



## CIPROFLOXACIN INDUCED FIXED DRUG ERUPTION: A CASE STUDY

**Dr. Vishnu Das<sup>\*1</sup>, Dr. Nikhila K. V.<sup>2</sup>, Dr. Lydia B. Peters<sup>3</sup>, Dr. Drisya Viswam<sup>4</sup>, Dr. Thomas Varghese<sup>5</sup> and Anson Mathew Joseph<sup>6</sup>**

<sup>1,2,3,4,5</sup>Doctor of Pharmacy (PHARM D), Sree Krishna College of Pharmacy and Research Centre, Parassala, Trivandrum-695502.

<sup>6</sup>Doctor of Pharmacy Intern (Pharm D), Sree Krishna College of Pharmacy and Research Centre, Parassala, Trivandrum-695502.

**\*Corresponding Author: Dr. Vishnu Das**

Doctor of Pharmacy (PHARM D), Sree Krishna College of Pharmacy and Research Centre, Parassala, Trivandrum-695502.

Article Received on 04/08/2017

Article Revised on 25/08/2017

Article Accepted on 15/09/2017

### ABSTRACT

Fixed drug eruption (FDE) is a distinctive type of cutaneous drug reaction that characteristically recurs in the same locations upon reexposure to the offending drug. FDEs are less common than exanthematous (morbilliform) eruptions, which occur in both sexes and in all age groups. FDEs account for 14 to 22 percent of cutaneous drug reactions. Drugs most frequently associated with FDE are antimicrobials, anticonvulsants, and nonsteroidal antiinflammatory drugs. Here, an uncommon case of ciprofloxacin induced fixed drug eruption was reported.

**KEYWORDS:** cutaneous drug reaction, urticaria, ciprofloxacin, morbilliform, vasculitis.

### INTRODUCTION

Adverse reaction to medication are common and often present as skin reaction. Morbilliform exanthem, urticaria, hypersensitivity syndrome, pseudolymphoma, photosensitivity, pigmentary changes, acute generalized exanthematous pustulosis, lichenoid dermatitis, vasculitis, Stevens-Johnson syndrome, or fixed drug eruption (FDE) are the common drug induced cutaneous reaction. The term fixed drug eruption describes the development of one or more annular or oval erythematous patches as a result of systemic exposure to a drug; these reactions normally resolve with hyperpigmentation and may recur at the same site with re-exposure to the drug. Repeated exposure to the offending drug may cause new lesions to develop in addition to "lighting up" the older hyperpigmented lesions.<sup>[1]</sup>

Fixed drug eruption (FDE) is a distinctive variant of drug induced dermatoses characterized by sharply demarcated, erythematous patches with/without blistering that develop within hours of administration of the causative drug and heals with postinflammatory residual hyperpigmentation. It usually recurs at the same site of the skin or mucous membrane upon subsequent exposure to the same/similar group of drugs. Fluoroquinolones are widely used antimicrobials, which cause cutaneous adverse drug reactions in about 1-2% of patients. Fixed drug eruptions may account for as much as 16-21% of all cutaneous drug eruptions. Several variants of fixed drug eruption have been described, based on their clinical

features and the distribution of the lesions like generalized or multiple, linear, bullous, urticarial, pigmented, non-pigmented, wandering, eczematous, psoriasiform, erythema dyschromicum perstans-like, vulvitis and oral fixed drug eruption.<sup>[2]</sup>

Here we describes a case of bullous fixed drug reaction induced by Ciprofloxacin. Ciprofloxacin is a antibiotics belong to fluoroquinolones. It acts by inhibiting the relaxation of DNA and inhibits DNA gyrase in susceptible organisms thereby promotes breakage of double-stranded DNA.

Fluoroquinolones commonly cause a morbilliform rash and/or photosensitivity, but rarely result in FDE. The few cases of fluoroquinolones induced fixed drug reactions reported in literature are typical localised FDR.<sup>[2]</sup>

### CASE SUMMARY

A 55yr old male patient came to the dermatology department with complaints of dark red patch on left palm since three days. At first it appears as a erythematous rash followed by darkening of the skin. On direct interaction with the patient, we came to know that he was free from diseases and medication except taking Tab. Ciprofloxacin 500mg twice daily for lower respiratory tract infection. On physical examination he was afebrile and his vitals are in normal range. Skin biopsy report reveals the presence of eosinophils and few neutrophils. We advised the patient to stop the drug to

check whether it because of adverse reaction of the drug. From this details, we identified this as a case of ciprofloxacin induced bullus FDR (fixed drug reaction). We advised regarding the cause of skin problem and advised to stop ciprofloxacin. We reported this to concerned doctor and by considering our intervention, Doctor told him to stop T. Ciplox and prescribed T. Celin 1-0-0, Tinactin cream for this bullus fixed drug reaction.



