

**Doxycycline induced fixed drug eruption: a case report****Isswariya Anandan, Nitya Selvaraj\*, Suganya Ganesan,  
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commercial use, distribution,  
and reproduction in any  
medium, provided the original  
work is properly cited.**ABSTRACT**

Fixed drug eruption (FDE) is an adverse drug reaction seen with various groups of drugs are antibiotics such as trimethoprim -sulphamethoxazole, penicillin, tetracyclines, non steroidal anti-inflammatory drugs like ibuprofen, aspirin etc. Doxycycline belongs to tetracycline groups of antibiotics. We herein present the case of Doxycycline induced fixed drug eruption. A 35-year - old man presented to our hospital, with a 2-day history of itching and hyperpigmentation over the chest. Patient developed skin lesion 2 days after and he started taking Doxycycline 100 mg twice a day for skin infections. Dermatological examination revealed multiple well defined hyperpigmented patches seen over the anterior aspect of the chest. Doxycycline was discontinued immediately, and the skin lesions resolved spontaneously within 2 weeks. Causality assessment by using Naranjo adverse drug reaction probability scale and WHO Uppsala monitoring scale categorize the reaction as Doxycycline was the probable cause for the adverse drug reaction. Severity assessment by using modified Hartwig and Siegel ADR severity assessment scale labelled the reaction as mild-level 2. The causative drug or drugs and cross reactants should be avoided in future to prevent recurrence of similar skin reactions.

**Keywords:** Antibiotic, Doxycycline, Fixed drug eruption, Tetracycline**INTRODUCTION**

Fixed drug eruption is a type of cutaneous adverse drug reaction.<sup>1</sup> The most significant findings of FDE are recurrence of similar skin lesions at the same site upon reexposure to the offending drugs.<sup>2</sup> It is characterized by sharply marginated, round to oval patch or plaque on a violaceous or dusky erythematous background.<sup>3</sup> Lesions may be solitary or multiple and sometimes it may present as vesicular or bullous.<sup>1</sup> Symptoms like pruritus and burning sensation are associated with FDE.<sup>3</sup> Pigmenting and non pigmenting lesions are seen. Pigmented lesions are seen with heroin addicts and non pigmented lesion seen with pseudoephedrine use.<sup>1</sup> Literature search reveals 2-5%

prevalence of cutaneous drug eruption are mainly due to FDE.<sup>4</sup> Doxycycline is an antibiotic belonging to the tetracycline group of antibiotics.<sup>3</sup> It inhibits bacterial protein synthesis by binding to 30S ribosomal subunit. It is commonly used to treat respiratory tract infections, intra-abdominal infections, rickettsial infections, sexually transmitted infections, skin and soft tissue infections.<sup>5</sup>

Being a cheaper and easily available drug, it is commonly prescribed by practitioners. Therefore, it is important to enlighten the importance of the adverse drug reaction caused by the commonly prescribed drug. So hereby we present a case of Doxycycline induced fixed drug eruption.

## CASE REPORT

A 35 year old man presented to our hospital with complaints of itching and hyperpigmentation over the chest for past two days. The patient stated that, the lesions developed after intake of doxycycline 100 mg twice a day which was prescribed for skin infections. He was not concurrently taking any other medications. On further questioning, the patient acknowledged the past history of similar illness following consumption of the same drug, which was confirmed from the old prescription.

Dermatological examination revealed multiple well defined hyperpigmented patch over the anterior aspect of the chest (Figure 1). Patient was afebrile. Complete blood count, renal function test and liver function test were within the normal limits. The patient was diagnosed as Doxycycline induced fixed drug eruption. Patient did not give consent for oral provocation test, patch test and skin biopsy. Patient was treated as outpatient, Doxycycline was discontinued immediately, and skin infections were treated with oral cetirizine 10mg and topical betamethasone for

two weeks. The lesions resolved with residual post inflammatory hyperpigmentation in two weeks. Patient was counselled, advised to maintain drug allergy card which included drugs to be avoided in future to prevent recurrence.



**Figure 1: Multiple hyperpigmented patch seen over the chest.**

**Table 1: Naranjo ADR probability scale.**

Question	Yes	No	Don't know	Score
Are there previous conclusion reports on this reaction?	+1	0	0	1
Did the adverse event appear after the suspect drug was administered?	+2	-1	0	0
Did the adverse reaction improve when the drug was discontinued, or a specific antagonist was administered	+1	0	0	+1
Did the adverse reaction reappear when the drug was re - administered	+2	-1	0	0
Are there alternate causes (other than the drug) that could solely have caused the reaction	-1	+2	0	+2
Did the reaction reappear when a placebo was given?	-1	+1	0	0
Was the drug detected in blood (or other fluids) in a concentration known to be toxic?	+1	0	0	0
Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0	0
Did the patient have a similar reaction to the same or similar drugs in any previous exposure	+1	0	0	+1
Was the adverse event confirmed by objective evidence	+1	0	0	+1
<b>Total score</b>				<b>6</b>

Scoring for Naranjo algorithm: >9 = definite ADR; 5-8 = probable ADR; 1-4 = possible ADR; 0 = doubtful ADR

Of all cutaneous adverse drug reactions 16-21% are mainly due to FDE and occurrence is common in India.<sup>6,1</sup> Based on the clinical features and distribution of lesions, FDE has been classified into various types like linear, bullous, generalized or multiple, pigmented, non-pigmented, eczematous etc.<sup>6</sup> Acute lesions usually develop within 30 min to 8 hours after exposure to the causative drug.<sup>7</sup> Sites involved in FDE are face, trunk, genitalia, lips and extremities. Drugs reported to induce FDE are antibacterial, antifungal, antipsychotics, analgesics etc.<sup>8</sup>

