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Case Report

FIXED DRUG ERUPTION, A NOVEL SIDE-EFFECT OF LEVOCETIRIZINE: A DOUBLE EDGED SWORD

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ABSTRACT

Fixed drug eruption (FDE) is a common drug reaction that often recurs at the same location after exposure to the same drug and is characterized by erythematous and edematous plaques**.** Rarely, antihistamines such as cetirizine, levocetirizine and loratadine, being antiallergic drugs, paradoxically produce FDE lesions. In this report, we present a 32-year-old female patient with levocetirizine induced fixed drug eruption. Her history also revealed similar lesions in the past after taking cetrizine. FDE to levocetirizine is very rare and documented in few cases. We report this case to highlight a novel side-effect of very commonly used drug.

KEY WORDS: Fixed drug eruption (FDE), anti-histamines, levocetrizine.

INTRODUCTION

Fixed drug eruption (FDE) is a common drug reaction that often recurs at same location after exposure to same drug and is characterized by erythematous and edematous plaques.[1] FDE is characterized by development of one or more annular or oval erythematous plaques, more commonly on the lips or genitalia or localized in any part of the body.[1] Lesions in FDE typically occur within a few hours or days after exposure to the offending drug, typically resolve spontaneously after discontinuation of the causative drug but leave a residual hyperpigmentation at the reaction site.[1] Rarely, antihistamines such as cetirizine and levocetirizine being antiallergic drugs, paradoxically produce FDE lesions.[2] In this report, we presented a patient with levocetirizine induced fixed drug eruption.

CASE HISTORY

A 32-year-old female presented with complaints of red flat lesion associated with itching and burning sensation over her right lower leg within 2 hours of taking levocetrizine 5mg/day for her recurrent urticarial rash. Cutaneous examination revealed well defined solitary erythematous patch seen over the right lower leg. Her history also revealed similar lesions in the past after taking cetrizine 5mg/day. There was no history of any other drug intake during this period. The lesion subsided with oral fexofenadine180mg 1-0-0 for 5 days, T.Methyl prednisolone 8mg 1-0-1 for 5 days and topical mometasone cream M-0-N for 5 days. She was advised to avoid both the drugs in the future. Oral provocation could not be performed as patient was unwilling.

