Case Report

Cetirizine-Induced Fixed Drug Eruption

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Abstract

Cetirizine, a piperazine-derivative second-generation antihistaminic, is used for a wide variety of disorders such as urticaria, eczema, and allergies. Adverse reactions due to this drug are usually rare, especially fixed drug eruption (FDE), a delayed cell-mediated hypersensitivity reaction, is scarce. Here, we report a case of cetirizine-induced FDE. A 34-year-old female developed hyperpigmented, itchy patches over both forearms, legs, feet, and right side of the chest after taking tablet cetirizine for dry cough with similar episode 2 years back on the same sites. The patient responded slowly with conservative treatment and the lesions disappeared after 10 days. She was advised to avoid the causative in near future. This case report highlighted FDE due to an antihistaminic which themselves will be prescribed to treat allergies.

Keywords: *Cetirizine, fixed drug eruption, hyperpigmented patches*

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Introduction

H_1-antihistamines are commonly used medication for a wide variety of disorders such as urticaria, eczema, allergic reactions, and allergic rhinitis. The second-generation antihistamines have specific receptor action with less side effects.[1] 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.[2] Hypersensitivity to H_1-antihistamines are usually rare and fixed drug eruption (FDE) reaction is scarce. This FDE usually appears as one or more annular, pruritic, well-circumscribed, oval, itchy, erythematous plaques, and sometimes vesicular or bullous. It occurs precisely at the same site and resolves spontaneously by stopping the causative drug with residual hyperpigmentation. The lesions usually occur on the hip, lower back, proximal extremities, lips, face, and genitals.[3]

Here, we report a case to emphasize on this uncommon reaction to a commonly used drug.

Case Report

A 34-year-old female came to the dermatology department of our hospital with complaints of hyperpigmented itchy patches over both forearms, legs, feet, and right side of the chest which occurred 8 h after the consumption of tablet cetirizine. She did not have any systemic complaints. Medical history revealed that symptoms developed following consumption of tablet cetirizine 10 mg (cetirizine hydrochloride, manufactured by Macro Pharmaceuticals, batch number MCTO0077) prescribed for dry cough and rhinitis by the general medicine department, and later, she was referred to dermatology department for the allergic lesions (FDE). There was no history suggestive of consumption of any herbal medication and over-the-counter drugs along with the above drug. History revealed that the patient had similar reactions on the same site before 2 years which manifested after taking tablet cetirizine for rhinitis. She has no other significant medical history.

On examination, the patient was conscious, well oriented, and afebrile. Vital signs were stable. The patient was not anemic, no cyanosis, and clubbing, and lymph

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nodes were normal. Local examination showed multiple, well-defined, violaceous patches over forearms, legs, feet, and right side of the chest. General investigations such as hemoglobin, total leukocyte count, differential leukocyte count, platelet count, blood urea, serum creatinine, and urine routine were normal. Patch test was not done because the patient refused to give the consent. Based on the clinical examination and history, the patient was diagnosed as cetirizine-induced FDE reactions [Figures 1 and 2]. The offending drug (tablet cetirizine) was stopped immediately and the patient was conservatively managed with tablet fexofenadine 180 mg once daily dose for a period of 7 days, topical application of betamethasone dipropionate 0.1% ointment once daily at night time for 1 week on the affected areas, and calamine lotion for local application twice daily. She responded slowly with recovery after 10 days and was advised to avoid cetirizine in the near future.

Naranjo's algorithm causality scale was used to assess plausible reaction due to cetirizine [Table 1].[4]

The WHO-Uppsala Monitoring Centre causality assessment system showed that the adverse reaction was "probable/likely" reaction to cetirizine [Table 2].[5] This case was reported to the nearby adverse drug reaction monitoring center.

Discussion

FDE usually presents with sudden onset of well-demarcated erythematous macules, evolving rapidly to violaceous edematous plaques, recurs on the same site within 30 min to 1 day of drug administration, and heals with residual pigmentation. This accounts for 16%–21% of all cutaneous reactions.[1]

FDE is believed to be a delayed-type hypersensitivity reaction, and the major contributing factor in the development of localized tissue damage is due to the activation of $CD8^+$ T-cells which has an immunologic memory retained in the lesions. This will trigger the lesion but not sufficient to damage the tissue extensively. In addition, $CD4^+$ T-cells contribute to the late stage of lesion development and get activated on rechallenge with the offending drug.[3] FDE has four stages including resting, drug intake, acute evolving, and resolution phases.[6] Histopathologically, FDE is characterized as marked, basal cell, hydropic degeneration with pigmentary incontinence. Epidermis and dermis show scattered keratinocyte necrosis with eosinophilic cytoplasm and pyknotic nucleus, lymphocytes, histiocytes, and neutrophils.[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] Literature search showed that few H_1-antihistamine-induced FDE were reported with diphenhydramine, cyclizine, phenothiazine, hydroxyzine, and loratadine.[9] Moreover, levocetirizine, a piperazine-derivative-induced FDE reactions, was also reported by Kim *et al*. and Harish *et al*.[10,11] Yet, another report by Jhaj *et al*. showed cross-reaction between cetirizine and levocetirizine.[12] Case reports highlighted FDE to levocetirizine with cross-reaction; other chemically related antihistamine members are also available.[13,14] Very few cases had been reported with cetirizine-induced FDE by Sonia and Ravikumar, Kränke and Kern, and Inamadar *et al*., which was confirmed by patch test, oral rechallenge test, etc.[6,15,16] Although oral rechallenge test is recommended for the diagnosis of FDE, in our case since the reactions manifested on the same site after 8 h of drug administration with one previous

