



Paracetamol Induced Fixed Drug Eruption- A Relatively Rare Case Report

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Abstract

A 40 years old male patient reported with multiple ulcerative lesions over oral mucosa and glans penis since last 1 day. He has taken tablet Paracetamol 500mg twice daily for one day for the management of fever. On physical examination, multiple ulcerative lesions over oral mucosa and glans penis were observed. Patient was hospitalized, symptomatically treated and Paracetamol was withdrawn. Patient recovered.

Keywords: Paracetamol, Fixed drug eruption, Hypersensitivity reaction

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Introduction

Bourns in 1889, 1st described the fixed drug eruption and in the 1894, the term fixed drug eruption, or “*éruption érythémato-pigmentée fixe*” was 1st given by Brocq.^{1,2} Fixed drug eruption is a cutaneous adverse drug reaction. It starts with the onset of rash at a fixed location on the body each time whenever a specific medication is used and with each time of recurrence, some additional sites can be involved and size can increase.³

Fixed drug eruption (FDE) is defined as “a same-site recurrence with exposure to a particular medication”. Fixed drug eruption is not uncommon reaction and is associated with more than 100 drugs/medications. Fixed drug eruptions are divided into two categories namely localized and generalized. These may be bullous or non-bullous.⁴ Among these categories

localized fixed drug eruptions with self-limiting ability is the most common presentation. Fixed drug eruptions can be scattered, solitary or generalized. It can take for eruption as long as two weeks to appear after the causative drug exposure but in most of the situation’s eruptions develop within 48 hours of the exposure of the drug. Most of the patients feel local symptoms such as such as itching and/or burning in association with the eruption.^{5,6,7}

The main line of management of all types of fixed drug eruptions is removal of causative agents, patient counselling and symptomatic treatment after elucidation of thorough history of medication and other chemical exposures, and also the prior episodes. Causative agent can be confirmed by using oral re-challenge test but it is highly risky and not recommended now a

days as it cause severe exacerbation or possible generalization hence patch test is preferred instead of oral re-challenge test.⁴

If causative agent of fixed drug eruption is not removed then there are chances of recurrence which can progress to increased inflammation, hyperpigmentation, and there is also the risk of a potentially generalized bullous fixed drug eruption which can be lethal. This generalized fixed drug eruption may resemble Stevens-Johnson syndrome or toxic epidermal necrolysis.⁴ There are not many cases of Paracetamol induced fixed drug eruption have been reported in literature.^{8,9} We report a case of Paracetamol induced fixed drug eruption with multiple ulcerative lesions over oral mucosa and glance penis.

Case Report

A 40-year-old male patient weighing 50 kg reported in the OPD of Dr. Panjabrao Deshmukh Memorial Medical College and Hospital with multiple ulcerative lesions over oral mucosa and glance penis since last 1 day. He was taking over the counter tablet Paracetamol 500mg twice daily orally in the last one day for the management of fever as he was suffering from the fever since last one day. He did not report taking any other medication or herbal products or any other alternative medications. He doesn't have past history of similar reactions to Paracetamol or any other medications. He denied engaging in high risk sexual activities. He was suffering from diabetes mellitus and hypertension. On the physical examination, multiple ulcerative lesions over oral mucosa and glance penis were observed. There were multiple fissures on the lower lip with erosive white plaques on the tongue and buccal mucosa and on glance penis. There was no lymphatic enlargement. Patient was hospitalized and patch test was performed which was positive for Paracetamol. Paracetamol was withdrawn and patient was treated with oral Cetirizine 10mg twice daily. Patient was recovered after the withdrawal of the drug.

Discussion

Although Paracetamol was synthesized in 1878 by Morse but first used clinically by von Mering in 1887. Later it was not in common use until

it's rediscovery by Brodie and Axelrod in 1950s. Since 1970s it is widely and most commonly used analgesic and antipyretic drug.¹⁰ Paracetamol (Acetaminophen) is one of the most popular and widely used over the counter drug for the treatment of acute and chronic pain and fever. It is the safest drug with very low incidence of side effects. It has no anti-inflammatory and antirheumatic activities unlike other non-steroidal anti-inflammatory drugs which produces gastrointestinal side effects and have potential for cardiorenal effects. But evidences are strong against the chronic use of Paracetamol as it increases the chances of gastrointestinal bleeding and a small (~4 mmHg) increase in systolic blood pressure. These effects show a degree of dose dependence.¹¹ Overall its adverse reactions are very rare but severe.

Usually, toxic drug eruptions induced by paracetamol are rare and these are usually of the fixed pigmenting type. These cutaneous adverse reactions which are rare due to Paracetamol, vary from transient pruritis or maculopapular rash to Stevens-Johnson syndrome and even fatal toxic epidermal necrolysis.^{12,13} In all fixed drug eruption cases, share of Paracetamol induced fixed drug eruption is only 1.5% and less.^{14,15} The fixed drug eruptions by Paracetamol is mainly present as maculopapular rash, cellulites like reaction, bullous reaction, or pigmenting type.¹⁶ In our case, fixed drug eruption due to paracetamol shows multiple ulcerative lesions over oral mucosa and glance penis. The exact pathogenesis of fixed drug eruptions is not known. Although one hypothesis suggests that the causative drug work as hapten which preferentially binds to basal keratinocytes and thus releases lymphokines and antibodies hence damaging the basal cell layer.¹⁷ According to another hypothesis fixed drug eruptions are classified as a type IVc immunologic reaction because of latent cytotoxic T cells in the lesions, which may become reactivated. There are also possibilities of genetic predisposition as an association with HLA class I antigens is found in such type of reactions.¹⁸

Only few cases of Paracetamol induced drug eruption have been reported. One such case was reported by Wilson HT (1975) in which the patient taken a chlormezanone-paracetamol

combination and to this combination fixed drug eruption developed.¹⁹ M Nino in 2009 reported a fixed drug eruption case with Paracetamol in a 2-year-old girl with bullous fixed drug eruption.²⁰ In 2015, Swati V. Raipurkar reported Paracetamol induced fixed drug eruption in a 2-year male child with Paracetamol syrup. The child had multiple purplish-livid bullae over the fingers of both the hands and over the chest with erosions with crusting over his lips.²¹ Kimmatkaar et al in 2018 reported a case of Paracetamol induced fixed drug eruption in a 7 years old male patient in whom left upper eyelid was involved. There was eyelid erythema and edema causing mild ptosis along with a well-defined area of bluish-purple discoloration of the lateral upper eyelid skin.²²

In our case, the diagnosis of Paracetamol induced fixed drug eruption was made, as the sequence of events; intake of Paracetamol after febrile illness followed by drug eruptions and recovery after Paracetamol withdrawal strongly were in favor of Paracetamol induced fixed drug eruption. According to the Naranjo probability scale,²³ Paracetamol induced fixed drug eruption was probable. Patient was explained about the drug reaction and counselled not to use the drug in future to avoid fixed drug eruption by Paracetamol.

Conclusion

In conclusion, we report a case of paracetamol induced fixed drug eruption involving oral mucosa and glans penis. Paracetamol is over the counter drug also widely prescribed by physicians. Clinician must be aware and should suspect if such reaction occurs while using Paracetamol. Reaction should be well documented in the case record of the patient and patient should be properly advised to avoid the drug to prevent further adverse reactions.

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