Original Article

A Study on Genital Fixed Drug Eruption in a Tertiary Care Hospital

Dermatology Section

SANJAY KUMAR KANODIA, AMOOLYA K. SETH, SHAILJA RATAN SHUKLA

ABSTRACT

Background: Genital fixed drug eruption (FDE) present as single oval lesion, most commonly over glans penis and are many times wrongly diagnosed and treated as sexually transmitted diseases.

Objectives: The aim of this study was to present a series of cases of genital lesions with fixed drug eruptions, diagnose the suspected drug and identify the change in pattern of drugs causing them.

Methods and Material: Patients with the genital FDE were interviewed for onset and duration the disease with history of all drugs taken and a list of suspected drugs was made for each patient. Rechallenge test (oral provocation test) was done for the suspected drug with a quarter of a single therapeutic dose, followed if necessary, by a step-wise increase to one half, one full and double of a dose for subsequent days. A definite erythema at or around the existing lesion was considered as positive provocation test.

Results: Thirty eight cases (35 males and 3 females) were enrolled in the study with clinical diagnosis of FDE. The lesions were most commonly present on the glans penis (68.42%) as hyperpigmented macule (47.36%) accompanied with pruritus (71.05%), burning (55.26%) and pain sensation (28.94%). Oral rechallenge test showed positive result in 29 cases with nimesulide (35.29%) as the most common offending drug followed by fluconazole (25.52%) and tetracycline (14.70%).

Conclusion: The study emphasizes the changing trend of genital FDE and the importance of oral provocation test for diagnosing genital fixed drug eruptions. The findings in this study is in contrast to the previous studies which showed antimicrobials (tetracyclines) as the commonest cause of genital FDE's.

Key Words: Fixed drug eruptions(FDE), Genital lesions, Oral rechallenge test (oral provocation test), Nimesulide

KEY MESSAGE

- With the changing trend, time and availability, nimesulide is emerging as common cause of genital FDEs.

INTRODUCTION

Genital lesions of any kind are a cause of confusion to the dermatologists, because of their varying possible causes. Genital fixed drug eruption (FDE) in particular, is the cause for apprehension in the sufferer. These appear as oval, erythematous macules and recur at the same areas following every administration of the responsible drug [1].The patients are often unaware of the nature of the drugs which are consumed by them and do not relate their complaints to the use of the drugs.

The incidence of FDE induced by a specific drug depends on the frequency of the agent which is used in a given part of the world [2]. Although a large number of drugs have been incriminated to cause FDE, certain drugs have been found to be responsible more often. The aim of this study was to identify the agents which commonly caused genital FDE in the patients of a tertiary care hospital in the post millennium era.

MATERIAL AND METHODS

This study was done from February 2009 to March 2011 after obtaining ethical approval from the institution where it was done. Patients with the clinical diagnosis of genital FDE were enrolled and interrogated regarding the onset and the duration of the disease. They were also asked about the history of all the drugs which they had taken. A list of suspected drugs was made for each patient on the basis of their detailed history. Systemic examination and routine blood examination along with liver and renal function tests were done for each patient. Sexually transmitted diseases were ruled out by the clinical examination and the relevant laboratory tests.

The rechallenge test (oral provocation test) was done for the suspected drug after taking a written consent from the patients. It was started with a quarter of a single therapeutic dose, followed if necessary, by a step-wise increase to one half, one full and double of a dose for subsequent days. A definite erythema at or around the existing lesion indicated a positive provocation test. The drugs which were used for the provocation test included nimesulide, ampicillin, teracycline, fluconazole, cotrimoxazole and aspirin as per the history of the suspected drugs for FDE. The rechallenge was considered to be negative if exacerbation of the lesion was not seen within 24 hours, even after the administration of the double dose. Biopsies were not done at the genital site in any of the cases because of ethical and medical reasons.

RESULTS

A total of thirty eight patients (35 males and 3females) with genital FDE, in the age group of 13 to 56 years (mean age = 27.5 years), visited the dermatology outpatients department. The duration of the lesions varied from 2 days to 3 years. A maximum number of patients had lesions on the glans penis (68.42%). Hyperpigmented macular lesions were present in 18 patients (60.52%). The most common symptoms which were presented by most of the patients were pruritus (71.05%), followed by a burning sensation (55.26%).

Out of the 38 cases, the rechallenge test was positive in 34 patients with various doses of drugs as shown in Table 2. The onset of the lesion was noticed as early as 3 hours to a maximum of 23 hours (mean=8.5hours) after the administration of the drug. Nimesulide was the most common offending agent, affecting 12 patients (35.29%), followed by fluconazole in 8(25.52%) and tetracycline in 5 patients (14.70%). The test was positive for half the drug dose in 18 cases, followed by positivity for a full dose in 9 and positivity for a 1/4th dose of the drug in 6 cases. We considered the drug to be responsible for FDE only, in cases where the rechallenge test was positive. The blood and systemic examination showed no abnormality in all the patients, except for one case where the liver function test results were marginally high [Table/Fig-1 & 2].

