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Case Report

A rare case report on linezolid induced fixed drug eruption

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ABSTRACT

Fixed drug eruption is a rare but significant adverse drug reaction characterized by recurrent, well-defined skin lesions that consistently reappear at the same anatomical sites upon re-exposure to the offending drug. This case report presents a 48-year-old female who developed hyperpigmented patches on her left thigh and axilla followed by the administration of linezolid, an antibiotic used for treating resistant gram-positive bacterial infections. Although Linezolid is generally well-tolerated, it can cause cutaneous reactions, with fixed drug eruptions being an exceedingly rare occurrence. The patient's condition improved significantly after discontinuation of linezolid and treatment with corticosteroids, antihistamines, and topical agents. This case underscores the importance for clinicians to consider FDE in the differential diagnosis of patients receiving linezolid, particularly when lesions appear in atypical locations such as the thigh and axilla. Additionally, it emphasizes the critical role of prompt drug cessation and appropriate symptomatic treatment in managing such adverse reactions, thereby improving patient outcomes and ensuring better clinical management.

Keywords: Fixed drug eruption, Linezolid, Adverse drug reaction, Case report

INTRODUCTION

Drug eruptions are one of the most frequently observed skin disorders in dermatology, presenting in diverse forms and often resembling other skin conditions. Many of these eruptions are nonspecific and can be triggered by a wide range of agents.[1] Fixed drug eruption (FDE) is a rare adverse drug reaction characterized by recurrent skin or mucosal lesions that consistently reappear at the same sites upon re-exposure to the offending drug.[2]

The skin is the most commonly affected organ in drug reactions, with up to 10% of hospitalized patients experiencing cutaneous adverse drug reactions (CADRs). While most CADRs are mild, 2 to 6.7% can be severe. FDE is a prevalent CADR, often ranking second or third among drug eruptions.[3] Its incidence varies regionally, 0.69% in Pakistan, 9% in Bangkok, 34% in South Korea, and 21% in Finland. In North India, FDE accounted for about 22% of cases. Reporting accuracy can be influenced by factors such as hyperpigmentation and misclassification.[4]

The most common causative agents are antibiotics like co-trimoxazole, sulphamethoxazole, trimethoprim, tetracycline, amoxicillin, ampicillin, and erythromycin; analgesics like metamizole, phenylbutazone, paracetamol, acetylsalicylic acid, mefenamic acid, diclofenac sodium, indomethacin, ibuprofen, and diflunisal; antiprotozoals like metronidazole and tinidazole; muscle relaxants like chlormezanone and orphenadrine; antifungals like griseofulvin; anticonvulsants like phenobarbital; anthelmintics like pyrantel pamoate and albendazole; antigout agents like allopurinol; and antispasmodics like belladonna.[5] Among

antibiotics, linezolid, an oxazolidinone, is highly effective against gram-positive bacteria, including resistant strains like methicillin-resistant staphylococci and vancomycin-resistant enterococci. It is used for treating skin infections, pneumonia, and other bacterial infections, with success rates over 80%.[6]

Although linezolid is generally well tolerated, with gastrointestinal issues being common, known cutaneous adverse effects include pruritus, macular exanthema, and maculopapular rash. Anecdotal reports have also highlighted angioedema, drug rash with eosinophilia and systemic symptoms, and leukocytoclastic vasculitis. Reports of linezolid-induced fixed drug eruption (FDE) are exceedingly rare.[7]

This case report highlights the relevance of documenting linezolid induced FDE, as it adds to the limited evidence on this rare adverse reaction and underscores the importance of recognizing and managing such unusual cutaneous reactions associated with this antibiotic.

CASE REPORT

A 48-year-old married female presented with abnormal uterine bleeding and a history of two previous normal vaginal deliveries (P2L2). An ultrasound revealed a bulky uterus with findings consistent with adenomyosis, confirmed by biopsy. Initial management included norethisterone, antibiotics, analgesics, and supportive medications. A follow-up ultrasound confirmed adenomyosis, and the patient was scheduled for a total abdominal hysterectomy with bilateral salpingo-oophorectomy. Preoperative preparation included an epidural-spinal anesthetic regimen. The surgery proceeded as planned.

