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Case Report

Multiple fixed drug eruptions

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ABSTRACT

Fixed drug eruptions (FDE) are a type of hypersensitivity reaction that occurs in response to certain medications, typically reappearing at the same site when the causative drug is reintroduced. These lesions may present as itchy, red patches, and, less commonly, painful hyperpigmented macules. FDE accounts for a small percentage of all drug reactions and can occur alongside other drug-induced conditions. This case report discusses a 25-year-old female with a history of FDE following the use of norfloxacin and tinidazole for burning micturition and abdominal pain. The patient exhibited well-defined erythematous patches, some associated with previous drug reactions. Discontinuation of the offending drugs and appropriate treatment led to the resolution of her FDE without the appearance of new lesions. Such cases emphasize the importance of early diagnosis and management of FDE in patients with a history of drug-induced skin reactions.

Keywords: FDE, Hypersensitivity reaction, Erythematous, Norfloxacin, Tinidazole

INTRODUCTION

Fixed drug eruptions (FDEs) are skin reactions linked to the administration of specific medications. These eruptions typically present as oval-shaped, red patches but may vary in appearance depending on the different forms of the condition. FDEs can develop on various body parts, including the face, tongue, hands, feet, torso, limbs, and genital areas. They often reappear at the same site as earlier reactions, so a history of lesions recurring in the same location should raise suspicion of FDE.[1] FDEs are a relatively rare condition, accounting for approximately 0.003% of all skin reactions in a U.S. study involving 2.7 million participants.[2] The precise mechanism behind FDE remains unclear, though antibodies, serum factors, and cell-mediated immune responses are thought to be involved. Antibody-dependent cell-mediated cytotoxicity is also believed to contribute to the development of the condition.[3] The key aspect in diagnosing FDE is the recurrence of lesions following the use of the triggering drug. The definitive diagnostic test is an oral challenge test, but obtaining patient consent can be challenging due to concerns about worsening symptoms. As a result, FDE should be the top differential diagnosis in patients with a history of repeated similar eruptions after taking a specific medication. The primary treatment involves promptly discontinuing the offending drug, followed by the administration of antihistamines and corticosteroids.[4]

This case highlights a typically fixed drug eruption induced by the combined use of norfloxacin and tinidazole.

CASE REPORT

A 25-year-old female patient presented with complaints of a painful, erythematous rash for the past three days. Her menstrual history revealed amenorrhea for the past two months. The patient reported a history of taking tablets Norfloxocin-Tinidazole, Mefenamic Acid, and Dicyclomine Hydrochloride for complaints of burning micturition and abdominal pain. She has a history of similar complaints at the age of 8 years after taking an

injection of penicillin, as well as 6 and 3 years ago, which were associated with blister formation after taking medications. Additionally, she mentioned developing hyperpigmented dusky erythematous macules on her thigh 4 years ago upon taking Ibuprofen for shoulder pain.

On examination, the patient was moderately nourished. There were no signs of anemia, cyanosis, or jaundice. Cutaneous examination revealed well-defined erythematous to bluish-grey pigmented patches surrounded by erythema and tenderness, located on both buttocks, the front of the abdomen, the trunk, and both breasts. The palms and soles were normal. Hyperpigmented dry patches were observed on both lips, along with erythema of the mucosa. Erythema and erosions were seen over the labia majora.

The offending drugs were discontinued immediately upon admission. The patient was administered injection Pheniramine Maleate at a dose of 2 mL intramuscularly twice daily for three days, followed by 2 mL intramuscularly once daily for one day, and subsequently 1 mL intramuscularly once daily for one day. Additionally, she was prescribed tablet Pheniramine Maleate 25 mg three times daily, tablet Ranitidine 150 mg twice daily, and tablet Paracetamol 500 mg twice daily. Glycerine was prescribed for topical application on the lips, and liquid paraffin for external application. Upon discharge, the patient showed no signs of new lesion development. The existing patches demonstrated reduced erythema and dryness, accompanied by a decrease in pain and itching. She was reassured and advised not to use a similar combination of drugs in the future and to avoid the following medications, as they are likely to trigger similar reactions: norfloxacin-tinidazole, penicillin, sulfa drugs, NSAIDs, ciprofloxacin, sparfloxacin, tetracycline.

DISCUSSION

FDEs are a specific type of drug reaction characterized by pruritic, well-defined, round or oval-shaped erythematous macules or edematous plaques that typically recur at the same locations upon re-exposure to the offending medication. These lesions usually heal independently, often leaving behind areas of hyperpigmentation.[5] Over 100 drugs have been linked to FDE, with some of the most frequently implicated being trimethoprim-sulfamethoxazole (and other sulphonamides), naproxen, ibuprofen, tetracyclines, other antibiotics (such as ampicillin and metronidazole), and barbiturates.[1] The number of diagnosed FDE cases is rising, partly due to greater awareness among physicians and the increased use of medications. FDE can affect individuals of all ages and both sexes, including infants and the elderly. However, most cases are observed in individuals aged 20-40 years.[6] The clinical presentation of FDE varies among individuals. The lesions may heal with or without residual pigmentation.[4] Norfloxacin is especially effective in treating urinary tract infections. While cutaneous side effects are rare, occurring in less than 1% of patients, they can include urticaria, rash, and pruritus. Quinolones, including norfloxacin, can trigger both IgE-mediated hypersensitivity reactions and delayed hypersensitivity reactions, such as FDE.[3] Tinidazole, a 5-nitroimidazole derivative, treats bacterial and protozoal infections. The mechanism of action of Tinidazole involves generating free radicals that cause damage to the pathogens. Tinidazole is metabolized into metronidazole, where the nitro group reacts with parasite ferredoxin to produce free radicals that kill the organism. Side effects of tinidazole can include nausea, vomiting, headache, fatigue, and a disulfiram-like reaction. There are only a few case reports documenting FDE associated with tinidazole.[4] FDE lesions arise when a sensitized individual reacts to a specific drug, with sensitization developing slowly in those who use the drug intermittently. These lesions feature intra-epidermal CD8+ T cells with an effector memory phenotype. Activated CD8+ T cells cause damage to basal keratinocytes and release cytokines, maintaining a delayed type IV hypersensitivity reaction at previous lesion sites. Repeated exposure increases skin hyperpigmentation, and drugs of the same class may cross-react with memory cells, causing similar lesions. The drug acts as a hapten, binding to basal keratinocytes and triggering hypersensitivity reactions.[7] Discontinuing the offending drug typically relieves the lesions. In rare cases, antihistamines and topical corticosteroids may be required for more severe conditions. While it is generally understood that FDEs arise due to "molecular mimicry," the reason why they consistently recur at the same site remains unclear.[8]

In this patient, the temporal relationship between the drug and the reaction, along with a positive de-challenge, confirms the classification of this as a certain type of adverse drug reaction according to Naranjo's scale.

CONCLUSION

FDE are a specific and increasing type of hypersensitivity reaction that may cause discomfort and lead to complications if not treated properly. This case gives us the importance of early recognition of the problem from a patient's history and examination with instant withdrawal of that causative drug. The satisfactory treatment outcome as well as no appearance of new lesions points out to the success of early cessation of the causative drug and the subsequent supportive measures. On the other hand, she was counselled to avoid certain drugs that could trigger new episodes in the future, thus highlighting the role of education in the management of recurrent FDEs.

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