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Cefuroxime Induced Multiform Erythema and Uveitis - A Case Report

Anna James[1], Anjali M[1*], Preethi Nivedhaa A[1], Chitra R[2]

1 Clinical pharmacist, Department of General Surgery, PSG Hospitals, Coimbatore. India.

1* Pharm.D Intern, Department of Pharmacy Practice, PSG College Of Pharmacy, Coimbatore. India.

1 Pharm.D Intern, Department of Pharmacy Practice, PSG College Of Pharmacy, Coimbatore. India.

2 Associate professor, Department of General Surgery, PSG Hospitals, Coimbatore. India.

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ABSTRACT

Introduction: Cefuroxime, a second-generation cephalosporin, is widely used for treating a variety of bacterial infections, including those caused by Gram-positive and Gram-negative aerobes, and serves as an alternative for beta-lactamase producing Neisseria gonorrhoeae. Although generally well-tolerated, cefuroxime is known to cause gastrointestinal symptoms and, in rare instances, severe reactions such as Clostridium difficile-induced colitis. Uncommon cutaneous reactions, including drug-induced lymphomatosis and erythema multiforme, have been scarcely documented. **Case Presentation:** We present a 51-year-old male with Type 2 diabetes mellitus and systemic hypertension who experienced left groin pain and inguinal lymphadenopathy. After a 10-day course of cefuroxime and doxycycline, the patient developed painful, erythematous, deep-seated vesicular lesions on his palms, without itching. Laboratory results revealed elevated inflammatory markers. The timing of the drug intake and symptom onset suggested a drug-induced hypersensitivity reaction. Despite its rarity, the symptoms were consistent with erythema multiforme and potentially uveitis induced by cefuroxime. **Importance of the Case:** This case is significant due to its demonstration of rare adverse reactions to cefuroxime, including erythema multiforme and possible uveitis. It highlights the need for awareness and investigation of atypical cutaneous reactions to cefuroxime, which can impact patient management and outcomes. The findings emphasize the importance of vigilant monitoring for rare adverse effects and the consideration of alternative treatments if such reactions occur. **Conclusion:** This report underscores a rare but significant adverse reaction to cefuroxime, including erythema multiforme and uveitis, likely due to Type IV hypersensitivity. Clinicians should be alert to these atypical reactions and consider them in differential diagnoses. Further research into the underlying immunological mechanisms could enhance understanding and improve patient care.

Keywords: Cefuroxime, Erythema, Uveitis and Rashes.

INTRODUCTION:

Cefuroxime, a novel semisynthetic cephalosporin for parenteral use, demonstrates resistance to beta-lactamases produced by staphylococci and most Gram-negative aerobic bacteria. It is particularly effective against bacteria resistant to cephalothin and is the most potent cephalosporin against gonococci and Hemophilus influenzae, especially beta-lactamase producing strains. Administered via intramuscular or intravenous injection, cefuroxime effectively treats a broad range of infections caused by Gram-positive and Gram-negative aerobes, excluding those caused by Pseudomonas aeruginosa or Bacteroides fragilis. It is beneficial for respiratory infections caused by Hemophilus influenzae and Streptococcus pneumoniae, and is effective against cephalosporin-resistant Klebsiella and Enterobacter species. Additionally, cefuroxime serves as an alternative to spectinomycin for beta-lactamase producing Neisseria gonorrhoeae infections. The drug is generally well tolerated and shows no nephrotoxicity at standard dosages. [1], [2]

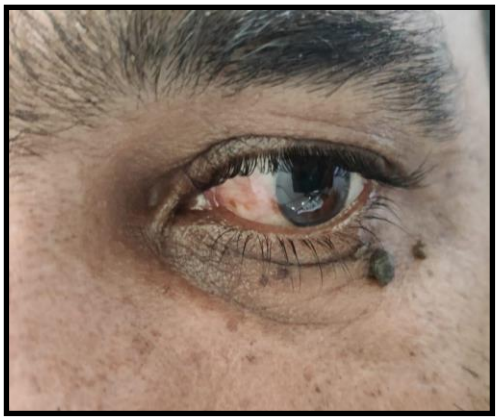
Cephalosporins are extensively used in treating various infections like septicemia, pneumonia, meningitis, and urinary tract infections due to their generally well-tolerated nature at standard doses. The sequential use of cefuroxime is favored for its efficacy and ease of administration in severe infections. Adverse effects occur in about 2.5% of cases, commonly manifesting as gastrointestinal symptoms such as mild nausea and diarrhea. Rare but serious reactions include Clostridium difficile-induced colitis and neurological symptoms like headache and dizziness. Hematological changes like low white blood cell count and allergic skin reactions are also reported. Uncommonly, cephalosporins have been linked to systemic conditions like Henoch-Schoenlein purpura and acute generalized exanthemata's pustulosis. Notably, cephalosporins have not previously been associated with atypical cutaneous lymphoid infiltrates resembling pseudo lymphoma, unlike other drugs. The exact mechanism behind this drug-induced lymphomatosis vascular reaction remains unclear, but it may involve the immunogenicity of the β-lactam ring in cephalosporins, which can form haptens and trigger delayed hypersensitivity reactions. [2], [3].

