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Fixed drug eruption due to fluoroquinolone group of drug ciprofloxacin – A case scenario and review of literature

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Abstract

Ciprofloxacin is a broad spectrum quinolone antibiotic which is used for treating a wide variety of infections. It inhibits cell division by inhibiting DNA gyrase and topoisomerase IV enzymes. The most common adverse reactions are mild nausea, vomiting and/or abdominal discomfort in 3% to 17% of patients, mild headache and dizziness in 0.9% to 11% of patients. Rashes including photosensitivity can also occur. We report a case of 62 years old male, admitted in the hospital with the history of itching, redness and raised multiple dark skin lesion over the chest, back and oral cavity, bilateral palms and upper limbs since 2 days. On examination, multiple well- defined hyperpigmented patches with peripheral erythema seen over chest, abdomen, and back. Hyperpigmentation of lips along with the erosion of buccal mucosa and angle of mouth; erythematous plaque and exfoliation were seen in the scrotal region. Palms and scalp were spared. The patient was then treated successfully with antihistamines and steroids. The Naranjo and WHO-Uppsala monitoring center scale showed as a "probable" adverse drug reaction. "Level 4b" severity was assessed using Modified Hartwig and Seigel severity assessment scale. The steroid was tapered and the patient was discharged with advice to avoid using ciprofloxacin (fluoroquinolones) group of drugs in future.

Keywords: Antibiotic; Ciprofloxacin; Fixed drug eruption; Antibiotic; Naranjo.

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1. Introduction

Fixed drug eruption (FDE) is most commonly seen with many antibiotics including Ciprofloxacin, Amoxicillin, Ampicillin, Cefixime, and other groups of drugs which are commonly used by any medical practitioners for common infections and injuries. [1] FDE accounts for 16-21% of all cutaneous drug eruptions. [2-3] It is one of the adverse drug reaction and termed as continuous fixed eruption occurring at any particular site due to the usage of the same drug. [4] FDE lesions are characterized by erythematous patches or bullous patches and regress with or without hyperpigmentation. [5] Ciprofloxacin is most the commonly used quinolone group of a drug as an antibiotic for the treatment of respiratory and urinary tract infections. [6] It also leads to adverse drug reaction like urticaria, nausea; vomiting and other cutaneous drug reaction like FDE, photosensitivity, bullous eruption, angioedema, and maculopapular rashes have been reported. [6] However, there were only a few cases reported regarding ciprofloxacin-induced FDE, Stevens-Johnson syndrome (SJS) and Toxic epidermal necrolysis (TEN). [7-9] Here, in this report, we discuss a case of ciprofloxacin-induced FDE.

2. Case Report

A 62 years old male was admitted in the hospital with the history of itching, redness and raised multiple dark skin lesion over the chest, back, oral cavity, bilateral palms and upper limbs since 2 days. A complete history was taken

which revealed that patient had taken one dose of ciprofloxacin prescribed by a Registered Medical practitioner for complaints of ulceration over the left 4th toe. He had a history of drug allergy for the past 4years. He stated that he has been admitted for similar two episodes in the past 5 and 10 months ago in our hospital which was due to the drug intake. However, he didn't have the older prescription and was unaware of the drug that resulted in the adverse reaction. So, we went through his record at medical record department of our hospital and found that the drug reaction was due to ciprofloxacin. On examination, multiple well- defined hyperpigmented patches with peripheral erythema seen over chest, abdomen, (Figure 1) and leg and foot (Figure 2). Hyperpigmentation of lips along with the erosion of buccal mucosa and angle of mouth (Figure 3); erythematous plaque and exfoliation were seen in the scrotal region. Palms and scalp were spared. All routine blood investigations were within normal limits. Hence, Ciprofloxacin was diagnosed as a cause of fixed drug eruption. Naranjo and WHO- Uppsala monitoring center scale showed as "probable" adverse drug reaction and Modified Hartwig and Seigel severity assessment scale showed "Level 4b" severity. The patient was withdrawn from the intake of T. Ciprofloxacin and was treated with Inj. Dexamethasone 1 ½ cc i.v. once daily, T. Prednisolone 30mg once daily, T. Ranitidine 150mg (1/2 hour before food) orally given, syrup potassium chloride 5ml twice daily, Fusidic acid cream E/A twice a day (sutured site) and other supportive measures were given. The patient improved and recovered from skin lesions within 10 days of treatment. The steroid was tapered and the patient was discharged with the advice to avoid using ciprofloxacin (fluoroquinolones) group of drugs in future.

