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Fixed drug eruption to cetirizine & levocetirizine: A case Report

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I. Introduction

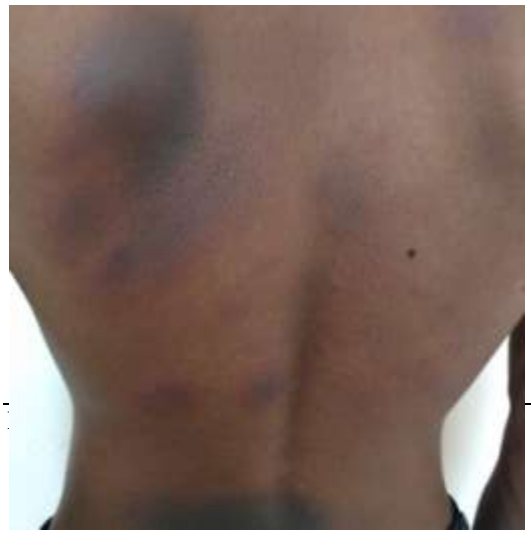
Cutaneous drug eruption is the most common adverse drug reaction attributed to a drug. Fixed drug eruption represents the most common cutaneous drug reaction in Indian patients[1].H1 antihistaminics are commonly used medications for a wide variety of disorders such as urticarial,eczema,allergic reactions,and allergic rhinitis.[2]Hypersensitivity to H1 antihistaminics are usually rare and fixed drug eruption reaction is scarce.

II. Case Report

A 15 year old male presented to our hospital with multiple,erythematous to violaceous ,painful patches distributed over dorsum of hand, flexor aspect of both forearms(Figure-2),rt arm &back(Figure 1). The patient gave history of ingestion of single tablet of cetirizine10mg for cold &fever about 4 days back . After about half an hour of taking medicine patient started getting tingling sensations on whole body which was followed by development of erythematous,painful patches first on back then over dorsum of hand which gradually progressed to involve whole body.The colour of patches gradually turned to violaceous.Patient then consulted some local doctor and was prescribed levocetrizine 10mg and omnacortil 10mg. After taking levocetrizine , within 15 minutes he again started developing erythematous patches over whole body on same sites as before. There was no history suggestive of consumption of any other medication or herbal medications along with the above drug.

On examination,the patient was conscious,well oriented,and afebrile.Vital signs were stable.The patient was not anaemic,no cyanosis or clubbing. Lymph nodes were normal.Local examination showed multiple,well defined,violaceous patches surrounded by erythema over forearms,arms,hand &back. General examination such as haemoglobin,TLC,Platelet count,blood urea,serum creatinine and routine urine were normal.Oral and genital mucosa were not involved.Patient refused for patch testing and oral provocation test.

Since the patient had not taken any other drug in last 4 weeks we suspect cetirizine to be the culprit.Based on the clinical examination and history, the patient was diagnosed as cetirizine and levocetirizine induced FDE.Use of Naranjo Adverse Drug Reaction (ADR) Probability Scale(Table-1) indicated a probable relationship between this cutaneous adverse effect and cetirizine &levocetirizine therapy in this patient.The offending drugs were stopped immediately and the patient was conservatively managed with tablet fexofenadine 180 mg twice daily and topical application of clobetasol propionate 0.05% once daily on affected areas for 7days.The patient recovered slowly after 10 days. The patient was advised to avoid cetirizine , levocetirizine and other piperazine derivatives in the near future.