## DISCUSSION

Fixed drug eruptions (FDEs) start as a few sharply demarcated erythematous macules that rapidly become erythematous plaques occurring more commonly on the lips, genitalia, and trunk. The prevalence of drug eruptions has been reported in the range of 2-5% and Fixed drug eruptions may account for as much as 16-21% (1). Ciprofloxacin is a widely used fluoroquinolone antibiotic, inducing cutaneous adverse drug reaction in 1 to 2% of treated patients.<sup>[3]</sup>

The term FDE was first introduced by Brocq in 1894.<sup>[5]</sup> Fixed drug eruption is a distinct variant of drug-induced dermatoses characterized by their relapse in the same location after the administration of the causative drug. We have recently shown that intraepidermal CD8+ T cells phenotypically resembling effector memory T cells are greatly enriched in the resting lesions of FDE. Although effector memory T cells have been implicated as the mediators of protection in epithelial tissues, our observation raises an alternative possibility that improper, enhanced or uncontrolled activation of intraepidermal T

cells could contribute to severe tissue injury. Until recently, however, their detrimental effects on epithelial tissues have rarely been examined. The focus of this review is on how intra-epidermal T cells originally evolved to protect tissue integrity can exert an opposite action that is deleterious to the host.<sup>[6]</sup>

Lesions heal with hyperpigmentation and occur in the same site with readministration of the responsible drug. In 30% of cases, macules may become vesicles and bullae, which may lead to a more severe reaction known as generalized bullous FDE resembling SJS-TEN. In patients with generalized bullous FDE, physical examination reveals clearly demarcated erythematous and edematous patches surrounded by bullae that contain clear fluid.<sup>[7]</sup>

Rechallenging the patient to the suspected offending drug is the only known test to possibly discern the causative agent, but that is unethical and not advisable. Therefore, certain causality assessment scales regarding drug reaction have been described like the Naranjo ADR probability scale, WHO-Uppsala Monitoring Centre causality assessment system and Hartwig scale.<sup>[7,8]</sup>

Treatment includes stopping the offending drug with oral and topical steroids, emollients, and oral antihistamines. Though usually not fatal, FDE can cause enough cosmetic embarrassment especially when they recur on the previously affected sites leaving behind residual hyperpigmentation.

In this, Naranjo's algorithm, was used to determine a plausible reaction due to ciprofloxacin. The following criteria were considered: There were previous conclusion reports on this reaction (+1); the adverse event appeared after ciprofloxacin was administered (+2); adverse event improved when ciprofloxacin was discontinued (+1); adverse event reappeared when the drug was re-administered (+2); Are there alternative causes that could have caused the reaction(+2);the reaction reappeared when a placebo was given (+1); drug detected in the blood (or other fluids) in a concentration known to be toxic (0); the reaction was more severe when the dose was increased or less severe when the dose was decreased (0); the adverse event confirmed by objective evidence (+1). Based on the total score of 10, this FDE was categorized as "definite" reaction to ciprofloxacin administration.<sup>[7]</sup>

According to WHO-Uppsala Monitoring Centre causality assessment system, the adverse reaction was found to be "probable/likely" reaction to ciprofloxacin.

## CONCLUSION

Pharmacovigilance for monitoring ADR by practicing physicians and clinical pharmacist is an essential armament of the clinical acumen. It is also important to report ADRs, which helps to detect and prevent drug reactions which in turn decrease the cost of treatment.

Ciprofloxacin is commonly used antibiotic and so it is important for prescribing physician to keep in mind that it can also lead to bullous FDR.

#### CONFLICT OF INTEREST

There is no conflict of interest for publishing the case report. The written consent signed solely by the patient was received before stating the study.

#### REFERENCE

1. Ronnau Ac, Sachs B, et al. Cutaneous adverse reaction to ciprofloxacin: Demonstration of specific lymphocyte proliferation and cross reactivity to ofloxacin in vitro. *Acta Dermatol Venereol*, 1997; 77: 285-8.
2. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4408714/>.
3. Sehgal VN, Srivastava G. Fixed drug eruption (FDE): Changing scenario of incriminating drugs. *Int J Dermatol*, 2006; 45: 897–908.
4. <https://www.ncbi.nlm.nih.gov/pubmed/12130946>.
5. F D Butler, D W James. Drug-Induced Bullous Disorders Clinical Presentation. 2016 Mar 29. Also available from: <https://www.google.co.in/emedicine.medscape.com/article/1062790-clinical>.
6. The use of the WHO-UMC system for standardised case causality assessment. [Last accessed on 2 Dec 2014]. Available from: <http://www-who.umc.org/graphics/24734.pdf>.
7. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther*, 1981; 30: 239-45.
8. Hartwig SC, Siegel J, Schneider PJ. Preventability and severity assessment in reporting adverse drug reactions. *Am J Hosp Pharm*, 1992; 49: 2229-32.