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Fixed drug eruption induced by topical olopatadine ophthalmic solution

SG Bilgili¹, AS Karadag¹, R Karadag²,
G Bulut³ and O Calka¹

Abstract

Fixed drug eruption (FDE) usually develops after oral administration and is described as a cutaneous reaction recurring at the same location each time the drug is taken. Olopatadine is both a H1 histamine receptor antagonist and a mast cell stabilizer, indicated for the treatment of allergic conjunctivitis. Here, we report a 14-year-old male patient who developed FDE localised on the lateral side of periorbital rim bilaterally, whilst applying olopatadine 0.1% ophthalmic solution for the treatment of allergic conjunctivitis. As far as we know, FDE due to olopatadine has not been previously reported in the literature. We deem it appropriate to report this case because FDE that results from the application of topical drugs is a rare event in the literature.

Keywords

fixed drug eruption, topically, olopatadine, antihistaminic drug

Introduction

Fixed drug eruption (FDE) is characterized by erythema, edema and occasional blistering reappearing at the same sites on the skin or mucous membranes after reexposure to an offending drug.¹ Eruption may begin within a few minutes or up to 8 h after drug intake. Typical lesions presented as round or oval, well-demarcated, erythematous-to-violaceous, slightly elevated plaques. Eruption most often manifests as a single lesion, but multiple lesions are not infrequent and eruption typically heals with residual hyperpigmentation.²

FDE is usually induced by a systemically administered medication. This study reports a case of FDE that developed after topical application of olopatadine.

Case

A 14-year-old boy was presented to our clinic with complaints of dark brown patches localised on the lateral margins of his eyes. He was prescribed topical olopatadine 0.1% ophthalmic solution for recurrent allergic conjunctivitis. On the 2nd day of the treatment, a rash consisting of violaceous, erythematous, itchy plaques 1–2 cm in diameter involving

periorbital areas appeared. Erythematous patches healed without any treatment in 1 month with a dark brown residual hyperpigmentation. There was a negative history of skin reactions and no history of any other drug intake during this period.

Dermatological examination of the patient disclosed darkly hyperpigmented patches of size between 1 and 2 cm in diameter over the lateral margins of the periorbital skin (Figure 1). Systemic examination was normal. Routine laboratory tests were unremarkable. Skin biopsy obtained from the hyperpigmented lesional skin showed thinning of the stratum malpighii, loss of rete ridges, vacuolar degeneration of the basal layer, pigment incontinence with capillary proliferation and perivascular

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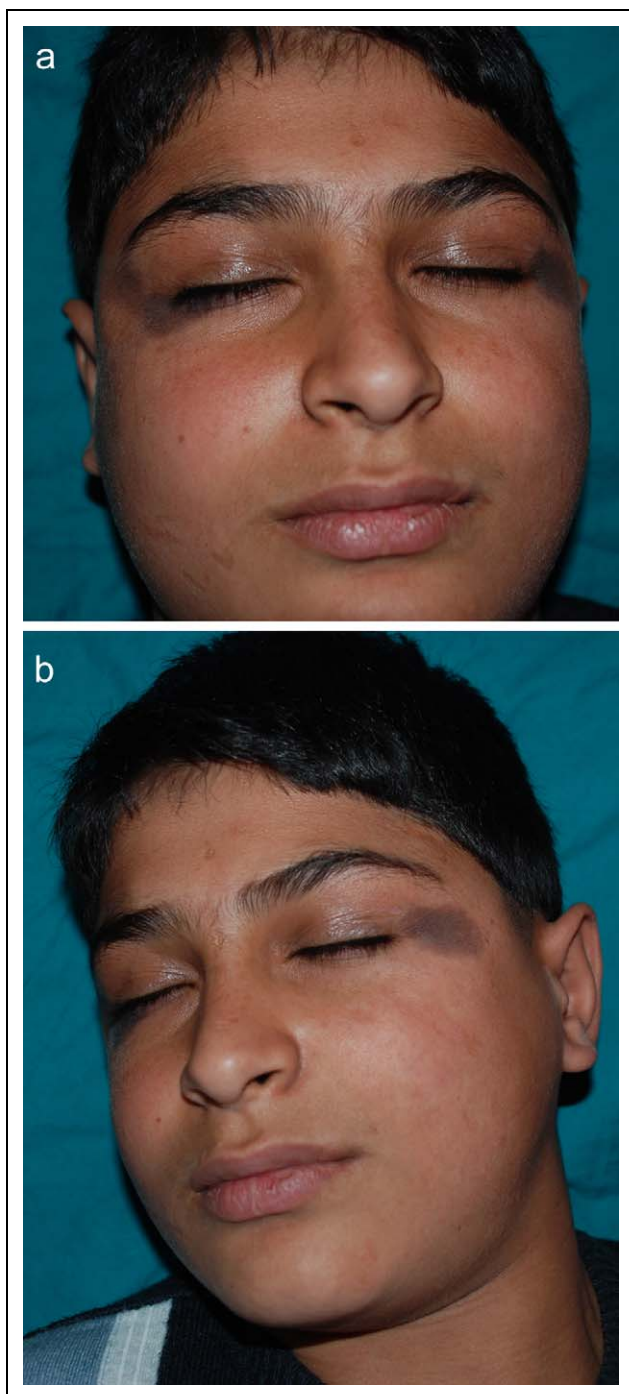


Figure 1. (a) Hyperpigmented macule at the lateral sides of both the eyes. (b) Hyperpigmented macule at the lateral side of left eye.

lymphocytic infiltration in the dermis (Figure 2). The diagnosis of FDE was based on the clinical and histopathological findings. Because our patient refused to give informed consent, we could not carry out patch testing with olopatadine to confirm the diagnosis.