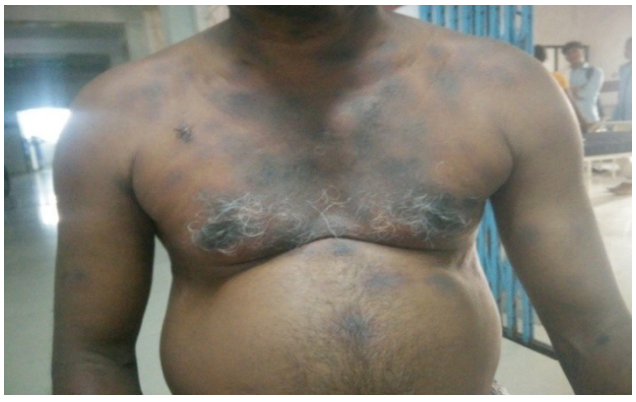

Figure 1: Multiple vesicular lesion with multiple hyperpigmented patches with erythema seen all over the chest and upper limbs

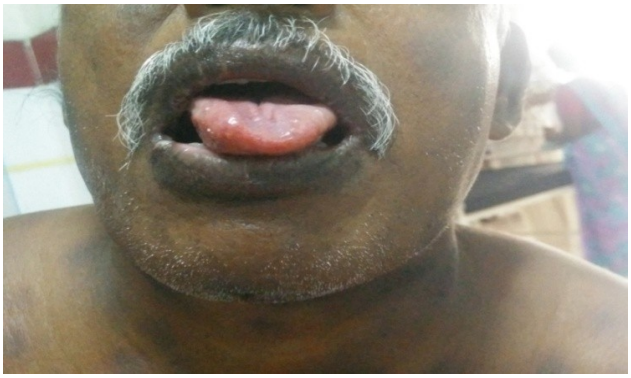

Figure 2: Multiple well-defined hyperpigmention macules are seen in the oral cavity on the mucosal side of lower lip, bucca erosion on both sides are seen

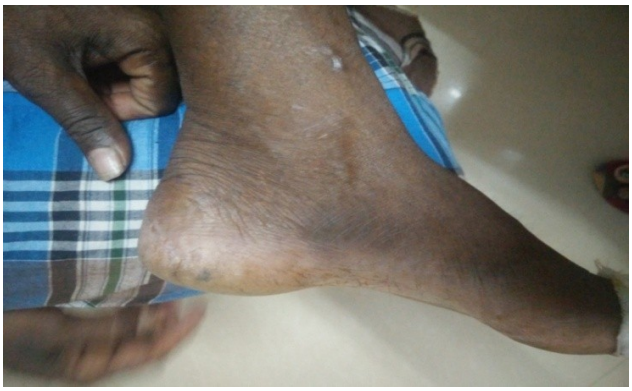

Figure 3: Hyperpigmented patches seen over left leg and foot

3. Discussion

FDE is found most commonly seen in the Indian population, may be due to genetic factors. Genetic susceptibility development maybe due to increased human leukocyte antigen-B22 possibly leading to FDE. [10] FDE is a distinctive drug-induced pattern identified by a recurrent eruption at the same site of skin or mucous membrane due to repeated administration of the drug. [4] FDE exact mechanism is unknown but suggested that it is due to delayed-type IVc hypersensitivity reaction of $CD8^+$ lymphocyte mediated reaction by the drug which may induce local reactivation of T-cell lymphocytes leading to release of lymphokines, mast cell, and antibodies, causing damage to the basal cell epithelium. [11] There is various drug involved in causing FDE are antipsychotics, antifungals, NSAIDs-Diclofenac, Paracematol, antibiotics. Antibiotics that are most commonly used are Penicillins, Cephalosporins, Ciprofloxacin, Ofloxacin, Cefixime etc. [1]