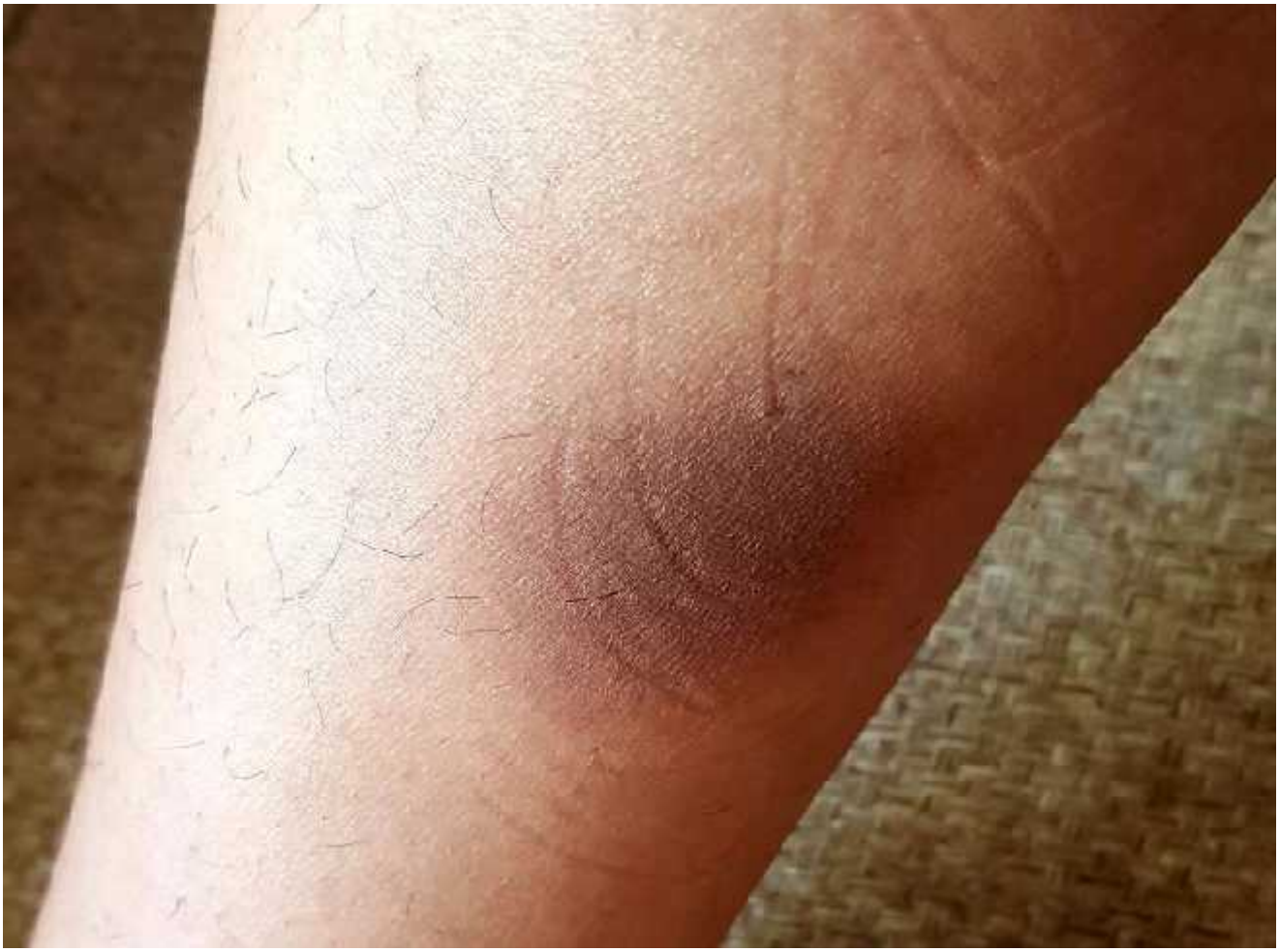

Fig 1: FIXED DRUG ERUPTION (FDE)

DISCUSSION

FDE is a common form of cutaneous adverse drug reactions whose exact etiology is unknown. They are caused by epidermal CD8 T cells, which are retained in the lesions forming an immunologic memory, which gets activated on re-challenge. Persistent expression of intercellular adhesion molecule by an abnormal subpopulation of keratinocytes facilitates the adhesion of lymphocytes that express lymphocyte associated antigen, which in turn liberates lymphokines, causing damage to epidermal cell layer. Oxidative stress parameters such as reduced glutathione, malondialdehyde, and inhibition of leukocyte migration have also been significantly noted in FDE. [3] FDE can occur with several drugs, common ones are sulfonamides, NSAID'S, antimicrobials and oral contraceptives. However, FDE due to antihistaminics are very rare. FDE reported to H1antihistaminics are cyclizine, diphenhydramine, phenothiazines, hydroxyzine, loratadine and in few cases with cetirizine and levocetirizine. [4] Development of FDE due to cetirizine and levocetirizine can be explained by the fact that both cetirizine and levocetirizine, along with hydroxyzine, have the same chemical node, i.e. piperazine; thus they have similar pharmacological profiles. While levocetirizine accounts for most or all clinical antihistaminic activity of racemic cetirizine, [5] the latter is itself a main metabolite of hydroxizine. When administered orally hydroxyzine is converted into cetirizine. Levocetirizine the latest (third generation) antihistaminicis the R-enantiomer of cetirizine. [4] There were a few reports of piperazine antihistamine induced delayed hypersensitivity reaction. [6] In 2002, Assouère et al. [6] reported that hydroxyzine induced same morphologic cutaneous eruption at the same site which cetirizine had induced drug eruption before. Interestingly, both the drugs are piperazine antihistamines. In 2007, Mariana et al reported one case of fixed drug eruption to cetirizine. [6] In 2009, a case of cetirizine induced anaphylaxis was reported. [7] FDE can be confirmed by oral provocation test, patch test, prick test and intradermal skin test. But provocation tests are

not done because of risks involved in this approach, namely anaphylactic reactions or intense lesional reactivation with a significant increase in the number of lesions. [8] In our patient, no oral provocation test and patch test was performed as patient was unwilling. The causal relationship between levocetirizine and the FDE was found to be definite according to the objective causality assessment by the Naranjo probability scale (Naranjo score = 10). [9] According to the World Health Organization-Uppsala Monitoring Center (WHO-UMC) criteria, [9] which were used for the evaluation of adverse drug reaction for causality assessment, the assigned causality category for this adverse drug reaction was revealed as "certain." FDE to levocetirizine is very rare and documented in few cases. Clinicians should have a high index of suspicion and should be aware of the possibility of reactions to antihistamine drugs, which themselves are very frequently prescribed to manage drug reaction. A patient with history of hypersensitivity to a certain antihistamine should be cautious about the possibility of cross reaction with other antihistamines of the same chemical class. Antihistamines with least structural resemblance to the offending agent should be used in such a patient. We report this case to highlight a novel side-effect of very commonly used drug.

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