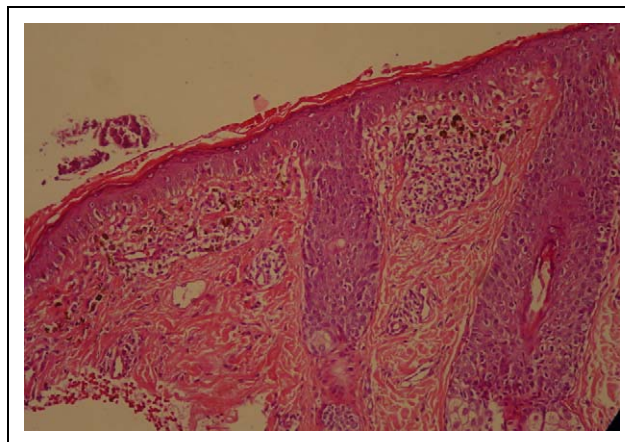


Figure 2. Thinning of stratum malpighi, loss of rete, vacuolar degeneration of the basal layer, incontinence of pigment, capillary proliferation of dermis and perivascular lymphocytic infiltration (hematoxylin-eosin stain, $\times 200$).

Discussion

FDE is caused by various drugs. Sulfonamides, tetracyclines, sulphone, penicillins, nonsteroidal anti-inflammatory drugs, barbiturates, phenolphthalein, aspirin and oral contraceptives are the most frequent offenders.³

FDE following the ingestion of H1 antihistamines is rare; but in a number of reports, H1 antihistamines such as loratadine, cetirizine and hydroxyzine were causative medications.^{3–5} The rich blood flow and the relatively small mass of the eye makes it especially sensitive to drug-induced adverse reactions. Drug molecules present in the system may become selectively deposited in specialized ocular tissues such as the cornea, lens and retina, which may therefore show individual sensitivities to drug toxicity.⁶ Olopatadine hydrochloride, a mast cell stabilizer and histamine receptor antagonist, has been shown to inhibit mast cell activation in an in vitro model of human mast cell culture, reducing histamine and TNF- α release and upregulating proinflammatory mediators in conjunctival epithelial cells.⁷ Olopatadine is the first dual-function antiallergic agent approved by the Food and Drug Administration for the treatment of the signs and symptoms of allergic conjunctivitis. The recommended dose for olopatadine hydrochloride 0.1% ophthalmic solution is 1 drop twice a day at an interval of 6–8 h.⁸ Our case developed FDE after the treatment with topical olopatadine ophthalmic solution.

FDE is frequently associated with oral intake of medications. To our knowledge, only one case report of FDE induced by intravaginal metronidazole has

been reported so far. All other reported eruptions were induced by the oral administration of drugs.⁹

Although the eruption can occur anywhere on the body, trunk, extremities, lips and genital regions are preferred locations.^{1,2} Eruption in our case was of unusual and rare localisation.

The pathogenesis of FDE still remains to be fully elucidated. However, it is thought to be immunological and type IV hypersensitivity reaction is suggested. Drug-induced enhanced expression of intercellular adhesion molecule-1 on lesional keratinocytes, persistence and increase of CD8+ T-cells at previously affected sites is suggested as the reason for recurrence of lesions at the same site upon readministration of the drug.^{1,2}

In the acute phase of the disease, histopathological examination reveals dyskeratosis, basal cell hydropic degeneration, dermal edema and perivascular lymphocytic infiltration in the upper dermis. In the healing phase, where regression of skin lesions occurs with residual hyperpigmentation, basal layer hyperpigmentation and melanin-laden macrophages are observed.² In our patient, skin biopsy specimen of hyperpigmented lesion was consistent with FDE.

Erythema multiforme, erythema dyschromicum perstans in its postinflammatory hyperpigmentation phase, lichen planus pigmentosus, urticaria pigmentosa and postinflammatory hyperpigmentation, which occurs after inflammatory dermatoses, should be considered in the differential diagnosis of FDE.^{2,10} On the basis of the history, clinical examination and histopathology, the diagnosis of FDE due to olopatadine was made.

Confirmation or a definitive diagnosis of FDE can be achieved by oral challenge test. But patients may experience serious flares, appearance of copious numbers of new lesions in previously uninvolved areas and anaphylactic reactions.³ In a study, lesional skin patch test positivity was found to be 43%.¹¹ Our patient refused skin patch testing with olopatadine ophthalmic solution, hence we could not confirm the diagnosis.

To the best of our knowledge, this is the first case report of FDE to olopatadine. Caution is advised when prescribing topical antihistamines because of the risk of FDE.

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