Fixed drug eruption due to metronidazole: a case report

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ABSTRACT:

Introduction:

Metronidazole is commonly used for the treatment of amebiasis, giardiasis and trichomonous vaginitis. Its side effects are relatively frequent and unpleasant, but nonserious. It has the potential to cause fixed drug eruption (FDE).

Case Presentation:

This 10 year male boy presented for the itching in some part of the body including an itchy, erythematous oval lesion over the right side of the lower part of anterior abdominal wall. He developed these problems after intake of metronidazole tablet. He was diagnosed to be a case of FDE due to metronidazole. This case of adverse drug reaction (ADR) was “probable” type (Score=7) of reaction based on Naranjo ADR probability scale and severity assessment showed “mild” type (level 2) based on Hartwig et al scale. The offending drug was stopped immediately and managed with deflazacort tablet 12 mg for 10 days and Fusidic acid+Betamethasone cream for topical application.

Discussion:

FDE due to metronidazole usually occur within 30 min to 8 hours following its administration and mean length of time from drug intake to the onset of symptoms is approximately 2 hr. Tissue damage in FDE results from the preferential activation of intraepidermal CD8+T cells

Key words: metronidazole, fixed drug eruption

INTRODUCTION:

Fixed drug eruption (FDE) is common type of drug eruption seen in skin clinics and it represents a unique cutaneous drug reaction (CDR) pattern characterized by skin lesion(s) that recur at the same anatomic site(s) upon repeated exposures to an offending agent.[1] Importance of FDE lies in the fact that commonly prescribed drugs may cause such reactions. Metronidazole and other nitroimidazole-derivatives are frequently and most commonly prescribed drugs and are also used by many people as self medication in this part of the world. Standard literature suggests that the side effects of metronidazole are relatively frequent and unpleasant, but

mostly nonserious. Case reports of FDE due to metronidazole are increasingly available now, including one case report by us from our Institute published online in 2012. [2,3,4,5]

We are presenting here a case of FDE due to metronidazole.

CASE PRESENTATION:

A 10-year-old boy presented with a history of itching in some part of the body including an itchy, erythematous oval lesion over the right side of the lower part of anterior abdominal wall (figure 1). Parents of the boy gave the history of intake of metronidazole tablet for dysentery 1 day earlier which is evinced by the strip of consumed metronidazole tablet brought along and produced in clinic. They also gave the history of a similar eruptive lesion, particularly in the same site in the same location, after he was given the same drug obtained from the same counter for an episode of diarrhoea on an earlier occasion few months back. Unlike this occasion, the reaction at that time appeared after few days of intake of the same tablet. On that occasion, the boy was stopped from further intake of the drug and lesion subsided spontaneously. However, the itchy lesion on the particular area of the anterior abdominal wall left behind with a residual hyperpigmentation which flared up on this occasion.

Initially, the case was suspected to be either arthropod bite reaction or erythema multiforme. However, there was no history of insect bite. Moreover, the lesion was not target shaped, which is typical of erythema multiforme. Therefore, the case was diagnosed as FDE due to metronidazole considering the temporal association of the reaction and intake of said offending drug. Our diagnosis was supported by literature review and previous experience of FDE due to metronidazole.

Complete blood count only was done as laboratory investigation and all the parameter showed within normal limits.

The FDE was managed with deflazacort tablet 12 mg for 10 days and Fusidic acid+Betamethasone cream for topical application. Follow up after 7 days of treatment showed subsided lesion except the hyperpigmented area. Patient's parents were counselled to be cautious while taking metronidazole and related drugs in future.

Oral challenge test was not done as it is risky and patch test is not available in our Institute. Therefore, causal relation between the drug and the adverse drug reaction was assessed by using assessment Naranjo et al`s[6] alogarithm. We observed that the patient presented with FDE immediately after the oral administration of metronidazole (+2) and the reaction improved following discontinuation of the drug (+1). Patient had similar episode of reaction to the same drug before (+1). There were no alternative explanations for the reaction (+2) to be considered in terms of temporal association. Moreover, previous reports (+1) suggest that metronidazole has the potential to cause FDE. Overall, the reaction was categorized as `probable` reaction as per our assessment (score = 7) based on the Naranjo ADR probability scale. The severity assessment of this case as per Hartwig et al[7] scale showed mild (level 2) type of ADR.

DISCUSSION:

Available literatures suggest that FDE due to metronidazole usually occur within 30 min to 8 hours following its administration and mean length of time from drug intake to the onset of symptoms is approximately 2 hr.[4] In our case it occurred on the first day of drug intake.

The characteristic features of FDE are that it usually appears as a solitary or a small number of pruritic, well circumscribed, erythematous macules that evolve into oedematous plaques. [1] These lesions typically recur at exactly the same anatomic sites with each administration of causative drug, but upon the discontinuation resolve spontaneously, leaving hyperpigmentation. [2] Unless exposed to the offending drug, the lesions remain silent and typically present as gray-brown macules or plaques for prolonged periods. Although FDE can occur anywhere on the skin and mucous membrane, the most commonly affected sites are lips, soles, palms, face, hands, feet, groin areas; interestingly herpes simplex virus (HSV) is frequently reactivated in these areas of healthy individuals.[8] The lesions, in some cases may become more widespread with bullous lesions[4] and systemic manifestations, such as high fever and arthralgia, mimicking Stevens–Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN). For these cases, new lesions in the previously uninvolved areas may also occur unless the causative drug is withdrawn.

FDE lesions initially appear when susceptible patients are sensitized to a particular drug; such sensitization occurs more rapidly in patients receiving the causative drug intermittently rather than those patients continuously receiving the drug. The period required for sensitization is highly variable depending on the patients, ranging from a few weeks to several years. [9]

The exact pathogenesis of FDE is yet to be well understood; yet it is now accepted that they occur as a result of an immunologically mediated inflammatory response. Recent literatures suggest that the tissue damage in FDE results from the preferential activation of intraepidermal CD8+T cells to directly kill surrounding keratinocytes and release large amounts of cytokines such as INFα into the local environment.[8]

The diagnosis of FDE is primarily based on the patient's history and clinical picture. In some cases an oral challenge may be done, but oral provocation carries a risk of generalized serious drug reactions. Patch testing has been utilized as an alternative to oral testing, but only positive tests are helpful. [5,8]

CONCLUSION:

Metronidazole is a commonly used drug in the management of amoebiasis, giardiasis, trichomonas vaginitis and anerobic bacterial infections. It is one of the most commonly used drugs in India due to wide prevalence of amoebiasis. Moreover, various combination preparations with other antimicrobials are readily available in Indian market and rampantly used by people. It is widely accepted now that it has the potential to cause FDE including bullous lesions. Patients should be discouraged from self medication and alerted to notify their physicians of all drug allergies they have experienced. Clinicians and Pharmacists should also be alerted that the most commonly used medication like metronidazole has proved their potential to cause FDE. However, more information is required to understand the exact pathomechanism of inflammatory skin diseases particularly in the context of the intraepidermal CD8+T cells as they may represent double edged swords of the skin immune system with protective and destructive capacity.

COMPETING INTEREST:

None

PATIENT CONSENT:

Obtained

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