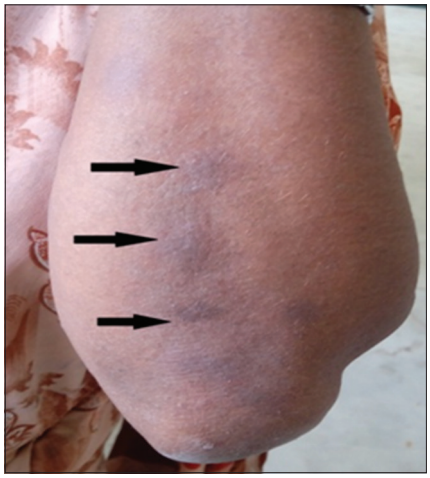

Figure 1: Lesion in the forearm

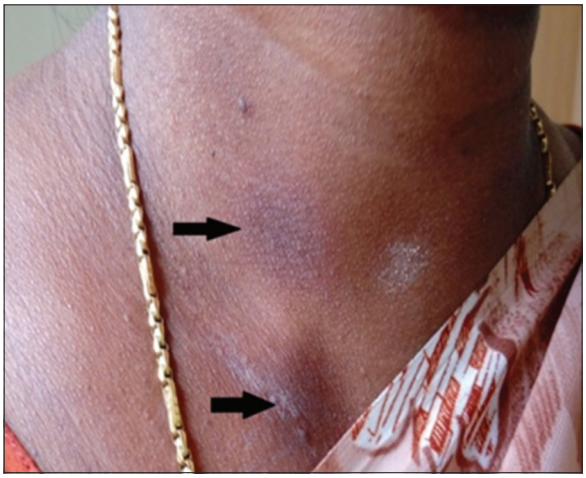

Figure 2: Lesion in the neck

Table 1: Naranjo's adverse drug reaction probability scale

Sl.No	Questions	Yes	No	Do not know
1	Are there previous conclusive reports on this reaction?	+1		
2	Did the adverse event appear after the suspected drug was administered?	+2		
3	Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	+1		
4	Did the adverse event reappear when the drug was readministered?			0
5	Are there alternative causes (other than the drug) that could on their own have caused the reaction?		+2	
6	Did the reaction reappear when a placebo was given?			0
7	Was the drug detected in blood (or other fluids) in concentrations known to be toxic?			0
8	Was the reaction more severe when the dose was increased or less severe when the dose was decreased?			0
9	Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1		
10	Was the adverse event confirmed by any objective evidence?			0
	Total score		7	

Causality score 7 suggestive of "probable" reaction to cetirizine

Table 2: World Health Organization - Uppsala Monitoring Center causality

Causality term	Assessment criteria
Certain	Event or laboratory test abnormality, with plausible time relationship to drug intake Cannot be explained by disease or other drugs Response to withdrawal plausible (pharmacologically, pathologically) Event definitive pharmacologically or phenomenologically (i.e., an objective and specific medical disorder or a recognized pharmacological phenomenon) Rechallenge satisfactory, if necessary
Probable/likely	Event or laboratory test abnormality, with reasonable time relationship to drug intake unlikely to be attributed to disease or other drugs Response to withdrawal clinically reasonable Rechallenge not required
Possible	Event or laboratory test abnormality, with reasonable time relationship to drug intake Could also be explained by disease or other drugs Information on drug withdrawal may be lacking or unclear
Unlikely	Event or laboratory test abnormality, with a time to drug intake that makes a relationship improbable (but not impossible) Disease or other drugs provide plausible explanations
Conditional/ unclassified	Event or laboratory test abnormality More data for proper assessment needed, or Additional data under examination
Unassessable/ unclassifiable	Report suggesting an adverse reaction Cannot be judged because information is insufficient or contradictory Data cannot be supplemented or verified

exposure 2 years back, the diagnosis was confirmed. To the best of our knowledge, cetirizine-induced FDE is the first case to be reported from South India.

The patient was treated with conservative management including topical emollients, corticosteroids, and oral antihistamines and discontinuing the offending drug. The patient was advised to avoid cetirizine and structurally similar compounds such as levocetirizine and also hydroxyzine due to the possibility of cross-reactions among them. This case was presented to document a rare side effect of a commonly prescribed drug, cetirizine.

Our case illustrates the clinically important but rare cutaneous reaction of cetirizine. Even though cetirizine has been widely prescribed with well-established safety, clinicians should have a high index of suspicion and aware of the likelihood of FDE to antihistamine drug, which themselves are very frequently prescribed to manage drug reactions. Deliberate medical and family history of allergic reactions due to any piperazine derivatives should be explored and prescribed with care.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Authors' Contribution

SG and MA: Manuscript writing, editing and manuscript review. SG,GMR and SM: Manuscript editing and Figure editing.

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Conflicts of interest

There are no conflicts of interest.

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