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Case Report

Cefotaxime-induced allergic reaction in a 4 years old boy: Case presentation and management strategies

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ABSTRACT

The present case study aims to report and analyze a hypersensitivity reaction to cefotaxime in a 4-year-old boy, highlighting the clinical presentation, diagnostic investigations, management, and classification of the adverse drug reaction using established systems. Cefotaxime, a third-generation cephalosporin, is a semisynthetic antibiotic derived from "cephalosporin-C," produced by the fungus *Cephalosporium*. A 4-year-old boy weighing 15 kg presented with a high-grade fever, cold, loss of appetite, and general weakness. He was admitted with a provisional diagnosis of Acute Febrile Illness (AFI) and initiated on parenteral cefotaxime (750 mg BD), along with paracetamol and febrinil. On the second day of therapy, he developed a hypersensitivity reaction characterized by a rash, prompting the discontinuation of cefotaxime. He was treated with antihistamines and hydrocortisone and switched to intravenous amikacin (100 mg BD). The Widal test was positive for antigen O++, with elevated C-reactive protein levels (1.86 mg/dl). Other tests, including dengue, urine analysis, and complete blood count, were within normal limits except for a slight elevation in white blood cells (8.62×10^9/L). Adverse drug reactions (ADRs) to cefotaxime can be classified using the Rawlins-Thompson and DoTS systems. The Rawlins-Thompson system categorizes ADRs into Type A (predictable pharmacological effects) and Type B (unpredictable and serious). The DoTS system considers dose relatedness, timing, and patient susceptibility, providing a comprehensive framework for understanding drug reactions. This case of cefotaxime-induced hypersensitivity falls under Type B in the Rawlins-Thompson classification and is characterized by the DoTS system. Clinicians should be vigilant for ADRs with cefotaxime, despite its general safety. Prompt recognition and management of hypersensitivity reactions are essential to prevent further complications. Discontinuing the offending agent and providing appropriate supportive care is crucial for patient recovery.

1. Introduction

Cefotaxime, a third-generation cephalosporin, is a widely utilized semisynthetic antibiotic derived from cephalosporin-C, a substance produced by the fungus *Cephalosporium*.[1] This antibiotic shares a structural relationship with penicillins, characterized by a dihydrothiazine ring joined to a β-lactam ring.[1,2] The development of cefotaxime involved modifications at positions 3 and 7 of these rings, resulting in various semisynthetic compounds with distinct pharmacokinetic properties and ranges of antimicrobial activity.[1] Cefotaxime demonstrates high efficacy against aerobic gram-negative bacteria, including species such as *Escherichia coli*, *Klebsiella*, and *Enterobacter*, as well as some gram-positive bacteria like *Streptococcus pneumoniae*.[1,3]

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However, it is ineffective against anaerobes, including *Pseudomonas aeruginosa* and *Staphylococcus aureus*.[1] Clinically, cefotaxime is indicated for the treatment of severe infections, particularly in immunocompromised patients. It is used to manage septicemias, hospital-acquired infections, and meningitis caused by gram-negative bacteria.[2] Cefotaxime can achieve significant cerebrospinal fluid (CSF) concentrations and is effective in treating bacterial meningitis.[2] Despite its broad-spectrum efficacy and general safety, cefotaxime, like other antibiotics, can cause adverse drug reactions (ADRs). These reactions range from mild gastrointestinal disturbances to severe hypersensitivity.[4] Hypersensitivity reactions to cephalosporins are relatively rare but can be life-threatening if not promptly identified and managed.[1,2] The potential for such reactions necessitates careful monitoring, especially in pediatric patients, who may be more susceptible to ADRs due to their developing physiology and immune systems.[4] This case report documents a hypersensitivity reaction to cefotaxime in a 4-year-old boy. The boy presented with a high-grade fever and was initially diagnosed with AFI. After being treated with cefotaxime, he developed a severe hypersensitivity reaction. This report details the clinical presentation, diagnostic workup, and management strategies employed in this case, aiming to provide insights into identifying and treating ADRs associated with cefotaxime.[2,3,5] Understanding the mechanisms and manifestations of drug hypersensitivity reactions is critical for clinicians to ensure patient safety. Early recognition and appropriate management of these reactions can prevent complications and improve clinical outcomes. This case underscores the importance of vigilance in monitoring ADRs and highlights the need for effective communication between healthcare providers and caregivers in managing paediatric patients.[2,4] The findings from this case report contribute to the broader knowledge base on antibiotic-induced hypersensitivity reactions and their management in paediatric practice.[2,6]

