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CIPROFLOXACIN AND METRONIDAZOLE INDUCED ADVERSE DRUG REACTION: A RARE CASE REPORT

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KEYWORDS :

INTRODUCTION

Fluoroquinolones are one of the oldest and widely used antimicrobials in day-to-day practice. As the name suggest, these are quinolones with one or more fluorine substitutions showing various spectrum of activity (effective against both gram-negative as well as gram-positive bacteria). It acts by interfering with bacterial DNA synthesis by inhibiting DNA Gyrase enzyme as well as topoisomerase IV enzyme. The damaged DNA hence formed is digested by exonucleases thereby exerting bactericidal action. These include drugs such as Ciprofloxacin, Norfloxacin, Ofloxacin, Levofloxacin, Moxifloxacin, Prulifloxacin, Pazufloxacin, Balofloxacin etc.[1] Among these, Ciprofloxacin is considered the prototype drug that was patented in 1983 by Bayer A.G. It was FDA approved for use in common infections like UTI, LRTI in 1987.[2] It is also used in several clinical conditions such as typhoid, bacterial gastroenteritis; chancroid; tuberculosis; meningitis; bone, soft tissue, gynecological and wound infections.[3,4]

Although Ciprofloxacin has good safety profile with mild to moderate side effects such as nausea, vomiting, bad taste, anorexia, headache, insomnia, restlessness, anxiety, impairment of concentration etc. It accounts for 1-2% of cutaneous drug reactions.[4-7] Several Case reports have been found to cause Fixed Drug Eruptions due to ciprofloxacin. Hereby, we came across such rare case report of FDE with Ciprofloxacin and Metronidazole.

Cutaneous ADR seen in about 1-2% cases. Fixed drug eruptions (FDE) accounts for 10% of all ADRs.

As the name suggests , the most common drugs causing FDE are co-trimoxazole(25%), NSAIDs (21.7%, Tetracycline (11.7%), ciprofloxacin (6.7%), amoxycillin (5%) and metronidazole (3.3%).

The shape of the eruptions can vary. These are generally oval erythematous patches. It is benign in nature and can affect any body part like face, tongue, hands, lips and even genitilia.

The severity of the reaction in FDE may increase after repeated exposure to the drug and may rarely progress to a clinical state called generalized bullous FDE. It may be clinically misdiagnosed as Stevens Johnson Syndrome and Toxic Epidermal Necrolysin.

CASE REPORT

A female patient aged 35 years visited dental OPD with complains of food lodgment and mild pain in upper back tooth region for last 2 months. She gave no past history of any medical or dental treatment. On examination, carious tooth with mild generalized gingivitis was found. A provisional diagnosis of Chronic Pulpitis was made. To confirm the diagnosis, she was advised for X-ray and routine blood investigations and was prescribed a fixed dose combination of tablet Ofloxacin (200mg) and Ornidazole (500mg) one tablet to be taken twice a day, tablet Ibuprofen one tablet to be taken three times a day, tablet Ranitidine one tablet to be taken before breakfast and tablet B-complex one tablet to be taken once daily. The duration of the treatment was for 7 days.

Based on the X-ray findings, a diagnosis of "Chronic Pulpitis" (in relation to right maxillary second molar) was made and the patient was advised for dental extraction of tooth under local anesthesia. After 7 days the patient underwent the procedure with 2% lignocaine with adrenaline (1:80,000). The immediate post extraction period was uneventful and the above treatment was continued for next 5 days.

On next follow-up visit, the patient complained of numbness and mild pain around extraction socket. Mild inflammation was seen and irrigation with normal saline was done in the affected part. The following drugs were then prescribed for a duration of 3 days.

Tablet Ciprofloxacin 500mg twice daily
Tablet Metronidazole 400mg three times a day
Tablet Ibuprofen 600mg twice a day
Tablet B-complex once daily
Tablet Ranitidine 150mg twice daily

Mouthwash Chlorhexidine to rinse mouth three times daily After 12 days, the patient presented again to the Dental OPD with lip discoloration on both the lips involving small area of the chin. The lesion started with lip dryness and mild itching within 2 days of starting the above-mentioned drug and it began to flare up gradually with discoloration. She gave no past history of any food or dug allergy. All drugs were stopped immediately and she was advised tablet cetirizine once daily and ointment containing a combination of three antibiotics (Polymyxin B, Neomycin, Bacitracin) and a steroid (Hydrocortisone) to be applied topically over the affected region twice daily and was referred to dermatology department for further management.

DISCUSSION

Various drugs have been implicated in the causation of fixed drug reactions, most commonly are trimethoprim-sulfamethoxazole (and other sulfonamides), naproxen, ibuprofen, tetracyclines, other antibiotics (ampicillin, metronidazole), and barbiturates. Many cases of these kind remain under-diagnosed or misdiagnosed.[8]

Fluoroquinolones are notorious drugs as they cause a wide variety of side effects. The case here is a Fixed Drug Eruption induced by ciprofloxacin. Bourns was the first to describe FDE in 1889 while the term FDE/ "eruption erythemato pigmentee fixed" was coined by Brocq in 1894. FDE are cutaneous manifestations of drug reaction that generally occurs at similar locations.[9] It affects all ages but is more common in young to middle aged adults[10].

