Scholars Journal of Applied Medical Sciences (SJAMS) **ISSN 2320-6691 (Online)**
Sch. J. App. Med. Sci., 2016; 4(4B):1183-1186 **ISSN 2347-954X (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublishers.com DOI: 10.36347/sjams.2016.v04i04.017

Case Report

Fixed Drug Eruption Due to Ornidazole- A Case Report

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Abstract: Fixed Drug Eruption (FDE) is classified as cutaneous drug reaction which recurs in the same locations upon systemic administration of the same drug. Vesicles and bullae may sometimes be found, and in some cases even these are confused with Stevens Johnson Syndrome (SJS) or Toxic Epidermal Necrolysis (TEN). A male patient, 62 years old, developed FDE with the use of ornidazole. On physical examination the lesions developed blisters and violaceous patches all over the body. On further enquiry he had developed similar four episodes earlier. The patient's lesions improved after discontinuation of ornidazole and with proper supportive therapy, steroids and antihistaminic. On drug rechallenge test, ornidazole was found to be causing FDE. He was advised to avoid ornidazole in future.
Keywords: Fixed drug eruption, ornidazole, Naranjo ADR probability scale

INTRODUCTION

Fixed drug eruption (FDE) symbolizes the most common cutaneous adverse drug reaction in Indian patients [1]. It is a unique drug induced reaction pattern distinguished by recurrence of eruption at the same location of the skin or mucous membrane with repeated systemic administration of the drug. It was first depicted by Bourns and soon after by Brocq [2]. It is accountable for about 10% of all adverse drug reactions. Drugs causing frequent fixed drug eruptions are fluconazole, ciprofloxacin, doxycycline, clarithromycin, NSAIDs, Trimethoprim, cotrimoxazole, phenytoin etc [3]. Among anti-protozoal drugs, metronidazole and tinidazole have been reported along with cross-sensitivity to each other to cause FDE [4]. Less number of cases is reported with ornidazole. Ornidazole is considered as antibacterial and antiprotozoal. It is converted into an active form by reduction of its nitro group, this binds to DNA and prevent nucleic acid formation; it is a bacteriostatic [5]. Mostly, the skin lesion is a dusky erythematous macule and is typically found on the extremities, lips, genitalia and perianal areas, even though any skin or mucosal surface may be involved. The skin lesions may present with a burning sensation which can be in multiple numbers or progress to the development of central vesicles and bullae, particularly after the repeated use of an agent [6].

CASE REPORT

We report a case of fixed drug eruption due to ornidazole in a male patient aged 62 years old admitted in the Dermatology department at Silchar Medical College and Hospital, Assam. We have taken the case as less number of cases of FDE is reported with Ornidazole. On 5th June 2015, after ingesting Tab. O2 (ofloxacin & ornidazole) prescribed for diarrhoea, the patient developed skin lesions within 2 hours, at first involving the trunk and the upper limbs, followed by lower limbs, oral mucosa and the genital region. There was no history of insect bite or other drug consumption. At first there was itching in the involved area. They soon started to turn red and developed blisters. Multiple hyper pigmented to violaceous patches and plaques developed with few having scaling. The lesions were circular, deeply erythematous plaques which occasionally developed central bullae (Fig 1). The lesions were multiple which ranged from 3cm×4cm to 5×6cm and were associated with burning and itching (Fig 2).The lesions were even witnessed in the genital area and oral mucosa (Fig 3 & Fig 4). The erythematous disseminated violaceous patches suddenly appeared on the next day over the penis soon after the emergence of lesions over the hands and the feet.

On further enquiry, the patient reported that he had experienced four such episodes of skin lesions previously at the similar sites following ingestion of medication. The first episode of skin reaction occurred

in June 2013. Such similar episodes were accounted in the month of September in 2014 followed by similar skin lesion in January and March in 2015. The skin reaction in the year 2014 and 2015 happened after taking antibiotics for diarrhoea. He failed to recall the drugs taken in 2013. This present episode of skin lesions in June 2015 was much more severe than the previous episodes.

The patient was admitted and was advised to stop the O2 tab immediately. Patient was in treatment for five days with supportive therapy with intravenous fluids. Treatment was symptomatic. Systemic antihistamines and topical corticosteroids were administered. It resulted in complete resolution of all lesions leaving residual hyper pigmentation of the involved skin sites. He was advised to come after fifteen days for drug re-challenge test.

On his next visit after 15 days, drug re-challenge test was performed with ofloxacin and ornidazole separately. On drug re-challenge, only ornidazole was found out to be causing these fixed skin eruptions. Naranjo causality assessment suggests that the drug reaction due to ornidazole was definite (Score-10). The patient was advised to avoid ornidazole in the future.

