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Case Report

Eruptions in focus: cefadroxil and the uncommon realm of fixed-drug reactions: a case report

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ABSTRACT

This case report explores a rare case of localized fixed-drug eruption (FDE) induced by cefadroxil, a first-generation cephalosporin. FDE, characterized by recurrent lichenoid lesions at specific sites upon drug exposure, is an immunological cutaneous adverse reaction. The incidence of FDE due to cephalosporins is infrequently reported, making this case noteworthy. We present a 51-year-old male who developed brownish-black patches and painful blisters on his extremities after initiating treatment with Cefadroxil for a minor toe injury. The patient's symptoms, clinical course, and subsequent recovery are detailed. Treatment involved corticosteroids, antibiotics, and topical agents. The report also provides immunological insights into FDE pathogenesis, involving CD8+ memory T cells, cytokine production, and the role of CD4+ regulatory T cells. While the exact pathogenesis of FDE remains elusive, this report sheds light on the mechanisms contributing to the self-limited nature of these eruptions. Causality assessment using the Naranjo algorithm categorized the association between cefadroxil and FDE as probable. This case report contributes to the limited literature on FDE caused by cephalosporins and underscores the importance of recognizing and managing such dermatological reactions. The broader implications of understanding FDE pathogenesis and the rarity of cephalosporin-induced cases provides valuable insights for clinicians and researchers.

Keywords: Cefadroxil, Immunological cutaneous adverse reaction, CD8+ memory T cells, Cytokine production, CD4+ regulatory T cells, Naranjo algorithm, Pharmacovigilance

INTRODUCTION

A fixed-drug eruption (FDE) is an immunological cutaneous adverse reaction characterized by sharply defined lichenoid lesion/s which occur/s at the same location every time there is exposure to the causative substance.[1] There are over 100 drugs associated with FDEs, but some of the most commonly implicated drugs include trimethoprim-sulfamethoxazole (and other sulphonamides), naproxen, ibuprofen, tetracyclines, antibiotics (ampicillin, metronidazole), and barbiturates. They are often underdiagnosed or mistaken for insect bites, urticaria, or other conditions; this is due to them being less common among drug reactions, multiple variants, and a general unfamiliarity of the condition by clinicians.[2]

FDE can occur in all ages, including children and the elderly, but it most commonly occurs in young- to middle-aged adults, with reported median ages ranging between

35 and 60.[3] FDE occurs essentially equally in men and women.[4] Its incidence, from different reports, varies from 2.5% to a high of 22% of all patients with cutaneous adverse drug reactions (CADRs).[5]

These cutaneous drug eruptions often appear as oval, erythematous patches but may have different clinical presentations based on the many variants of the condition. They may occur anywhere on the body, including the face, tongue, hands, feet, torso, extremities and genitalia.[6]

Cephalosporins are bactericidal beta-lactam antibiotics, widely prescribed worldwide, FDE due to cephalosporins is rarely reported. There are 5 generations of cephalosporins. Here we present a case of localised FDE due to first generation cephalosporin-cefadroxil reported in our AMC of a tertiary care teaching rural hospital. To our knowledge, this is the first case report of cefadroxil induced localised FDE.

CASE REPORT

A 51-year-old male presented to the OPD of Pravara rural hospital with localised brownish black patches and painful blisters on the bilateral upper and lower extremities. Patient was apparently alright when he suddenly got injury on his left toe with a nail, for which he visited a local doctor and was prescribed with tab cefadroxil, tab paracetamol and tab levocetirizine. After consumption of tab cefadroxil, next day morning he had itching in his extremities. Due to the itching, he stopped the drug on his own. Following the next day-2 days later he developed circular hyperpigmented black, itchy and painful patches on his both the hands, feet, forearm and groin. The patches on his hands and feet became diffuse due to constant itching. After which the patient came to the OPD of Pravara rural hospital. The patient was admitted and the blood reports showed raised ESR.

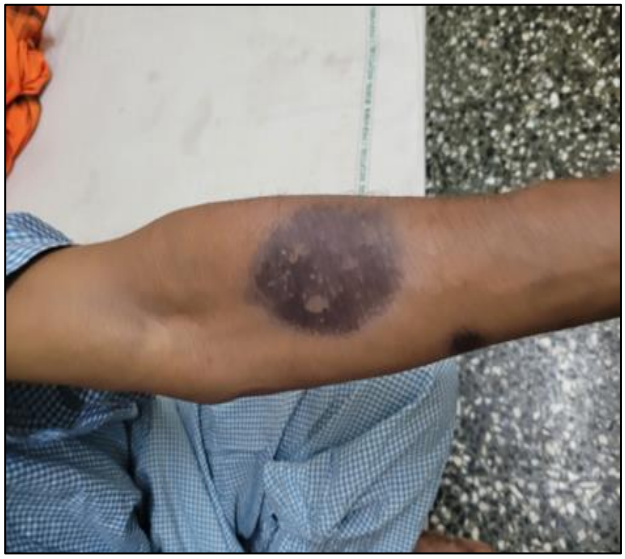

Figure 1: Localised circular brownish black patch on the arms.