2. Case Report

2.1. Study design

The case report design is a descriptive study focusing on a single patient case.[6] The case was reported at the District Civil Hospital, Osmanabad, Maharashtra, India. A clinical assessment like clinical history collection, including presenting symptoms, duration, physical examination findings, vital signs, and initial laboratory investigations (complete blood count, C-reactive protein, urine analysis, Widal test, Dengue test, etc.) was obtained from the hospital database. In the present case, the subject is a minor the oral consent was obtained from a legally acceptable person (The subject's mother). The study adheres to ethical guidelines for reporting patient information and maintained confidentiality. Cefatoxime-associated ADR is based on the application of classification systems (Rawlins-Thompson and DoTS) to categorize the hypersensitivity reaction.[7]

2.2. Case details

A 4-year-old boy weighing 15 kg was admitted to the outpatient department (OPD) at the Government Civil Hospital in Osmanabad with a high-grade fever of 110ºF persisting for 4-5 days. Additional symptoms reported by the caretaker included a cold, loss of appetite and general weakness over the same period. There was no history of vomiting. Following an initial consultation with a physician, the boy was admitted to the paediatric department with a provisional diagnosis of AFI.

2.3. Initial treatment regimen

On the first day of admission, the following treatment regimen was initiated with parenteral cefotaxime 750mg administered BD; Injection of Paracetamol 200 mg administered OD; Injection of Febrinil 75mg administered immediately upon admission; Paracetamol syrup 250 mg/5 ml administered every 6 hours to manage fever.

2.4. Investigations and reports

The following diagnostic tests were advised to identify the underlying cause of the AFI Complete Blood Count (CBC); C-reactive protein (CRP); Urine Analysis; Widal Test and Dengue Test. On the second day, the test results were as follows Widal Test Positive for antigen O++; C-Reactive Protein (CRP) Elevated at 1.86 mg/dl (Reference value: <1 mg/dl); Dengue Test Negative, Urine Albumin and Urine Sugar Nil; No Abnormality Detected (NAD) in Urine Microscopic Examination (ME); Complete Blood Count (CBC) includes White Blood Cells (WBC) 8.62 × 10^9/L; Hemoglobin (Hb) 11.6 mmol/L; Platelets 246 × 10^9/L [Table 1].

2.5. Clinical Course

On the second day of cefotaxime therapy, the patient developed a generalized rash characterized by erythematous, maculopapular lesions, indicating a hypersensitivity reaction to cefotaxime [Fig 1]. His temperature was recorded at 99ºF. Immediate action was taken to discontinue cefotaxime.

2.6. Management of hypersensitivity reaction

Injection Avil (Pheniramine Maleate) 5.6875mg/0.5 mL was administered, with an injection of hydrocortisone 75 mg, to manage the hypersensitivity reaction. Following the discontinuation of cefotaxime due to the adverse reaction, the treatment regimen was adjusted to include intravenous Amikacin 100 mg administered BD.