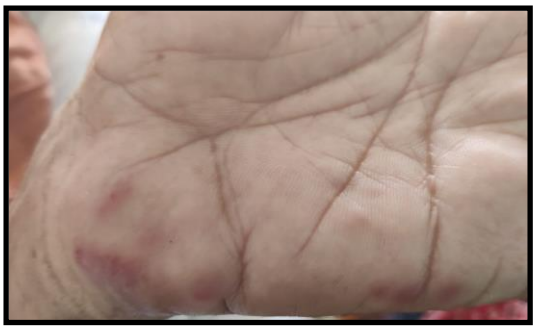
CASE REPORT:

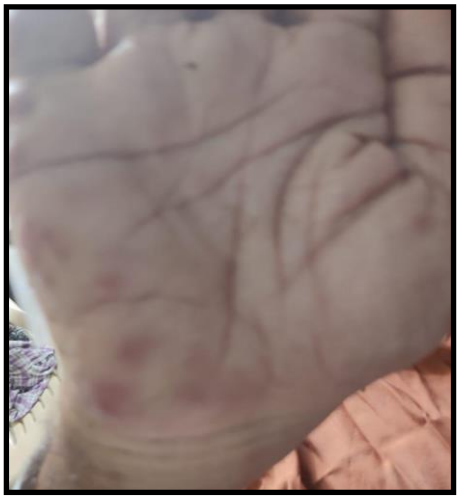
A 51-year-old male with a medical history significant for Type 2 diabetes mellitus (DM) diagnosed 2 years ago, systemic hypertension (SHTN) diagnosed 1 month ago, and resolved tuberculosis 31 years prior, presented with a 2-week history of left groin pain. He was admitted to the general surgery ward where evaluation revealed left inguinal lymphadenopathy measuring 4x4 cm. On admission, he was conscious, oriented, with normal cardiovascular and respiratory findings. Abdominal examination revealed non-tenderness, and neurological examination was non-focal neurological deficit. He had tenderness over left inguinal region suggestive of lymphadenitis. Vital signs were stable with a pulse of 90 bpm, blood pressure 130/70 mmHg, and respiratory rate 20 breaths per minute. He reported normal sleep patterns, bowel habits, and a mixed diet.

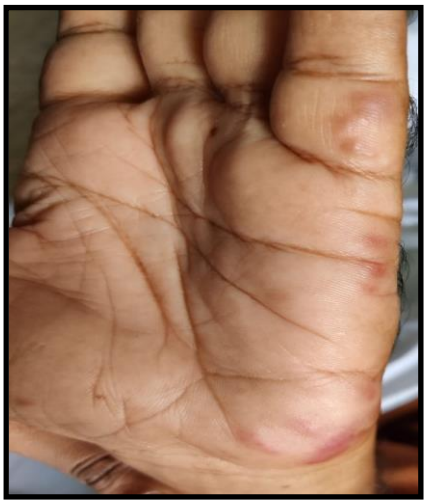
During hospitalization, the patient was found to have painful lesions on his palms, described as erythematous, deep-seated vesicles. These lesions began approximately 4 to 5 days after completing a 10-day course of cefuroxime and doxycycline, prescribed prior to admission. The patient reported painful lesions associated without itching. Laboratory investigations revealed a hematocrit of 35%, hemoglobin level of 12 g/dL, total leukocyte count of 14.1 x 10^3/µL with a differential count of 68.9% polymorphs, 19% lymphocytes, 9.9% monocytes, and 1.1% eosinophils. The erythrocyte sedimentation rate (ESR) was significantly elevated at 120 mm/1st hour. Blood glucose was 212 mg/dL, blood urea 19 mg/dL, serum creatinine 0.66 mg/dL, and electrolytes were within normal limits (sodium 132 mEq/L, potassium 3.84 mEq/L, bicarbonate 21.7 mEq/L). Urinalysis showed amber, light turbid urine with glucose 3+, WBC 3+, and RBC 39 per high-power field, suggestive of a mixed urinary tract infection.