Figure 2 (A-C): Diffuse brownish black patches on the extremities.

The patient was treated with tab prednisolone and broad-spectrum antibiotics. He was given clobetasol and Neomycin ointment to be applied on the hands and feet and Fusidic cream to be applied on the groin twice a day. IV fluids to correct the electrolyte imbalance and high protein diet was advised. No new skin lesions developed after stopping the cefadroxil and changing to cefuroxime. Causality assessment using Naranjo causality assessment algorithm was probable. After 3 days, the patient's condition improved, the lesions were resolved and healed. The patient was discharged with a medication card and advised to show the medication card whenever he visits physician next time in future for any treatment.

DISCUSSION

Cefadroxil is a first-generation cephalosporin with broad spectrum activity useful in the treatment of mild to moderate susceptible infections like tonsillitis, urinary tract infections, reproductive tract infections and skin infections and for patients allergic to penicillin. FDE due to cephalosporins is quite rare.

FDE is mediated by CD8+ memory T cells that reside in the basal layer of the epidermis of resting FDE lesions.[7] Within 24 hr of ingestion of a culprit medication, these CD8+ T-cells migrate upward in the epidermis, produce cytokines such as interferon-gamma and TNF-alpha, and take on the phenotype of a natural killer cell, expressing the cell surface molecule CD56 as well as the cytotoxic molecules granzyme B and perforin.[7-9] This activity leads to the epidermal necrosis that is observed in FDE.[9] At the same time, CD4+ Foxp3+ regulatory T cells migrate into the epidermis, curbing the damage inflicted by the CD8+ T cells.[7] The action of the CD4+ regulatory T cells, which includes the production of the anti-inflammatory cytokine IL-10, explains the self-limited nature of the FDEs.[9]

Till now pathogenesis of FDE is unknown but cell-mediated immunity, certain serum factors, and antibodies are some of the causative factors. FDE occurs by a CD8+-mediated reaction which is a delayed type hypersensitivity reaction. The offending drug activities CD8+ cells by damaging surrounding keratinocytes and release cytokines such as interferon gamma in localized epidermal and dermal tissue which cause localized tissue damage.[10] The most commonly used drugs which cause FDE are Paracetamol, metronidazole, tetracycline, cotrimoxazole, diclofenac, tinidazole, mefenamic acid, metamizole, erythromycin, ibuprofen, ampicillin, phenobarbitone, phenylbutazone, albendazole, clindamycin, indomethacin, belladonna, griseofulvin, allopurinol, diflunisal and acetylsalicylic acid.[11]

Cephalosporins have many side effects but FDE due to cefadroxil has been rarely reported. A single case of FDE due to ceftriaxone of cephalosporin class has been reported earlier in Turkish Woman and a case of FDE due to cefaclor-second generation cephalosporin has been reported.[12,13]

Treatment of FDE is mainly focussed on identifying the causative agent and avoiding it. Treatment is symptomatic and systemic anti-histaminic and topical steroids are required with broad spectrum antibiotics if infection is suspected.

A study conducted by Jung et al in Korea reported that the most common causative agents for FDE were NSAIDS followed by antibiotics but cefadroxil was not reported in the study.[14] Since cefadroxil is a commonly prescribed antibiotic, this case report serves as a cautionary note of rare but possible outcome.

CONCLUSION

This case report sheds light on the intricate landscape of FDEs, emphasizing their immunological nature and the challenges associated with diagnosis and management. FDEs, often go underdiagnosed due to their rarity, varied clinical presentations, and limited awareness among clinicians. The presented case of localized FDE induced by cefadroxil, a widely prescribed first-generation cephalosporin, adds to the limited literature on cephalosporin-induced FDEs. The clinical course, treatment, and causality assessment using the Naranjo algorithm highlight the importance of recognizing and addressing such dermatological reactions promptly. The rarity of FDEs induced by cephalosporins, despite their widespread use, emphasizes the need for continued vigilance in pharmacovigilance efforts. As we strive to unravel the complexities of FDEs and their causative factors, this case report provides valuable insights for clinicians, dermatologists, and researchers alike, contributing to the broader field of pharmacovigilance and drug safety.

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