Table 1: Diagnostic test results and clinical significance

Diagnostic Test	Result	Reference Value	Clinical Significance
Widal Test	Positive for antigen O++	-	Suggests possible typhoid fever or enteric fever; further investigation is needed for confirmation [8]
C-reactive protein (CRP)	Elevated at 1.86 mg/dL	<1 mg/dL	Indicates inflammation or infection; elevated levels support the presence of an acute inflammatory response [9]
Dengue Test	Negative	-	Rules out dengue fever as the cause of illness [10]
Urine Analysis	Urine Albumin: Nil	-	No proteinuria was detected; which suggests the absence of nephrotic syndrome or significant renal involvement [11]
	Urine Sugar: Nil	-	No glucosuria was detected; which rules out diabetes mellitus or significant renal glucose loss [12]
Urine Microscopic Examination	No Abnormality Detected (NAD)	-	No signs of urinary tract infection or other abnormalities [13]
Complete Blood Count (CBC)	White Blood Cells (WBC): 8.62 × 10^9/L	4.0-11.0 × 10^9/L	Within normal range; indicates no significant leukocytosis or leukopenia [14]
	Hemoglobin (Hb): 11.6 mmol/L	11.0-13.5 mmol/L (for children)	Within normal range for age; no evidence of anaemia
	Platelets: 246 × 10^9/L	150-450 × 10^9/L	Within normal range; suggests no significant thrombocytopenia or thrombocytosis

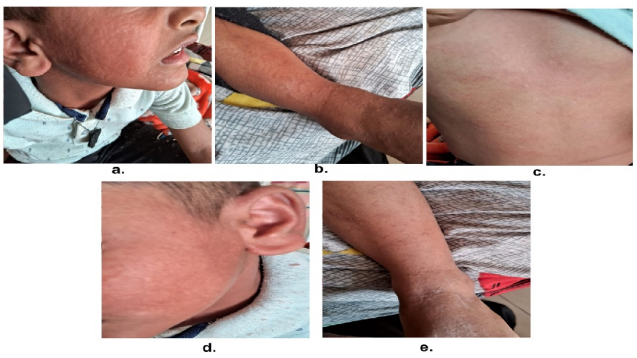

Figure 1: Image showing to allergic reaction to cefotaxime on face, legs, and stomach

3. Discussion

Adverse drug reactions (ADRs) pose significant challenges in clinical practice, ranging from mild discomfort to life-threatening conditions. Understanding and categorizing these reactions are crucial for effective pharmacovigilance and patient safety. The Rawlins-Thompson and DoTS classification systems offer distinct approaches to classifying and analyzing ADRs, providing valuable frameworks for clinicians and researchers. The Rawlins-Thompson system, established in 1981, divides ADRs into two main types. Type A (Augmented) reactions result from the known pharmacological actions of the drug. They are dose-dependent and occur in a quantitatively exaggerated manner. Type A reactions are often predictable and more common.[17] Type B (Bizarre) reactions are unpredictable and idiosyncratic. They are qualitatively abnormal and appear unrelated to the drug's pharmacology. Type B reactions tend to be more serious, with a higher risk of fatalities. The DoTS classification system focuses on three key factors that influence the occurrence and manifestation of ADRs. Dose-relatedness examines whether the adverse reaction correlates with the dose of the administered drug. Certain reactions, such as nephrotoxicity from aminoglycosides, exhibit clear dose-related patterns.[18,19] Timing considers the temporal relationship between drug administration and the onset of the adverse reaction. Immediate reactions (e.g., anaphylaxis shortly after drug infusion) highlight acute timing-related ADRs. Susceptibility factors in individual patient characteristics that predispose them to adverse reactions. Age, genetic predisposition, underlying diseases, and concomitant medications can influence susceptibility.[15] The DoTS framework provides a comprehensive approach to analyzing ADRs beyond the drug's inherent properties, incorporating the dynamic interaction between drug exposure, timing of onset, and patient-specific factors. In the case of cefotaxime, a third-generation cephalosporin widely used for its efficacy against gram-negative bacteria, adverse reactions can vary from mild gastrointestinal upset to severe hypersensitivity reactions.[13,14] The DoTS system