Characteristics	Site and type of lesion	Number
Site of genital lesions	Glans	26 (68.42%)
	Prepuce	3 (7.89%)
	Coronal sulcus	1 (2.63%)
	Penile shaft	1 (2.63%)
	Scrotum	1 (2.63%)
	Vagina	1 (2.63%)
	Vulva	2 (5.26%)
Extra genital lesion	Oral mucosa	4 (10.52%)
	Cutaneous	8 (21.05%)
Type of lesion	Hyperpigmented Macule	18 (47.36%)
	Erythematous Macule	9 (23.68%)
	Erosive	6 (15.78%)
	Maculoerosive	3 (7.89%)
	Bullous	2 (5.26%)
Associated symptoms	Pruritus	27 (71.05%)
	Burning sensation	21 (55.26%)
	Pain	11 (28.94%)
	Burning micturition	3 (7.89%)

[Table/Fig-1]: Characteristic features in patients with fixed drug eruptions

DISCUSSION

The observations of the present study implicated nimesulide as the most common agent which caused genital FDE, which differed from the findings of other studies. In earlier studies, antimicrobials were the most commonly implicated drugs for FDE, with tetracycline on the top of the list in the three series [2-5]. In studies on genital FDE in the premillenium era, tetracycline was the widely used drug. In the context of NSAIDs also, acetyl salicylic acid and phenylbutazone were found to be the most common offending agents in these studies.

Nimesulide is a nonsteroidal, anti-inflammatory agent with anti-pyretic and analgesic properties, which is commonly prescribed in India [6].The dermatological side effects which were previously reported with respect to its use were pruritus, urticaria, purpura, maculopapular rash and localized toxic pustuloderma [7, 8].There are only a limited number of studies on FDE which are the secondary effects of nimesulide [9,10]. To the best of our knowledge, there is no previously reported study which has expressed nimesulide as the common cause of genital FDE.

With the changing times, the trend of drug use also changes. The increasing use of nimesulide and fluconazole, with the over- the-counter availability of these drugs in the Indian market, could be one of the reasons for the increased reporting of their adverse effects. The under reporting of the side effects of nimesulide in the western literature may be possibly due to its non-availability in these countries.

This study also emphasizes the importance of the rechallenge test (oral provocation test) for pin pointing the diagnosis of fixed drug eruptions, specifically so in genital cases where a biopsy is not possible due to the chances of scarring and for ethical reasons. The provocation testing is both safe and reliable and it must be done to confirm the cause of the fixed drug eruptions [11]. The administration of graded doses is a rational approach so as to elicit the signs of reactivation at the minimum dose [12].

It is interesting to note that in our study, only three females reported with genital FDE, who were referred by gynaecologists for ruling out venereal diseases. This can be explained on the basis of the stigma and embarrassment due to genital problems in females, because of which they probably do not report to dermatology outdoors.

As FDE are sometimes confused with multiple venereal diseases, it is of utmost importance for all the medical specialists to study the entity of and to identify genital FDE clinically and by doing the provocation test so that these cases are not missed.

Suspected Drugs	Positive Rechallenge test				Total (n = 34)*
	¼ Drug dose	½ Drug dose	1 Drug dose	Double Drug dose	
Nimesulide	2	6	4	–	12 (35.29%)
Fluconazole	2	4	2	–	8 (25.52%)
Tetracycline	1	3	1	–	5 (14.70%)
Acetyl salicylic acid	–	3	1	–	4 (11.76%)
Cotrimoxazole	1	2	–	–	3 (8.82%)
Ampicillin	–	–	1	1	2 (5.88%)
Total	6	18	9	1	34

[Table/Fig-2]: Results of Rechallenge test with suspected drugs in patients with fixed drug eruptions
*Out of total 38 cases, 34 cases showed positive result and 4 cases negative result to rechallenge test.

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AUTHOR(S):

1. Dr. Sanjay Kumar Kanodia
2. Dr. Amoolya K. Seth
3. Dr. Shailja Ratan Shukla

PARTICULARS OF CONTRIBUTORS:

1. Asst.Professor, Department of Dermatology, Venereology and Leprosy, National Institute of Medical Science & Research, Nims University, Jaipur-303121.
2. Associate Professor, Department of Psychiatry, National Institute of Medical Science & Research, Nims University, Jaipur-303121.
3. Professor & Head, Department of Dermatology, Venereology and Leprosy, National Institute of Medical Science & Research, Nims University, Jaipur-303121.

NAME, ADDRESS, TELEPHONE, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Sanjay Kumar Kanodia
C-90, Sethi Colony, Jaipur-302004
Phone numbers-09928977411
Facsimile numbers 01412607053
E-mail: drskin2@gmail.com

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