Tinidazole a nitroimidazole derivative antiprotozoal is widely used in the treatment of diarrhoea in India. However, these FDC are not a part of WHO essential medicine list. Incidence of FDE, drug-induced anaphylaxis and erythema multiforme and vomiting have been reported with the use of Ciprofloxacin/tinidazole combination.[2,3,5]

Adverse drug reaction to this FDC makes it difficult to determine the possible offending drug due to cross sensitivity. Though rechallenge with the offending drug is the gold standard for confirmation of FDE, in this case it was not attempted as the patient was not willing for the fear of aggravation of the lesions.

Fixed drug reaction was seen in a case report with ofloxacin followed by recurrence of the reaction with ciprofloxacin after a gap of one year suggesting possibility of cross reactivity with fluoroquinolones. On the contrary, in our case report no such cross-reaction appeared in patient taking Ofloxacin with ornidazole 15 days back. The reaction appeared 2 days after taking ciprofloxacin and metronidazole. This was a rare occurrence and a very unusual one. (R-7)[11,12]

The pathogenesis of this reaction could be due to CD8+ memory T cells which resides in the basal layers of epidermis. On consumption of the offending drug, these CD8+ cells migrate to epidermis, causing release of cytokines and hence the FDR[13].

The ADR in this scenario was evaluated for causality assessment using World Health Organization-Uppsala Monitoring Centre Causality Assessment Scale and it was found to be probable. The severity was assessed by using Modified Hartwig & Siege scale. It was of mild severity. The preventability was assessed using Modified Schumock & Thornton scale and this case was found to be probably preventable.

This rare case is presented to create awareness about FDE associated with this type of very commonly prescribed antibiotics.

CONCLUSION

Pharmacovigilance for detecting, assessing, understanding and preventing ADR is an essential knowledge for health care professionals. It is important to report ADRs which can help to detect and treat drug reactions decreasing morbidity and mortality and in turn decrease the cost of treatment. Judicious use of the ciprofloxacin/metronidazole is required in view of cosmetic disfigurement seen with FDEs. Patients should be counselled on recurrence of FDE with the offending drug and possible cross-reactions of similar medications.

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(World Health Organization (WHO) -Uppsala Monitoring Centre. The Use of the WHO-UMC System for Standardised Case Causality Assesment[14].

REFERENCES

1. Mac DougallConan. “DNA disrupters:Sulfonamides, quinolones and Nitroimidazoles.” Goodman & Gillman's The Pharmacological Basis of Therapeutics. Laurence L Brunton, Bjorn C Knollmann.14th Edition. Mac Graw Hill,1138-1146
2. Sharma PC,Jain A, Jain S,Pahwa R,Yar M S.Ciprofloxacin: review on developments in synthetic, analytical, and medicinal aspects. J Enzyme Inhib Med Chem.2010 Aug:Aug(4):577-89 (Cross Reference)
3. Sulfonamides, cotrimoxazole and quinolones. Essential of Medical Pharmacology. K D Tripathi,8th edition,Jaypee.755-765
4. Beauduy Camille E, Winston Lisa G. Sulghonamides, Trimethoprim & Quinolones. Basic and Clinical Pharmacology. Bertram G Katzung, Todd W Vanderah. 15th edition, Mc Graw Hill Range. (1245-53)
5. Nair PA. Ciprofloxacin induced bullous fixed drug reaction: Three case reports. J Fam Med Primary Care 2015; 4:269-72.
6. Ravishankar M, Deepika G, Shwetha S. Ciprofloxacin induced fixed drug eruption. Int J Basic Clin Pharmacol 2014; 3:1096-7.
7. Parikh N, Sood S, Chaudhary R, Malhotra S, Patel P.Ciprofloxacin and metronidazole induced fixed drug eruption. Natl J Integr Res Med 2018; 9(5):58-60
8. Shaker G, Mehendale T, De La Rosa C (August 23, 2022) Fixed Drug Eruption: An Underrecognized Cutaneous Manifestation of a Drug Reaction in the Primary Care Setting. Cureus 14(8): e28299
9. c Eruption. Medicina 2021, 57, 925. https:// doi.org/10.3390/medicina57090925
10. Zaouak, A.; Ben Salem, F.; Ben Jannet, S.; Hammami, H.; Fenniche, S. Bullous fixed drug eruption: A potential diagnostic pitfall:A study of 18 cases. Therapies 2019, 74, 527–530.)[CrossRef]
11. Meenakshi R, Nitya S, Kiruthika S, Shanthi M.Fixeddrug eruption associated with fixed combination of fluoroquinolone-nitroimidazole.Int JBasic Clin Pharmacol 2021;10:576-7.
12. Kameswari PD, Selvaraj N, Adhimoolam M. Fixed drug eruptions caused by cross-reactive quinolones. J Basic Clin Pharma 2014;5:54-5.
13. Mizukawa, Y.; Yamazaki, Y.; Shiohara, T. In vivo dynamics of intraepidermal CD8+ T cells and CD4+ T cells during the evolution of fixed drug eruption. Br. J. Dermatol. 2008, 158, 1230–1238. [CrossRef]
14. [Available from: https://www.who.int/docs/defaultsource/medicines/pharmacovigilance/whocausality-assessment.pdf.[Last accessed on 2023]