

Fixed drug eruption to rupatadine with positive patch tests on non-lesional skin

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Fixed drug eruption (FDE) is a unique cutaneous adverse drug reaction characterized by skin lesions that recur on the same sites upon re-exposure to the same or a related drug.¹ FDE can be caused by a vast number of drugs (>100 described), mostly non-steroidal anti-inflammatory drugs (NSAIDs), antibiotics, and anticonvulsants. Although rare, FDE has also been described with H₁-antihistamines.^{2,3}

CASE REPORT

A 62-year-old man with a personal history of allergic rhinitis and hypertension reported two episodes of sudden onset of erythematous-violaceous lesions on the cervical, suprapubic, and penile regions that recurred in the same locations and progressed to residual brownish-grey pigmentation, clinically typical of FDE (Figure 1). He reported taking rupatadine (Rinialer) on the preceding days in the context of exacerbation of allergic rhinitis, in addition to his medication (irbesartan, hydrochlorothiazide and bisoprolol) for his chronic condition.

He was advised to stop rupatadine and 2 months after patch testing was performed with the European Baseline Series, with the powder of rupatadine in water and 30% pet., and with other antihistamines (diphenhydramine 1% pet., hydroxyzine 1 and 10% pet. [Chemotechnique Diagnostics, Vellinge, Sweden], levocetirizine [xyzal] 30% pet., loratadine 20% pet., desloratadine [Aerius] 30% pet.). Allergens were applied in occlusion on the back for 48 hours and rupatadine and the related antihistamine, desloratadine, were also applied on residual lesions for 24 and 48 hours. Positive reactions (++) were observed only for rupatadine in water and pet. on the normal skin of the back at day (D) 2 and D3 (Figure 2A), whereas patch testing performed on lesional areas with rupatadine in water and pet. and desloratadine were repeatedly negative, both in the suprapubic and cervical lesions (Figure 2B). A patch test with rupatadine (30% pet. on normal skin) was repeated and was positive at D2. A skin biopsy of this test, performed with the patient's informed consent, showed an interface dermatitis with vacuolization of the basal layer associated

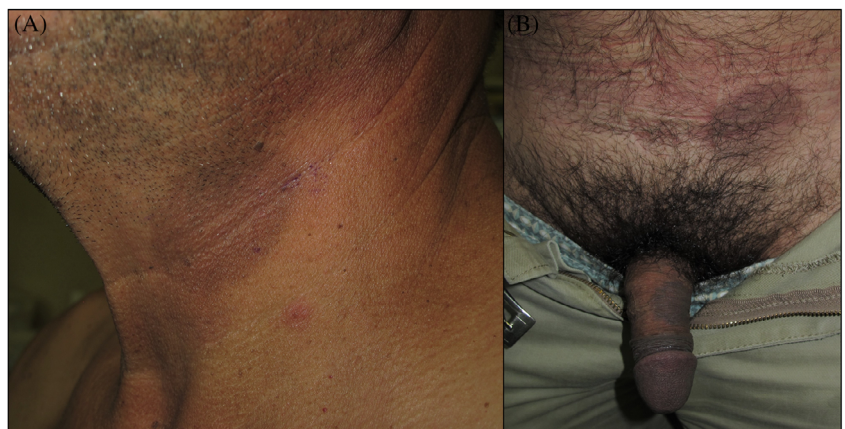


FIGURE 1 Pigmented round to oval lesions on the cervical (A), suprapubic and (B), penile regions, characteristic of fixed drug eruption



FIGURE 2 (A), Results of patch testing on the back, revealing a positive (++) reaction to rupatadine “as is” in water and 30% pet.; (B), patch testing performed on a lesional site, which gave a negative result

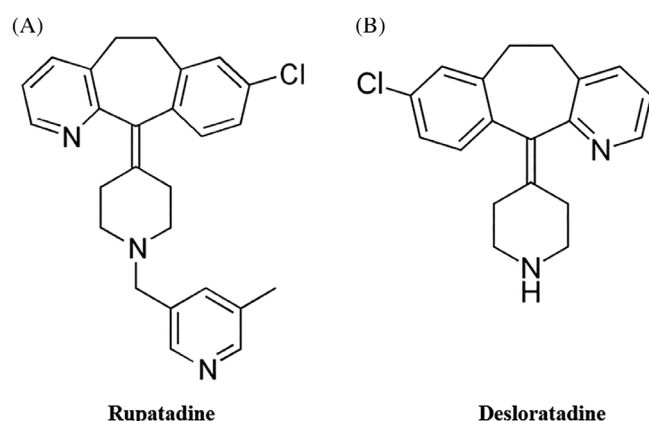


FIGURE 3 (A), Structure of rupatadine and (B), its major metabolite desloratadine, which share an important moiety in their structure

with a spongiotic dermatitis with lymphocyte exocytosis and a perivascular lymphomononuclear infiltrate with rare eosinophils. Patch testing performed with rupatadine 30% pet. in 15 controls (5 M/10F, mean age 47.1 years) was negative.

DISCUSSION

This is a typical case of a FDE caused by rupatadine, a second generation H_1 -antihistamine, approved for the treatment of allergic rhinitis and chronic urticaria.⁴ A single case of FDE has previously been described and confirmed by oral provocation,⁵ not by patch testing.

Interestingly, and in contrast to the usual notion that patch tests are positive only in residual lesional areas where drug-specific T cells are retained in the epidermis for a long time,^{6,7} in our case, epicutaneous tests were positive exclusively on a non-lesional skin area. This was a specific reaction as we had 15 negative controls. It was not probable that we tested a non-pigmented residual area as the patient reported no lesion on the back. When we repeated the test in another non-lesional area it was still positive. Also, we avoided the refractory

period reported after an acute reaction, as patch testing was performed more than 2 months thereafter. Moreover, histopathology showed aspects that exhibited a mixture of eczema and FDE, with a lichenoid pattern and vacuolization of the basal cell layer, which we have shown previously in other patch tests in FDE.⁸

We also want to highlight that there was no cross-reaction in patch tests with other antihistamines, namely between rupatadine and its major metabolite, desloratadine, which share an important moiety in their structure (Figure 3).⁴

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

Joana Calvão: Conceptualization; data curation; formal analysis; investigation; writing-original draft; writing-review and editing. **José Cardoso:** Formal analysis; investigation; resources. **Margarida Gonçalves:** Conceptualization; data curation; formal analysis; investigation; supervision; validation; writing-review and editing.

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