

RABEPRAZOLE-INDUCED FIXED DRUG ERUPTION: A RARE CASE REPORTBALAJI O¹, AMITA D¹, NAVIN PATIL^{2*}¹Department of Pharmacology, Kasturba Medical College, Manipal, Karnataka, India. ²Department of Medical Oncology, Kasturba Medical College, Manipal, Karnataka, India. Email: navin903@gmail.com

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ABSTRACT

Among cutaneous adverse drug reactions, fixed drug eruption is the most common cutaneous drug reaction among the Indian population. The drugs most commonly implicated in fixed drug eruption are analgesics and antibiotics. Here, we report a case of fixed drug reaction caused by rabeprazole.

Keywords: Fixed drug eruption, Rabeprazole, Proton-pump Inhibitor, Naranjo's scale.

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INTRODUCTION

An adverse reaction is defined as an appreciably harmful or unpleasant reaction, resulting from an intervention related to the use of a medicinal product, which predicts hazard from future administration and warrants prevention or specific treatment, or alteration of the dosage regimen, or withdrawal of the product. Most common among them is cutaneous adverse drug reactions [1] with fixed drug eruption being the most common cutaneous drug reaction among the Indian population [2]. The drugs most commonly implicated in fixed drug eruption are analgesics and antibiotics [2]. Here, we report a case of fixed drug reaction caused by rabeprazole.

CASE REPORT

Informed consent was obtained from the patient. A 26-year-old male came with complaints of rounded reddish erythematous bright red macular patches over the right thumb of size 1 cm × 1 cm, right index finger of size 0.5 cm × 0.5 cm, and mucosa of the upper lip of size 2 cm × 2 cm with edematous plaques. Patient also had tingling and burning sensation with itching. Past history of patient reveals on and off fever, cough, and expectoration since 3 months and treatment with paracetamol and rabeprazole. Patient said similar lesion appeared over his index finger and it subsided after he finished his course of treatment. He did not report it to a physician. There is no other significant medical history or exposure to other drugs. Two weeks back, patient was treated for the same condition with Dolo 650 mg thrice daily and rabeprazole 20 mg twice daily. After taking medications for 1 day, the patient developed reddish macules, and doctor advised her to stop rabeprazole. She was then continued with paracetamol, and patient lesion slowly subsided on treatment. Rechallenge was not performed as the patient did not give consent, and causality assessment was performed using Naranjo's scale. Severity and preventability assessment was performed using Hartwig's scale and Thornton's scale, respectively.

DISCUSSION

In 1894, Brocq coined the term fixed drug eruption ("erytheme pigmenté fixe") after investigating three patients on antipyrine presenting with erythematous pigmented eruptions [3]. A fixed drug eruption is a skin lesion characterized by bright red, rounded erythematous macules with edematous plaques that appear at the same site within 30 minutes to 12 hrs after the administration of the causative drug. Lesions are usually solitary initially and then later after repeated exposure can present as multiple lesions occurring at the same site of increasing size as well

as new lesions over other sites. Common sites of involvement include hand, feet, genitalia, periorbital, perioral, and perineal areas [4].

Pathogenesis mainly involves infiltration of the CD8 cells into the epidermis, and an intellectual memory is created. When the offending drug is administered, these cytotoxic cells get activated and produce a cascade of inflammatory cytokines mainly interferon-alpha [3]. These cytokines cause apoptosis of keratinocytes leading to epidermal injury presenting as eczema, macules, blisters, and plaques. Acute stage is characterized by epidermal necrosis progressing with dermal lymphocytic infiltration ultimately resulting in deposition of melanin in epidermis in chronic lesions [4].

Many drugs cause fixed drug eruptions, and common ones are included in Table 1 [4]. Rabeprazole is a substituted benzimidazole, a proton-pump inhibitor [5]. It is mainly used in the treatment of peptic ulcer, gastroesophageal disorder, and also in *Helicobacter pylori* infections. It causes adverse effects such as diarrhea, headache, dizziness, and confusion with the prevalence of cutaneous reactions ranging from 0.5% to 1.5%. Cutaneous reactions present as angioedema, urticaria, anaphylaxis, maculopapular rashes, hyperpigmentation, erythema multiforme and erythroderma, exfoliative dermatitis, and bullous eruption [4].

Table 1: Common drugs causing fixed drug eruptions

Sulfonamides (cotrimoxazole)
Tetracyclines
Penicillin
Erythromycin
Clarithromycin
Metronidazole
Ciprofloxacin
Rifampicin
NSAIDs
Barbiturates, benzodiazepines
Lamotrigine
Fluconazole
Cetirizine
Omeprazole and lansoprazole
ACE inhibitors
Hormonal preparations

NSAIDs: Nonsteroidal anti-inflammatory drugs, ACE: Angiotensin-converting enzyme

Table 2: Adverse drug reaction assessment

Naranjo's scale	Probable
Hartwig's scale	Mild severity
Thornton's scale	Not preventable

As per literature, only a few cases of fixed drug eruptions have been reported with proton-pump inhibitors mainly omeprazole [6-9]. In our patient, rabeprazole was given and other drugs causing it was ruled out. Causality, severity, and preventability assessment as per Naranjo's, Hartwig's, and Thornton's scale was found to be probable, mild severity, and not preventable, respectively (Table 2) [10].

CONCLUSION

Since a probable causal relationship is established and rabeprazole being a commonly prescribed drug for peptic ulcer disease, history of previous drug exposure and any cutaneous adverse drug reactions to proton-pump inhibitors should be recorded. Immediate discontinuation of drug is warranted if the patient complains of fixed drug eruption and proper treatment should be given. This case also suggests increased need for improved post-marketing surveillance to combat the emergence of new adverse drug reactions attributed to changing trends in drug utilization. Further retrospective as well prospective clinical trials can be undertaken to find out the exact incidence and prevalence of fixed drug eruptions with proton-pump inhibitors in future in India.

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