Other etiological factors known to precipitate FDE lesions are food, ultraviolet radiation and genetically predisposed individuals.<sup>9,10</sup>

Polysensitive FDEs are caused by piroxicam and cotrimoxazole, tenoxicam and trimethoprim - sulfamethoxazole and various anticonvulsants.<sup>9</sup> Food product which contains beta lactam and macrolide antibiotics residue are known to cause hypersensitive reactions.<sup>11</sup>

**Table 2: WHO-UMC causality categories.**

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 pharmacologic 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 explanation
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

**Table 3: 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

Doxycycline being a broad spectrum antibiotic, used to treat various bacterial infections. Adverse effects of doxycycline are nausea, vomiting, diarrhea, hepatotoxicity, renal toxicity, skin rashes and phototoxicity. Similar cases have been reported earlier.<sup>5</sup>Treatment should mainly depend upon duration, number and severity of lesions. If FDE is symptomatic then the skin lesions can be treated with systemic antihistamines and topical corticosteroids.<sup>7</sup> In case of severe generalized bullous fixed drug eruption warrant the attention and aggressive management of Stevens- Johnson syndrome or toxic epidermal necrolysis.<sup>12</sup>

Main pathophysiology of FDE is interleukin mediated survival of memory of T cells. Interleukin -20 is responsible for site specificity of lesions.<sup>7</sup> Localized tissue damage is due to intraepidermal clusters of differentiated CD8 positive T cells. On activation, resting T cells kill the surrounding keratinocytes, which in turn release cytokines such as interferon gamma. CD8 positive T cells, CD4 positive cells and neutrophils are recruited in FDE site resulting in tissue damage.<sup>9</sup>

In this patient, lesions developed within 3 hours of exposure and Causality assessment was done by using Naranjo adverse drug reaction probability scale and WHO

Uppsala monitoring scale. Naranjo's score was 6 and WHO Uppsala monitoring scale both categorize the adverse reaction as probable (Table 1 and Table 2).<sup>13,14</sup> Severity assessment was done by modified Hartwig and siegel ADR severity assessment scale labeled the reaction as mild - level 2 (Table 3).<sup>15</sup> Based on the scale and severity assessment it was concluded that "Doxycycline was the probable cause for the adverse drug reaction".

## CONCLUSION

FDE is definitely preventable by early identification, withdrawal and avoidance of offending drugs as well as their cross reactants. Clinicians should counsel the patient and create awareness about the adverse drug reaction. A drug allergy card should be given to patients and instructed to be shown to the doctor every time, while he is in need to take treatment. Thus, knowledge of drugs known to produce FDE is very much essential and should be taken into consideration before prescribing them to patients.

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## REFERENCES

1. Pai VV, Bhandari P, Kikkeri NN, Athanikar SB, Sori T. Fixed drug eruption to fluconazole: A case report and review of literature. Indian J Pharmacol. 2012;44:643-5.
2. Lee AY. Fixed Drug Eruptions: Incidence, recognition, and avoidance. Am J Clin Dermatol. 2000;1(5):277-85.
3. Podder I, Chandra S, Das A, Gharami RC. Doxycycline induced generalized bullous fixed drug eruption. Indian journal of dermatology. 2016 Jan;61(1):128.
4. Krahenbuhl-Melcher A, Schlienger R, Lampert M, Haschke M, Drewe J, Krahenbuhl S. Drug-related problems in hospitals: a review of the recent literature. Drug Saf. 2007;30(5):379-407.
5. Nitya S, Deepa K, Mangaiarkkarasi A, Karthikeyan K. Doxycycline induced generalized bullous fixed drug eruption - A case report. J Young Pharm. 2013;5(4):195-6.
6. Jain PS, Jain PA. Bullous, Fixed Drug Eruption to Ciprofloxacin: A case report. J Clin Diagn Res. 2013 Apr;7(4):744-5.
7. Das A, Sancheti K, Podder I, Das NK. Azithromycin induced bullous fixed drug eruption. Indian J Pharmacol. 2016;48:83-5.
8. Sehgal VN, Srivastava G. Fixed drug eruption (FDE). Changing scenario of incriminating drugs. Int J Dermatol. 2006;45:897-908.
9. Lim WK, Kim DH, Jin SY, Choi YS, Lee SH, Huh HJ, et al. A Case of Fixed Drug Eruption Due to Doxycycline and Erythromycin Present in Food. Allergy Asthma Immunol Res. 2013 Sep;5(5):337-9.
10. Pellicano R, Lomuto M, Ciavarella G, Di Giorgio G, Gasparini P. Fixed drug eruptions with feprazone are linked to HLA-B22. J Am Acad Dermatol. 1997;36:782-4.
11. Dewdney JM, Maes L, Raynaud JP, Blanc F, Scheid JP, Jackson T, et al. Risk assessment of antibiotic residues of beta-lactams and macrolides in food products with regard to their immuno-allergic potential. Food Chem Toxicol. 1991;29:477-83.
12. Lipowicz S, Sekula P, Ingen-Housz-Oro S, Liss Y, Sassolas B, Dunant A, et al. Prognosis of generalized bullous fixed drug eruption: Comparison with Stevens-Johnson syndrome and toxic epidermal necrolysis. Br J Dermatol. 2013;168:726-32.
13. 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(2):239-45.
14. Hartwig SC, Siegel J, Schneider PJ. Preventability and severity assessment in reporting adverse drug reactions. Am J Hosp Pharm. 1992;49:2229-32.
15. The Use of the WHO-UMC System for Standardised Case Causality Assessment. Available at: <http://www.who-umc.org/Graphics/24734.pdf>. Accessed on 2018 Aug 04.

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