Based on clinical presentation and temporal relationship to drug intake, the patient was concluded to have multiforme erythema and uveitis likely induced by cefuroxime. He was treated symptomatically with 1 g paracip (paracetamol) intravenously, topical corticosteroid Flutarate (fluticasone) for the cutaneous lesions, oral analgesic T.vorth tp (tapentadol).Additionally, he received 1 g intravenous Augmentin(Amoxicillin and clavulanic acid) for ongoing management of his infection, and antihypertensive therapy T.Hypertel (20 mg telmisartan) for his systemic hypertension and T.Gemer 0.5mg for type 2 DM. He was advised to avoid cephalosporin class of drugs.









Discussion:

Cefuroxime, a second-generation cephalosporin, is generally well tolerated, with the most frequent adverse effects being gastrointestinal symptoms and uncommon severe responses such as Clostridium difficile-induced colitis and neurological problems. Cefuroxime induced uveitis is very rare. In 2013, Duncombe et al. reported a rare case where a patient developed severe bilateral uveitis seven days after starting moxifloxacin for bacterial sinusitis and acute bronchitis treatment [4]. The link with cutaneous responses, including uncommon diseases such as Henoch-Schönlein purpura and systemic exanthemata's pustulosis, is well recognized but less prevalent. [4], [5].

The patient's deep-seated vesicular lesions, together with the temporal link to cefuroxime usage, point to an unexpected medication response. Drug-induced lymphomatosis and erythema multiforme are uncommon but can develop with cephalosporins, presumably due to immune-mediated hypersensitivity responses. The patient reported with left groin discomfort and erythematous vesicular lesions on his hands, which appeared immediately after finishing a treatment of cefuroxime and doxycycline. The temporal relationship between drug consumption and symptom onset raises the possibility of drug-induced erythema multiforme and potentially uveitis. The presence of palm lesions and systemic symptoms necessitated distinction from other possible causes, such as viral, autoimmune, or systemic disorders. Given the patient's history and recent medication usage, drug-induced responses were prioritized during the diagnostic process. The emergence of erythema multiforme might be linked to delayed hypersensitivity reactions, particularly Type IV hypersensitivity, in which T-cell-mediated responses to drug haptens cause cutaneous symptoms. This is consistent with the timing and appearance of the patient's symptoms after exposure to drugs. Cefuroxime's β-lactam ring may behave as a hapten, attaching to proteins and activating immunological responses. This immunogenic process may explain the patient's unique skin response. The patient received symptomatic therapy, which included paracetamol for pain alleviation, topical corticosteroids for skin lesions, and oral analgesics. These treatments are useful for treating symptoms caused by drug-induced cutaneous responses. Transitionin from cefuroxime to Augmentin for continuous infection control, as well as managing systemic hypertension and type 2 diabetes, enables complete care while avoiding cephalosporins to prevent adverse reactions from occurring again. [6], [7]

Conclusion:

This case report describes a rare but serious adverse response to cefuroxime that manifested as erythema multiforme, skin lesions, and uveitis. The time link between medication administration and symptom start clearly indicates a drug-induced hypersensitivity reaction, most likely mediated by type IV hypersensitivity mechanism. Although cefuroxime is typically well tolerated, the incidence of unusual responses such as those described highlights the importance of closely monitoring patients on cephalosporin medication[8]. In this situation, symptomatic therapy was combined with other medicines to provide good infection control while preventing further cephalosporin exposure. The findings emphasise the need of taking drug-induced responses into account when treating individuals with atypical cutaneous symptoms. Further investigation into the immunological processes behind such

unusual responses might improve our understanding and guide future treatment options. Clinicians should be aware of and take into account these potential side effects when diagnosing and treating individuals with similar symptoms [9], [10].

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Conflict of Interest Statement:
The authors have no conflicts of interest to declare.

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