Postoperatively, the patient was treated with Inj. Paracetamol 1 g as needed, Inj. Tramadol 100 mg IV BD, Inj. Cefotaxime 1 g IV BD for 3 days, Inj. Metronidazole 500 mg IV TDS for 3 days, Inj. Ranitidine 50 mg IV BD, Inj. Ceftriaxone 1 g IV BD for 5 days starting from postoperative day 4, Tab. Metronidazole 400 mg TDS from day 4, Tab. Paracetamol 500 mg TDS, Tab. Ranitidine 150 mg BD, Tab. B-complex, Tab. Vitamin C, Tab. FST, Tab. Calcium, Tab. Amlodipine 5 mg (if needed), Tab. CPM 4 mg OD, Cap. Bifilac BD, Tab. Chymoral Forte 1 Lakh AU TDS, and Tab. Linezolid 600 mg BD starting on postoperative day 9. Topical treatment with ointment mupirocin 2% was also administered. Following the administration of medications, she developed itching and red-coloured skin lesions over the left thigh and axilla on day 11. Her medical history showed no prior history of adverse drug reactions or allergies to any drug. She was then referred to the dermatology department for further evaluation.

The dermatological evaluation revealed erythematous, hyperpigmented patches over the left thigh and axilla. (Figure 1) Examination showed multiple well-defined central hyperpigmented patches with surrounding pale erythema. The oral and genital mucosa, as well as the palms and soles, were normal. Based on the appearance of well-defined hyperpigmented patches two days after the administration of Tab. Linezolid 600 mg BD, and the resolution of symptoms following its discontinuation, a diagnosis of linezolid-induced fixed drug eruption was made. The Naranjo's causality assessment score was determined to be 8, indicating a probable association, which further supports the diagnosis.

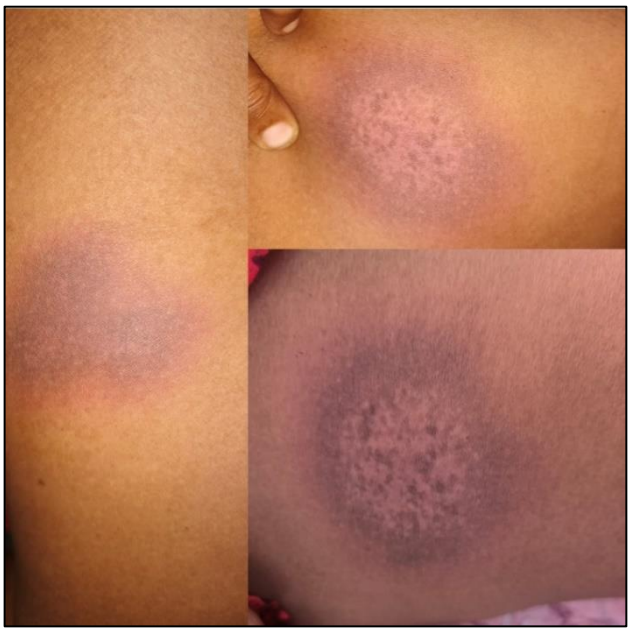

Figure 1: Erythematous, hyperpigmented patches over the left thigh and axilla on day 3 of onset, prior to initiation of treatment.

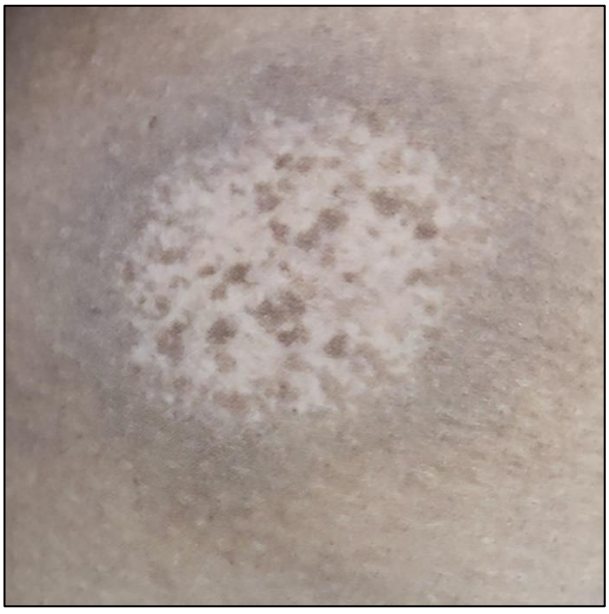

Figure 2: Resolution of erythematous, hyperpigmented patches observed after 3 days of treatment.

