Case Report

Ceftriaxone Induced Cardiopulmonary Arrest: A Fatal Case Report

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Abstract

Ceftriaxone is the most commonly used antibiotic in Pakistan which is well-tolerated and rarely cause fatal adverse reactions. Here, we underline a fatal cardiopulmonary arrest post-ceftriaxone administration. A nine-year-old girl was presented to the emergency department with complaints of sore throat and a small abscess on the cheek. She was prescribed ceftriaxone 0.5 g intravenously STAT (immediately) and amoxicillin syrup (125 mg/5ml) 1 tablespoon BID (twice a day) for 5 days. Earlier, the patient was alert and oriented but she had a fall and became unconscious within a minute of receiving a ceftriaxone injection. She was given emergency treatment for shock and cardiopulmonary resuscitation was performed for approximately 20 minutes. She was declared dead, with cardiopulmonary arrest reported to be the cause of death. In conclusion, this was a fatal case of cardiopulmonary arrest following anaphylaxis to ceftriaxone (Naranjo adverse drug reaction probability score = 5). Therefore, healthcare professionals should be mindful of anaphylaxis possibility in patients receiving ceftriaxone.

Keywords: Adverse drug reaction, Anaphylaxis, Cardiopulmonary arrest, Ceftriaxone

Introduction

Beta-lactam antibiotics, particularly penicillins and cephalosporins, are the most frequently used agents for the treatment of common infectious diseases [1]. Among the cephalosporin sub-class, ceftriaxone is the most widely used antibiotic in clinical practice in Pakistan [2, 3]. It is a semisynthetic, broad-spectrum, third-generation cephalosporin for intravenous (IV) or intramuscular administration. It is usually well-tolerated and hypersensitivity related to ceftriaxone occurs in 1-3% of the cases whereas anaphylaxis, the most serious of all allergic reactions, events are rare [1, 4]. Early recognition and aggressive treatment are pivotal for the successful management of anaphylaxis [5]. However, diagnosis and management are challenging since these adverse reactions are often acute and unpredictable. Here, we underscore a fatal cardiopulmonary arrest post-ceftriaxone IV injection in a nine-year-old child.

Case Presentation

A nine-year-old girl was presented (August 30, 2019) to the emergency department of the District Headquarter Hospital Pakpattan, Pakistan with chief complaints of sore throat and small abscess on the cheek. She was prescribed ceftriaxone 0.5g IV STAT (immediately) and amoxicillin syrup (125 mg/5ml) 1 tablespoon BID for 5 days by the physician. She was administered ceftriaxone 0.5 g after reconstitution in solvent (water for injection). Earlier, the patient was in a conscious state and was well oriented but within a minute of administration of the injection, she had a fall and became unconscious. She was given hydrocortisone sodium 100 mg IV and normal saline 500 ml. Following that, her condition kept deteriorating and she was injected atropine and adrenaline, 0.3 mg of each agent every 3-5 minutes, a total of 3 shots. She was resuscitated for approximately 20 minutes but expired. The physician declared it to be a cardiopulmonary arrest, the main cause of her sudden death.

Results and Discussion

Adverse drug reactions account for 4.2-30% of hospital admissions in the United States and Canada, 5.7-18.8% in