Table 2: Reported case studies of cefotaxime in children

Hypersensitivity Reaction	Case Description	Dose and Duration	Country	Ref
Anaphylaxis	A 5-year-old boy experienced anaphylactic shock within minutes of receiving cefotaxime for an ear infection, showing symptoms such as respiratory distress, hypotension, and generalized swelling.	Dose: 100 mg/kg/day, Duration: Single dose	Turkey	5
Maculopapular Rash	A 7-year-old girl developed a diffuse maculopapular rash three days after starting cefotaxime for a respiratory tract infection, which resolved upon discontinuation of the antibiotic.	Dose: 50 mg/kg/day, Duration: 3 days	India	6
Toxic Epidermal Necrolysis (TEN)	A 12-year-old girl presented with TEN, characterized by widespread skin detachment and necrosis, two weeks after cefotaxime treatment for sepsis, necessitating intensive care and supportive treatment.	Dose: 100 mg/kg/day, Duration: 14 days	Belgium	15
Stevens-Johnson Syndrome (SJS)	A 10-year-old boy developed SJS with extensive mucocutaneous involvement, including blistering and peeling of skin, within a week of cefotaxime administration for a bacterial infection.	Dose: 80 mg/kg/day, Duration: 7 days	India	2
Serum Sickness-like Reaction	An 8-year-old boy developed a fever, rash, and joint pain ten days after starting cefotaxime for a urinary tract infection, with symptoms resolving after stopping the medication and administering steroids.	Dose: 50 mg/kg/day, Duration: 10 days	USA	16
Eosinophilia	A 6-year-old girl developed marked eosinophilia two weeks after beginning cefotaxime for pneumonia, which resolved following cessation of the drug.	Dose: 60 mg/kg/day, Duration: 14 days	Italy	3

allows clinicians and researchers to classify these reactions based on Dose-Relatedness: While cefotaxime is generally well-tolerated, hypersensitivity reactions such as those observed in pediatric patients can be dose-independent and unpredictable.[13,15] Timing: Hypersensitivity reactions typically manifest within hours to days after drug exposure, emphasizing acute timing-related ADRs in clinical settings. Susceptibility: Pediatric patients, due to their developing immune systems, may exhibit increased susceptibility to hypersensitivity reactions, necessitating careful monitoring and management.[2,10] The Rawlins-Thompson and DoTS classification systems complement each other in providing a comprehensive understanding of ADRs associated with cefotaxime and other drugs. While Rawlins-Thompson categorizes reactions based on pharmacological mechanisms, DoTS offers a nuanced approach considering dose, timing, and patient susceptibility.[6,20] This integrated approach enhances pharmacovigilance efforts, facilitates targeted interventions, and improves patient outcomes by mitigating risks associated with ADRs. Future research should focus on refining these frameworks, incorporating genomic and biomarker data to enhance predictive capabilities and personalized medicine approaches in ADR management.[21]

4. Conclusion

This case underscores clinicians' need to remain vigilant for ADRs, even with widely used and generally safe antibiotics like cefotaxime. Prompt recognition and management of hypersensitivity reactions are crucial to prevent further complications and ensure patient safety. Discontinuation of the offending agent and appropriate supportive care are essential steps in managing such reactions. In pediatric patients, the potential for hypersensitivity reactions requires careful monitoring and communication between healthcare providers and caregivers. This case also highlights the

utility of classification systems like Rawlins-Thompson and DoTS in understanding and managing ADRs. Clinicians should know these frameworks to anticipate better, identify, and address adverse reactions in their practice. Ultimately, this case contributes to the broader knowledge base on antibiotic-induced hypersensitivity reactions and their management in pediatric practice. It emphasizes the need for ongoing research and education to enhance the safety and effectiveness of antibiotic therapy in children.

5. Limitations of Case Study

The report is based on a single patient, making it difficult to generalize the findings to a broader population. The specific case may not reflect typical responses or hypersensitivity reactions in other patients. The case does not mention long-term follow-up, leaving uncertainty regarding the patient's recovery and whether there were any delayed reactions or complications following the hypersensitivity episode. Further diagnostic testing, such as skin testing or drug provocation tests, is absent. The report does not explore specific patient factors that may have predisposed the child to an ADR, such as genetic markers, atopy, or prior exposure to cephalosporins or beta-lactam antibiotics.

6. Source of Funding

None.

7. Conflict of Interest

None.

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