

Fixed drug eruption with rupatadine: A rare case report

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ABSTRACT

Fixed drug eruption with rupatadine is a very rare type of drug reaction. A 25 years old man presented with recurrent attacks of fixed drug eruption on the face, trunk, and extremities for one and a half years. Rupatadine was not listed as an offending drug in the first two episodes. In the second and third attacks, the patient himself suspected that the drug was a culprit. The supervised oral challenge test was positive with Rupatadine. Patch test was also done in lesional and nonlesional skin but the result was equivocal. Skin biopsy for histopathology report was in favor of fixed drug reaction. Naranjo scale was definitive to drug reaction with rupatadine fumarate. This case is reported to notice a rare reaction of a commonly used antihistamine.

KEY WORDS: Fixed drug eruption, FDE, Fixed drug reaction, Rupatadine, Antihistamine

INTRODUCTION

Rupatadine is a dual histamine H1 receptor and platelet activating factor (PAF) receptor antagonist. During allergic response mast cells undergo degranulation, releasing histamine and other proinflammatory cytokines. Histamine acts on H1 receptors to produce symptoms of nasal blockage, rhinorrhea, itching, and swelling. PAF is produced from phospholipids cleaved by phospholipase A2.^{1,2} It acts to produce vascular leakage which contributes to rhinorrhea and nasal blockage. By blocking both the H1 receptor and PAF receptor, Rupatadine prevents these mediators from exerting their effects and so reduces the severity of allergic symptoms. Headache, dizziness, dry mouth, fatigue, tiredness and weakness, nausea, abdominal pain, diarrhea, vomiting, constipation, and skin rashes are the common

adverse effects of Rupatadine.³ This drug has to be used with precautions in pregnant and lactating mothers, in cases with liver and renal impairment, while driving, and along with alcohol. Severe cutaneous adverse reaction with rupatadine has not yet been listed. Fixed drug reaction was found in very few cases reports worldwide.

Rupatadine is a newer dual inhibitor of histamine H1 and PAF-receptors. We evaluated the evidence for its mechanism of action that includes anti-inflammatory effects in addition to a powerful inhibition of H1 and PAF receptors.

The clinical efficacy and safety of rupatadine, and importantly its longer-term utility in everyday life was assessed in several studies. Rupatadine is a well-known effective and well-tolerated treatment for allergic rhinitis and chronic spontaneous urticaria.⁴

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CASE REPORT

A 25-year-old man presented with multiple itchy hyperpigmented patches all over his body for one and a half years. Which intermittently became erythematous and fluid filled, on taking some medications. The patient had witnessed 4 such episodes in the last one and a half years. The lesions at first appeared as dusky bullae surrounded by erythematous halo. In every episode, the old lesions had become active and new lesions also appeared. Between the episodes that lasted for around 2 weeks, the lesions remained as asymptomatic brown to black well-defined patches. Oral mucosa, hair, and nail had never been involved. With that features the patient was labeled as lichen planus pemphigoid, lichen planus pigmentosus, and lichenoid drug eruption on different occasions. On that basis, the patient was prescribed oral corticosteroids (1mg/kg) and oral rupatadine fumarate for 2 weeks and rupatadine had to continue after steroid withdrawal. The patient noticed that rupatadine was the offender's drug and therefore he was referred to a tertiary care hospital. The lesional skin biopsy for histopathology and direct immunofluorescence(DIF) was done and the diagnosis of fixed drug reaction was finally made. The oral provocation test was done with informed written consent and with a full set of a severe reaction management team. One-fourth of the rupatadine fumarate tablet was given. The patient complained of itching and redness of a few lesions after around one and a half hour. Previously, a trial with a placebo drug was also done to check the psychological impact like FDR, but there was no result. A patch test was done with the application of the crushed tablet mixed with petroleum jelly on an intact patch but no reaction was noticed.



Fig. 1 Hyperpigmented patches of FDE



Fig. 2 FDE due to rupatadine

The patient was assessed with the Naranjo scale and the score was calculated at 9, which was definitive for a drug reaction to rupatadine. Finally, the case was labeled as FDR due to rupatadine fumarate.

DISCUSSION

Rupatadine is a non-sedating long-acting second-generation oral antihistamine drug. It has strong antagonist activity on both histamine H1 receptors and platelet-activating factor (PAF) receptors. The use of rupatadine is indicated in adult and adolescent patients with allergic rhinitis and chronic spontaneous urticaria. A very

good safety profile of rupatadine has been evidenced in various studies. Rupatadine is free from anticholinergic effects. It is a safe and potent antihistamine in our daily practice. Fixed drug reaction is an unusual finding not only for rupatadine but also for any type of antihistamine. Delayed diagnosis is common for its rarity of occurrence. In the present case, the diagnosis was made after a course of one and a half years. Fidan *et al* reported the first case of rupatadine-induced FDE in 2011.⁴ They confirmed the case with an oral provocation test. Whereas, Calvao *et al* confirmed a case with patch test at nonlesional and lesional skin.⁵ In our case, we did both oral provocation test and patch test. The provocation test was suggestive of rupatadine-induced FDE but the patch test result was equivocal. The patient was warned to avoid all brands and forms of rupatadine in future.

A fixed drug eruption (FDE) is a cutaneous adverse drug reaction due to Type IV or delayed cell-mediated hypersensitivity. Antihistamines, antagonize the action of histamine during an allergic reaction as well as any drug reactions.^{5,6} We justified the case with the Naranjo Algorithm of Adverse Drug Reaction (ADR) Probability Scale to assess whether there was any relationship between FDE and rupatadine, by using a simple questionnaire to assign probability scores. The ADR Probability Scale scoring was done by a third party and that was verified with our score. The score was 9 on both sides and it was considered a definite drug reaction for rupatadine.⁷ On the Naranjo scale, the total score range varies from -4 to +13. The reaction is considered definite if the score is 9 or higher; probable if 5 to 8; possible if 1 to 4; and doubtful if 0 or less. The other tests that can be done for FDE

are patch tests, lymphocyte transformation tests (LTTs), and provocation tests for evaluating non-immediate reactions to drugs.⁸

Suspicion, oral challenge, and re-challenge test positivity and definitive Naranjo scale score were confirmatory of FDE to rupatadine in our case.

CONCLUSION

Rupatadine hydrochloride is a safer potent antihistamine that may cause fixed drug reaction. Physicians should be watchful in prescribing rupatadine in the future.

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