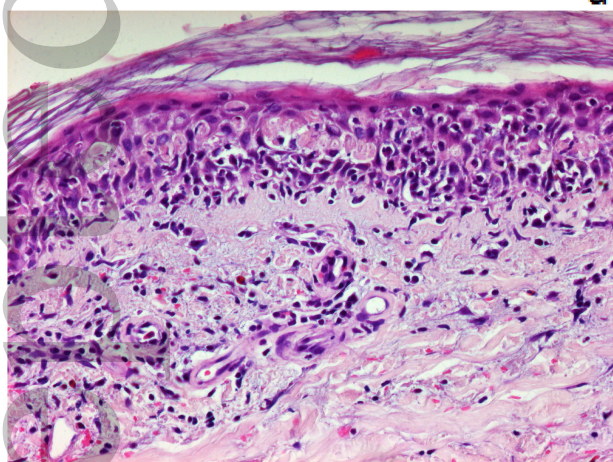
FIGURE LEGENDS

Figure 1: Left eye clinical appearance 6 hours after nimesulide ingestion (**1a**). Skin rash appearance, 12 hours after nimesulide ingestion (**1b**). Histopathology demonstrating lichenoid perivascular dermatosis with focal oedema and multiple apoptotic keratinocytes and eosinophils (**1c**).

Figure 2: Clinical presentation on 2-weeks control: the left eye (**2a**) and the back of the patient (**2b**) showing post-inflammatory residual hyperpigmentation.



a



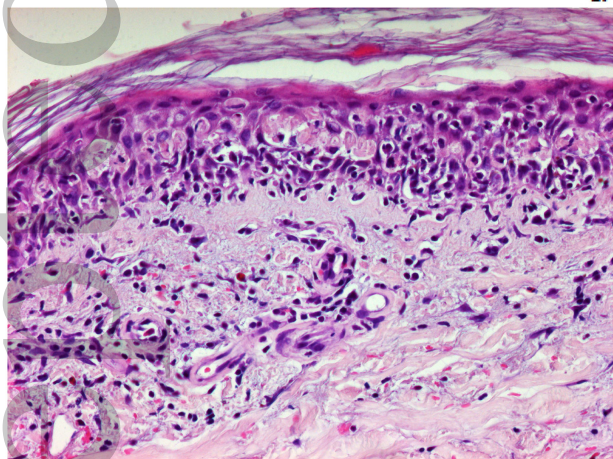
c



b



a



c



b