

Fixed drug eruption in male genitalia: A cross-sectional study from Iran

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Background: Fixed drug eruption (FDE) is an uncommon adverse reaction to medications. Mucosal areas, particularly the male genitalia, are favored sites. To our knowledge, no study has investigated the causative agent(s) in FDE occurring on male genitals of Iranian patients. So, we conducted a study to determine the most common agents and areas of involvement in fixed genital drug eruption of male patients.

Methods: Diagnosis of FDE was supported by a positive history and physical examination. Data including age, site of lesions, time interval between drug administration and FDE development was collected and analyzed.

Results: The age range of the 36 male patients was 17 to 60 years with a mean age \pm standard deviation of 36.1 ± 10.9 years. The most common causative drug was co-trimoxazole in 33 patients (91.7%). In the genital area, the most frequent involved site was the glans penis in 22 patients (61.1%), followed by the penis shaft in 11 patients (30.6%) and the scrotum in 2 patients (5.6%).

Conclusion: The most common causative drug is co-trimoxazole and the most common site is the glans penis.

Keywords: fixed drug eruption, drug reaction, male, genitalia

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INTRIDUCTION

Fixed drug eruption (FDE) is an uncommon adverse reaction to medications, presenting as oval, erythematous macules in the same site or sites each time the responsible drug is administered^{1,2}. Mucosal areas, particularly male genitals, are favored sites¹. It seems that the incidence of FDE depends on the frequency of the administration of medications in a given part of the world³.

To our knowledge, there is no study investigating the causative agent(s) in FDE occurring on male genitals of Iranian patients. So, we conducted a study to determine the most common agents and areas of involvement in fixed genital drug eruption.

PARTICIPANTS AND METHODS

This cross-sectional study was conducted on male patients referring to the Dermatology Clinic of Ghaem Hospital, Mashhad, Iran from December 2005 to December 2010. A diagnosis of FDE was supported by a positive history and physical examination. Inclusion criteria were a compatible history and typical clinical lesions on the male genital area. The exclusion criterion was the lack of a reliable history of drug consumption. Thirty-six male patients were diagnosed with FDE on the genital area. Sexually transmitted diseases were ruled out by clinical examination and relevant laboratory tests. Data, including age,

site of lesion(s), and time interval between drug administration and FDE development were collected and analyzed using SPSS (SPSS Inc., Chicago, IL, USA) version 11.5. The Ethics Committee of Mashhad University approved the study, and all patients signed informed consent before entering the study.

RESULTS

The age range of the patients was 17 to 60 years with a mean age \pm standard deviation of 36.1 ± 10.9 years. The time interval between drug exposure and the development of genital FDE ranged from 1 day to 7 days with an average of 2.85 ± 2.1 days. Eleven patients (30.6%) had a history of the same lesions in the past.

Eighteen patients (50%) had erythema in the genital area and 18 patients (50%) had erythema and erosion in the genital area. The most common causative drug was co-trimoxazole in 33 patients (91.7%), followed by aspirin, norfloxacin, and erythromycin, each used by 1 patient (2.8%).

In the genital area, the most frequent involved site was the glans penis in 22 patients (61.1%), followed by the penis shaft in 11 patients (30.6%) and the scrotum in 2 patients (5.6%). One patient (2.8%) had lesions on the penis shaft and scrotum at the same time.

Considering the involvement of other skin areas together with genital lesions, 27 patients (75%) had no lesions elsewhere, 5 patients (13.9%) had lesions on the upper extremity, 2 patients (5.6%) had lesions on the lower extremity, and one patient (2.8%) had lesions on the lip at the same time.

DISCUSSION

FDE, first described by Bourns in 1889, is a distinctive drug-induced dermatosis characterized mainly by sharply marginated, round or oval itchy plaques of erythema and edema becoming dusky violaceous or brown, and sometimes vesicular or bullous¹⁻³. Lesions recur at the same sites of the skin or mucous membrane upon repeated uptake of the causative agent¹⁻³. In our study, 18 patients (50%) had erythema and 18 patients (50%) had erythema and erosion, which shows that the most common signs of FDE in our region are erythema and erosion.

Histopathology of FDE in its classical form reveals a lichenoid or erythema multiform-like changes. FDE is believed to be a type IV immune reaction, mediated by CD8 lymphocytes, wherein the offending drug may induce local reactivation of memory T cell lymphocytes localized in the epidermal and dermal tissues and targeted initially by the viral infection^{1,2,4}. Since it is more common in some parts of the world, such as India, a genetic predisposition might play a role^{5,6}.

Our patients were mostly in the age group 20-30 years, which shows that FDE is mainly a disease of young and middle aged adults.

The mystery of site preference in FDE is still not resolved. The most common sites are the genitalia in males and the extremities in females^{6,7}. Considering the site of genital involvement, the glans penis was the most frequent site of involvement in our study, and FDE lesions were mostly solitary.

According to several studies, the most common medications causing FDE are antibiotics (trimethoprim-sulfamethoxazole, tetracycline, penicillin, and erythromycin), followed by non-steroid anti-inflammatory drugs (NSAIDs; diclofenac sodium, aspirin, naproxen, and ibuprofen)^{1,8,9}. The findings of this study showed that the major causative drug for FDE of the male genitalia was co-trimoxazole which is in concordance with the findings of other studies^{10,11}. However, two studies from India implicated tetracycline and nimesulide as the most common culprit in genital FDE, respectively^{12,13}. Other medications more commonly associated with FDE of the penis include tetracyclines, acetaminophen, and laxatives containing phenolphthalein¹⁴. Isolated involvement of the glans penis in 16 patients was mostly due to co-trimoxazole in one series¹¹. Some studies have suggested a significant relationship between specific medications and the clinical pattern and anatomic distribution of the lesions in FDE, such as tetracycline involving only the male genitalia, while co-trimoxazole affecting genitals in addition to other anatomic areas^{15,16}, but a generally significant relationship has not been established^{17,18}. A case of unilateral non-pigmenting FDE in both the genital and extra genital areas has been reported due to co-trimoxazole¹⁹.

There are no definitive laboratory tests to confirm a diagnosis of FDE. Oral provocation with the suspected agent is the only reliable method in

most cases¹. Consequently, the key to managing fixed drug eruptions of the penis is a thorough history with particular note of medications used intermittently, while excluding other conditions, as well.

Eleven patients (30.6%) had a history of same lesions in the past, which could be due to the ignorance of the patients or/ and the physicians who were unable to attribute FDE to the medication. It shows how significant it is for dermatologists to be familiar with the disease and its recurrent nature after rechallenge with the offending drug.

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