The dermatologist recommended immediate discontinuation of Tab. Linezolid from the postoperative regimen on day 11 and she was prescribed with Tab. Prednisolone 20 mg OD for two days, along with Tab. Ranitidine 150 mg BD, Tab. Chlorpheniramine maleate 4 mg OD, and ointment Betamethasone (0.1%). A follow-up review was scheduled to assess the patient's response to the treatment. At the follow-up review after three days, significant improvement in the patient's skin lesions was observed. The erythematous and hyperpigmented patches had notably diminished (Figure 2).

DISCUSSION

FDE is characterized by recurrent erythematous or hyperpigmented lesions at the same site upon re-exposure to the offending drug. In this case, the patient developed a well-defined hyperpigmented patches on the left thigh and axilla shortly after initiating treatment. The diagnosis was confirmed clinically when the skin lesions began to improve following the discontinuation of linezolid, and no new lesions appeared thereafter. Further Naranjo's causality assessment scoring supports the confirmation of diagnosis.[8]

The mechanism behind FDE involves the activation of CD8+ T lymphocytes, which migrate to the intraepidermal spaces and release cytotoxins like perforin and granzyme B, leading to apoptosis of basal keratinocytes. The offending drug acts as an antigen triggering this response. However, further damage occurs through the recruitment of CD4+ T cells, additional CD8+ T cells, and neutrophils, which disrupt the dermo-epidermal junction. Mast cells, though not primary contributors to inflammation, enhance T-cell activation via TNF-alpha release. Once the drug is discontinued, the inflammatory cells undergo apoptosis, clearing from the affected area within weeks. Some CD8+ T cells convert into memory cells, which remain dormant in the upper dermis, ready to reactivate if the same or a cross-reactive drug is reintroduced, causing the recurrence of FDE at the previously affected site.[9]

Despite extensive literature searches, only one report of linezolid-induced FDE was found Inamadar et al, highlighting the rarity of such occurrences. Unlike the more commonly reported locations of FDE, which typically involve the trunk or limbs, this case presents with lesions specifically confined to the thigh and axilla.[7] This unique site of involvement underscores the necessity for clinicians to consider FDE in the differential diagnosis for patients on linezolid who develop skin lesions, even when they present in atypical locations.

The timely discontinuation of linezolid was crucial in managing this case of FDE, as prompt removal of the offending agent and symptomatic relief can prevent progression to more severe reactions and avoid persistent hyperpigmentation.[10] post-diagnosis, the patient was treated with corticosteroids to reduce inflammation, antihistamines to alleviate itching, and topical treatments to manage skin symptoms. Antihistamines are effective in alleviating itching associated with FDE and raising awareness among healthcare professionals about this condition can lead to prompt diagnosis and treatment, improving patient outcomes by facilitating early cessation of the offending drug and speeding up symptom resolution.[11]

For future clinical practice, it is essential for clinicians to be vigilant for rare cutaneous reactions like FDE when prescribing linezolid, even if such reactions are uncommon.

CONCLUSION

This case report illustrates a rare case of FDE induced by Linezolid, a potent antibiotic used for treating resistant Gram-positive bacterial infections. Despite the general safety profile of Linezolid, this case underscores the potential for its rare cutaneous adverse reactions. It also emphasizes the importance of vigilant monitoring for adverse drug reactions, particularly with medications that are effective but have a known risk profile. Documenting such rare reactions contributes to a better understanding of the full spectrum of drug-induced skin conditions and can aid in improving patient safety and clinical management.

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