Ciprofloxacin, is the drug which is cause for FDE in question in the present case and it is in use since 1986 [12]. As it possess the properties like good tolerability and excellent tissue penetration has been used extensively in more than 56 countries. Due to its broad spectrum activity against gram positive and gram negative organisms, and easy dosage schedule; ciprofloxacin remains as one of the most popular antibacterial among the dermatologists till date. [12] Ciprofloxacin is most widely used for infections like respiratory tract infection, UTI, bones, and soft tissue infection as it penetrates the skin and mucous membrane easily. [6] It is effective both as an oral and parenteral form. [5] The most common renal adverse effects are crystalluria, haematuria, interstitial nephritis and acute renal failure, particularly with ciprofloxacin. [13-14] The increased reports of neurological ADRs to fluoroquinolones and their serious effects were reasons for recent the change in labeling of this class of drugs and revision of the boxed warning by the FDA (USFDA, 2016). [15] This also contributes to the restricted use of fluoroquinolones in Europe (EMEA 2008). [16] Few cases have been reported earlier with ciprofloxacin-induced erythema multiforme, SJS, vasculitis, hypersensitivity reaction and anaphylaxis. [7-8] FDE due to ciprofloxacin has been reported rarely. Ciprofloxacin-induced FDE is mostly found in male patients (4.7%) who are relating to our case too. [17]

Here in this case report, we reported a case of 62 years old male patient with FDE after intake of oral ciprofloxacin for ulcer of the left 4th toe as prescribed by a medical practitioner outside and after immediate stoppage of drug symptoms got subsided. Proper complete history of the patient regarding drug intake is important to avoid drug-induced ADR. Because in our patient there was the previous history of drug allergy of two episodes for the same drug and the patient was unaware about the drug details. Therefore immediate identification of patterns of an adverse reaction is important, besides the prompt withdrawal of drug and specific treatment are more essential to decrease morbidity.

Table 1: Naranjo's ADR Probability Scale

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

Table 2: Modified Hartwig and Seigel Severity Assessment Scale

Category	Assessment based on the level of severity
Mild	LEVEL 1: An ADR occurred but required no change in treatment with the suspected drug **Or** LEVEL 2: The ADR required that treatment with the suspected drug be held, discontinued, or otherwise changed. No antidote or other treatment requirement was required. No increase in length of stay (LOS)
Moderate	LEVEL 3: The ADR required that treatment with the suspected drug be held, discontinued, or otherwise changed. **And/Or** An Antidote or other treatment was required. No increase in LOS **Or** LEVEL 4a): Any Level 3 ADR which increases length of stay by at least 1 day **Or** LEVEL 4b): The ADR was the reason for the admission
Severe	LEVEL 5: Any Level 4 ADR which requires intensive medical care **Or** LEVEL 6: The adverse reaction caused permanent harm to the patient **Or** LEVEL 7: The adverse reaction either directly or indirectly led to the death of the patient

The Naranjo's scale shows a probability with scale scoring 8 as seen in (Table 1), WHO - Uppsala monitoring also showed the "probable" category of ADR with reasonable time relationship to drug intake, Response to withdrawal was clinically reasonable. [18-19] Modified Hartwig and Seigel severity scale showing "level- 4b" severity which implies that ADR required the treatment with the suspected drug is withheld, or discontinued, and other treatment was required and also increase in length of stay for 10days due to ADR caused by the drug intake (Table 2). [20] Therefore it is necessary to create awareness among people about the ADR due to drug intake.

4. Conclusion

Thus it's prime to get aware of drugs that lead to ADR or FDE. Patients should have a medical allergy card mentioned about the allergic drug details that cause ADR and should be instructed to carry with them whenever they visit for any treatment to hospitals/clinics. Doctors should be spending time on educating the patient by proper counseling about ADR and explain about its importance to the patient. Not only that but also reporting of ADR to ADR monitoring centers which helps other doctors to get aware of possible side-effects of the drug. Hence, general practitioners and physician's and should be cautious while prescribing ciprofloxacin (fluoroquinolones) group of drugs in the future to avoid ADR.

Conflicts of interest: Nil
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