



Cefotaxime-induced near-fatal anaphylaxis in a neonate: A case report and review of literature

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Abstract

A case of 7-day-old male neonate with cefotaxime-induced near-fatal anaphylaxis is being reported. Child was started on intravenous cefotaxime on day 3 of life in view of early-onset sepsis with pneumonia, following which there was clinical improvement. Child was then shifted out of intensive care to general ward for completion of antibiotic course. One day prior to the planned discharge, child suddenly developed poor sensorium, flaccidity, apnea, and cyanosis within seconds of receiving intravenous cefotaxime and was found to have bradypnea with bradycardia. Prompt resuscitation was carried out with artificial ventilation, adrenaline, and steroids. Spontaneous breathing reappeared and the clinical condition improved.

Keywords: Anaphylaxis, cefotaxime, neonate

Introduction

Cefotaxime is a third-generation cephalosporin antibiotic with broad-spectrum activity against Gram-positive and Gram-negative bacteria. It is being widely used in the treatment of empirical neonatal infections.[1] Unlike other third-generation cephalosporins, cefotaxime rarely causes anaphylaxis.[2] We report a case of intravenous cefotaxime-induced near-fatal anaphylaxis in a 7-day-old neonate treated for early-onset sepsis.

Case Report

A 3-day-old male neonate was presented with complaints of poor feeding and respiratory distress in the form of fast breathing and retractions for 2 days duration.

The baby was born at term, to a primi-gravida mother by spontaneous vaginal delivery following an uneventful antenatal period with birth weight 2.7 kg. The mother was booked and immunized with two doses of tetanus toxoid during pregnancy. The baby cried immediately after birth and colostrum was given. Baby was apparently normal for 24 hours following which the symptoms started. There was no history of seizures, jaundice, or poor sensorium. There was no history of allergy in the mother or family. On examination, baby had tachypnea with mild grunting, scattered crepitations, and conducted sounds on respiratory examination. Other systems were within normal limits. Initial septic screen was negative. Chest X-ray showed bilateral para-cardiac infiltrates. A diagnosis of early-onset sepsis with pneumonia was made. The child was supplemented with oxygen and was put on intravenous cefotaxime and gentamicin. Cefotaxime was given at a dose of 100 mg/kg/day in two divided doses and gentamicin at a single morning dose of 4 mg/kg. Symptoms improved within 3 days of antibiotic therapy and feeds were started. Blood culture was sterile. The child was shifted to general ward from neonatal intensive care unit (NICU) for completion of antibiotic course. On day 6 of antibiotic therapy, child developed sudden poor sensorium, flaccidity, apnea, and

cyanosis within seconds following administration of a night dose of cefotaxime. There was no evidence of extravasation of the drug. On examination, child had feeble respiratory attempts and bradycardia. Baby was given 100 mg of intramuscular adrenaline and cardiopulmonary resuscitation was done. Child was intubated and artificial ventilation was given for 10 minutes. Heart rate picked up as spontaneous respirations appeared regularly. Child was extubated immediately and readmitted in NICU and was monitored for the next 48 hours. Subsequent doses of cefotaxime were withheld and steroids were added. Child improved well and was shifted to the general ward after 2 days and discharged.

Discussion

Cefotaxime primarily acts by inhibiting bacterial cell wall synthesis. This is brought about by binding with penicillin-binding proteins which in turn inhibits the final transpeptidation step of peptidoglycan synthesis in bacterial cell wall. This arrest in cell wall assembly leads to bacterial lysis by cell wall autolytic enzymes.[2] The incidence of adverse reactions with cefotaxime ranges from 1% to 10%. Common reactions include rash, pruritus, diarrhea, nausea, vomiting, and pain at injection site. Life-threatening reactions are extremely rare and accounts for <1% which includes anaphylaxis, arrhythmia, and acute renal failure.[2,3]

Anaphylaxis is an acute severe type I hypersensitivity reaction developing over minutes to hours with multisystem involvement due to the systemic effects of histamine release.

Immune system gets sensitized to an allergen after initial exposure. On a subsequent exposure, massive mast cell degranulation and release of inflammatory mediators occur, leading on to severe anaphylactic reaction resulting in circulatory collapse, laryngotracheal edema, and spasm.[4] Anaphylaxis is a medical emergency which usually requires resuscitation measures such as airway management, supplemental oxygen, large volumes of intravenous fluids, and close monitoring. Administration of adrenaline is the treatment of choice with antihistamines and steroids often used as adjuncts.[4]

In the present case, cefotaxime-induced anaphylaxis was diagnosed on the basis of a typical history of an anaphylactic episode following the intravenous injection of cefotaxime. A skin-challenge test was not performed. There is no skin test that can reliably predict whether a patient will manifest an allergic reaction to the cephalosporins.[5] The timing of symptoms and clinical picture were in favour of drug-induced anaphylaxis. Sensitization might have occurred during previous injections, although the latency for anaphylaxis after a first sensitizing dose is usually longer. No history of sensitization *in utero* or through breastfeeding secondary to maternal exposure to cefotaxime was present. The diagnosis of drug-induced anaphylaxis is a presumption as history, and findings were not suggestive of other possible causes such as aspiration, abuse, and sudden infant death syndrome. Causality assessment of the case was done using Naranjo Adverse Drug Reaction Probability scale.[6] The score on Naranjo adverse drug scale was 6, suggesting a "probable" relationship of the reaction with the drug.

The child presented with sudden poor sensorium, flaccidity, apnea, and cyanosis which is in sharp contrast to the classical symptoms of anaphylaxis. The most common organs affected in anaphylaxis include: Skin (80–90%), respiratory (70%), gastrointestinal (30–45%), heart and vasculature (10–45%), and central nervous system (10–15%).[4] Skin involvement presents as urticaria, itchiness, flushing, and angioedema, while dyspnea, wheeze, and stridor are the chief respiratory manifestations. Gastrointestinal symptoms such as crampy abdominal pain, diarrhea, and vomiting can be present. Other findings include arrhythmias, loss of consciousness, and hypotonia. The clinicians should have a high index of suspicion and should be aware of all possible presentations of anaphylaxis.

An anaphylactic reaction occurs only in previously exposed and sensitized patient. An anaphylactoid reaction can occur following a single, first-time exposure even in nonsensitized patients. The term anaphylaxis is often used to refer both the conditions. Our case fits more into anaphylactoid reaction in view of the onset of reaction and lack of previous exposure. Moreover, anaphylactic reaction requires an average period of 10 days from the time of initial exposure for sufficient antibody production to occur.

Similar life-threatening anaphylactic reactions have been reported with ceftriaxone.[7,8] In one case, anaphylaxis

occurred with the first dose and in the other, after receiving multiple doses. Hypersensitivity could not be demonstrated by skin testing in both cases and also by ceftriaxone-specific IgE. However, in one infant, controlled, intravenous challenge was clearly positive. We did not attempt intravenous challenge test due to ethical concerns. Although cross-reactivity is common within cephalosporins and between cephalosporins and penicillins, recent studies have concluded that cephalosporins can be used in penicillin allergy and vice versa.[9,10] The explanation which is being offered is that the R1 side chain rather than the beta-lactam structure, shared by penicillins and cephalosporins, plays a critical role in determining the specificity of immunologic reactions to cephalosporins.[9]

We have reported a rare case of cefotaxime-induced anaphylaxis in a neonate treated for early-onset sepsis. The clinicians should be aware of this possibility of potentially fatal adverse effect occurring with intravenous cefotaxime.

Footnotes

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Conflict of Interest: None declared.

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