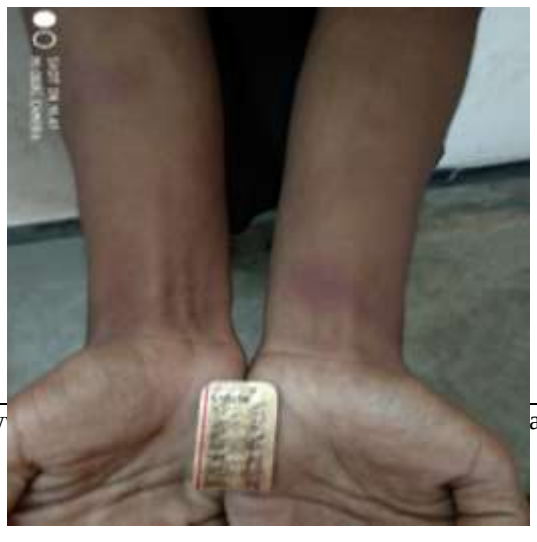


Fig 1: Lesion on back

Fig 2: Lesion on forearm with culprit drug

III. Discussion

FDE was first described by Bourns in1889; five years later, it was termed by Brocq as "eruption erythemato-pigmentee fixe.[3] Fixed drug eruption usually presents with sudden onset of well-demarcated erythematous macules, evolving rapidly to violaceous edematous plaques,recurs on the same site within 30 minutes to 1 day of drug administration, and heals with residual pigmentation[2].Sensation of burning often precedes the appearance of these lesions. The lesions may be solitary or multiple. The most common sites are the genitalia in males and the extremities in females.[4] They may be bullous, pigmented, or nonpigmented. Pigmented lesions can be seen in pigmented individuals and heroin addicts. Nonpigmented lesions are reported with pseudoephedrine use.[5]This accounts for 16-21% of all cutaneous reactions.

The pathomechanism of FDE is not well understood.Drug induced tumor necrosis factor-α(TNF-α)-dependant –keratinocyte ICAM-1 expression has been found in lesional skin,suggesting that it provides a localised initiating stimulus for the activation of disease-associated epidermal T cells.Intraepidermal CD-8+ T cells that are distributed along the epidermal basal layer and have the capacity to rapidly produce large amount of IFN-Y are likely to be a major actor in the epidermal injury observed in FDE lesion.[6]

Histologically, FDE is characterized by marked basal cell hydropic degeneration with pigmentary incontinence. Scattered keratinocyte necrosis with eosinophilic cytoplasm and pyknotic nucleus (civatte bodies) are seen in the epidermis. Infiltration of lymphocytes, histiocytes, and neutrophil polymorphs is evident in the upper dermis.[7]

Common drugs involved with FDE are antibiotics (e.g., trimethoprim, erythromycin, penicillin, and tetracycline), anticonvulsants (e.g., phenobarbitone and phenytoin) and other drugs such as phenolphthalein and nitroimidazole, as well as nonsteroidal anti-inflammatory drugs (e.g., aspirin, naproxen, diclofenac sodium, and ibuprofen)[8].The H1-antihistaminics implicated in FDE are diphenhydramine, cyclizine, phenothiazines, loratadine, hydroxyzine, and in few cases with cetirizine and levocetirizine.[9]

Cetirizine, a piperazine-derivative, second-generation nonsedative antihistaminic, has minimal anticholinergic effect with few cutaneous side effects. It has negligible penetration into the brain with relatively higher incidence of drowsiness compared to other second-generation antihistamines.[10]To the best of our knowledge, there are only six case reports of FDE to cetirizine[9]. Moreover, levocetirizine, a piperazine-derivative-induced FDE reactions, was also reported by Kim *et al*. and Harish *et al*.[11,12]Another report by Jhaj *et al*. showed cross-reaction between cetirizine and levocetirizine.[13]

Cetirizine and levocetirizine,being anti-allergic medications are rarely suspected of causing hypersensitivity reaction or FDE.Based on proper history,clinical examination and past history of drug reactions a high degree of suspicion should be kept in mind for probability of drug reactions to antihistaminics.

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Table 1

Naranjo's adverse drug reaction probability scale

Questionnaire	Yes	No	Do not know
Are there previous conclusive reports on this reaction?	+1	0	
Did the adverse event appear after the suspected drug was given?	+2	-1	
Did the adverse reaction improve when the drug was discontinued or a specific antagonist was given?	+1	0	
Did the adverse reaction appear when the drug was readministered?	+2	-1	
Are there alternative causes that could on their own have caused the reaction?	-1	+2	
Did the reaction reappear when a placebo was given?	-1	+1	
Was the drug detected in any body fluid in toxic concentrations?	+1	0	
Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	
Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	
Was the adverse event confirmed by any objective evidence?	+1	0	

Scoring >9= definite ADR; 5-8= probable ADR; 1-4= possible ADR; 0= doubtful ADR

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