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Australia, and 2.5-10.6% in Europe [6]. Children and elderlies are amongst the most vulnerable populations for such reactions. Around 2-5% of adverse drug reactions in children lead to hospitalization, and up to 39% of adverse drug reactions in children can be fatal [7]. The present case report is one such example. This case highlighted the cautions needed to be taken before ceftriaxone therapy. The treatment provided for the condition of the patient was deemed irrational as there was no need to use ceftriaxone for a small skin abscess as it may drain naturally, or heal with oral antibiotics only. Incision and drainage of pus along with antibiotics therapy are usually reserved for large abscesses. Moreover, there was also no need for an IV antibiotic (ceftriaxone) for the patient's mild upper respiratory infection. Irrational use of antibiotics is common in Pakistani healthcare settings and it can be attributed to the lack of standard treatment guidelines at national as well as institutional levels [2, 3]. It is important to mention that the patient was alert and conscious before the IV administration of ceftriaxone and had a fall within a minute post-dose. Additionally, the patient did not show any typical signs and symptoms of anaphylaxis before the fall. The patient remained in the emergency room for 45 minutes during which she was given emergency treatment for shock and cardiopulmonary resuscitation performed but the patient expired. It is also pertinent to mention that important information (drug allergies) was not obtained before the administration of ceftriaxone. The anaphylactic reaction typically presents with symptoms like bronchoconstriction, generalized edema, and rash along with hypotension. However, signs and symptoms of anaphylaxis can be unpredictable and may vary from one patient to another and one reaction to another. Hence, the absence of one or more of the common symptoms does not rule out anaphylaxis reactions [5]. Mortality associated with anaphylaxis usually occurs as a consequence of respiratory or cardiovascular failure, or both [5]. Therefore, in the present case, cardiopulmonary arrest following anaphylaxis to ceftriaxone (Naranjo ADR probability score = 5) [8] was the probable cause of death. Published literature related to ceftriaxone-induced anaphylaxis [9-19] is shown in **Table 1**. Moreover, a 10-year review (1998-2008) of reported cases to the Iranian Pharmacovigilance Centre showed that the most frequently reported serious events with ceftriaxone were cardiac arrest and anaphylactic and anaphylactoid reactions [20]. They reported that out of 232 deaths related to various medicines in their database, 49 were linked with ceftriaxone, with cardiac arrest as the leading cause of death.

Table 1. Published data related to ceftriaxone-induced anaphylaxis

Authors	Age (years), gender	Adverse reaction	Fatality
Saritas *et al*. [9]	31, male	Cardiac arrest within one minute of ceftriaxone administration. The time of onset was suggestive of ceftriaxone-induced anaphylaxis	No
Shrestha *et al*. [10]	9, male	ceftriaxone-induced anaphylaxis	No
Riezzo *et al*. [11]	59, Male	Ceftriaxone-induced anaphylaxis	Yes
Aboul-Fotouh *et al*. [12]	44, Male	Cardiac arrest following anaphylaxis to ceftriaxone	No
Kumari *et al*. [13]	22, Male	Ceftriaxone-induced anaphylaxis	No
Calapai *et al*. [14]	4, Male	Ceftriaxone-induced anaphylaxis	Yes
Pasquale *et al*. [15]	77, Male	Ceftriaxone-induced anaphylaxis	No
Bhagwat and Saxena [16]	52, Male	Ceftriaxone-induced anaphylaxis	Yes
Imam and Ibrahim [17]	31, Female	Ceftriaxone-induced anaphylaxis	No
Badar [18]	36, Male	Ceftriaxone-induced anaphylaxis	No
Rozeeta *et al*. [19]	31, Female 21, Female	Acute respiratory distress syndrome secondary to Ceftriaxone-induced anaphylaxis	No

Conclusion

This was a fatal case of cardiopulmonary arrest post-ceftriaxone administration. To minimize ceftriaxone associated adverse events in the future, the following points must be taken into account by the healthcare providers;

1. Avoid the unnecessary use of antibiotics. Avoid using ceftriaxone for indications not approved for its use. Do not use it for common cold and flu or infections that could be treated by oral antibiotics.
2. Always inquire patients about any allergies. Preferably, perform drug-hypersensitivity testing according to the guidelines before administration. Do not inject ceftriaxone in patients with a previous history of allergic reactions to ceftriaxone or other cephalosporin antibiotics
3. A shock response team for managing any acute hypersensitivity reactions should be available wherever a test dose or subsequent doses of ceftriaxone are administered.
4. Ideally, ceftriaxone dose should be given via IV infusion lasting at least 30 min or by IV injection over 5 minutes.
5. Do not administer ceftriaxone and calcium-containing fluids/solutions within 48 hours of each other.

6. Do not use diluents containing calcium (Ringer solutions or Hartman's solution) to reconstitute ceftriaxone or to further dilute an already reconstituted vial.
7. Report all the adverse drug reactions to the hospital and national pharmacovigilance center.

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ETHICS STATEMENT: This case report was in accordance with the ethical principles laid down in the amended Declaration of Helsinki. Permission to report this case was obtained from the Medical Superintendent of the DHQ Hospital Pakpattan.

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