Table I: Naranjo ADR probability scale

Questionnaire	Yes	No do not know
Are there previous conclusive reports on this reaction?	+1	0
Did the adverse event appear after the suspected drug was given?	+2	-1
Did the adverse reaction improve when the drug was discontinued? or a specific antagonist was given?	+1	0
Did the adverse reaction appear when the drug was read ministered?	+2	-1
Are there alternative causes that could on their own have caused? the reaction?	-1	+2
Did the reaction reappear when a placebo was given?	-1	+1
Was the drug detected in any body fluid in toxic concentrations?	+1	0
Was the reaction more severe when the dose was increased or less? Severe when the dose was decreased?	+1	0
Did the patient have a similar reaction to the same or similar drugs? In any previous exposure?	+1	0
Was the adverse event confirmed by any objective evidence?	+1	0

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

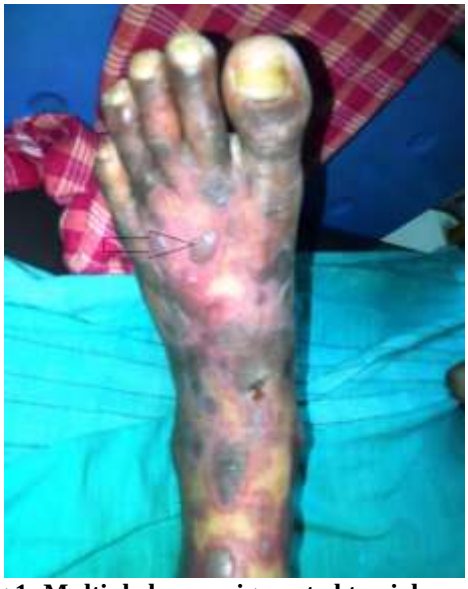

Fig 1: Multiple hyper pigmented to violaceous patches with central bullae

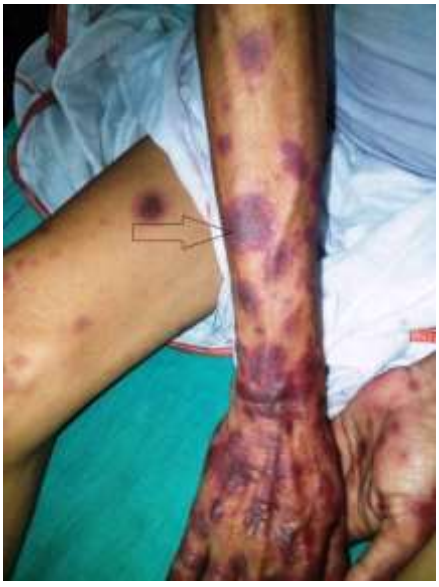

Fig 2: Recurrent hyper pigmented patches over the forearm and the lower limbs

Fig 3 Healed penile lesion

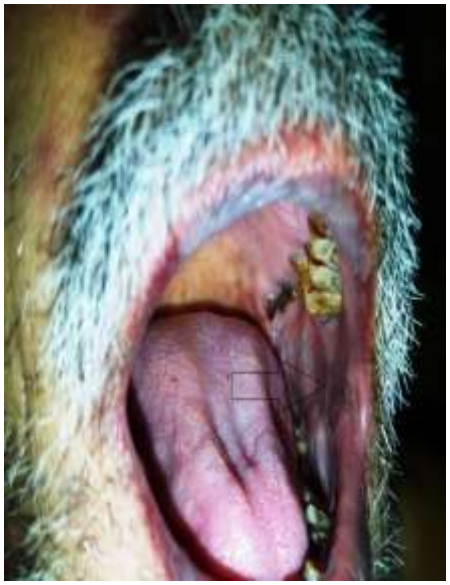

Fig 4: Oral mucous plaques

DISCUSSION

The incidence of FDE worldwide varies from time to time and place to place; entirely depending on the use of the drugs by that particular population [7]. The most definite trait of FDE is reactivation of the inflammatory process in the previously involved site (s) with each subsequent exposure. The characteristic morphology of FDE lesion is dusky red painful patches that leave long-lasting or permanent deep post inflammatory hyper pigmentation [8]. The exact pathogenesis of FDE is unidentified, although antibodies, antibody dependent cell mediated cytotoxicity and serum factors have been accounted. Intra epidermal clusters of differentiated CD8-positive T cells at the FDE lesion site contribute to localized tissue damage. Resting T cells are not cytolytic, but upon activation, they kill the surrounding keratinocytes and release cytokines such as Interferon gamma. Additional CD8-positive T cells as well as CD4-positive T cells with neutrophils are drafted to the lesion, resulting in tissue damage [9]. FDE is generally solitary in the early assault, but with each subsequent exposure, the number of involved sites may increase and preexisting sites may enlarge in size. The lesion builds up within 30 minutes to 8 hours of taking a drug [10]. In the present case, the lesions started building up within 2 hours after intake of ornidazole. With the crowding of new medications and preservatives inside medications, physicians are seeing both typical and unusual presentations of FDEs often imitating dermatologic entities such as erythema multiforme, SJS, TEN, cellulitis, paronychia, and bullous pemphigoid [11]. To confirm the diagnosis of FDE different skin tests including patch, prick and oral challenge test with suspected are done. However, the identification usually relies on typical clinical manifestation of lesion(s), the path of recurrent attacks preceded by the use of same drug [12]. Our case was confirmed with drug rechallenge test after fifteen days of the episode of FDE. Repeated attacks of FDE would always result in pigmentation. Almost all the patients with recurrent FDE had residual pigmentation. Almost all the patients with recurrent FDE had residual pigmentation. The main goal of treatment is to identify the causative agent and avoid it; if not the treatment for FDE would be symptomatic. Systemic antihistamines and topical corticosteroids therapy is satisfactory. The clinician should consider discontinuing all but the essential drugs required for the patient care. The patients may possibly be prescribed with the medications with the same pharmacological effects but with different chemical structures from those of drugs in problem [13]. In the present case, the patient had residual hyper pigmentation. He was advised to avoid ornidazole in future. This case highlights the fact that not only the dermatologists but also the physicians must take precautions while prescribing medication with proper drug history.

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