Case Report

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Anaphylactic shock caused by a selective allergy to ceftriaxone: A case report

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ABSTRACT

Ceftriaxone has been widely used due to once daily dosing. However, case with anaphylaxis secondary to ceftriaxone has been documented and the other β-lactam might be a caution. **Objective:** To reported an 89-year-old patient who had history of Type I hypersensitivity to ceftriaxone. **Results:** This case could be received imipenem following by piperacillin/tazobactam for a few days with a good clinical outcome before antibiotic de-escalation. After switching to ceftriaxone, this pateint developed anaphylactic shock and the appropriate resuscitation was performed immediately. Subsequently, she had sepsis several times treated by ampicillin, cloxacillin, piperacillin/tazobactam, and imipenem without any serious events. With our case report, the other β-lactam might be therapeutic choices in the case of selective allergy to one of them, but it can be hard to know except, they have experienced such medications. Moreover, the rechallenge β-lactam in Type I hypersensitivity does not routinely reintroduce. **Conclusion:** Thus, the other classes of antimicrobial agents, not β-lactam, are the preferred options.

INTRODUCTION

Ceftriaxone, a third-generation parenteral cephalosporin is a broad spectrum coverage Gram-positive and Gram-negative bacteria [1]. This agent has been widely used due to once daily dosing, making convenient administration in hospital and in most outpatient antimicrobial therapy (OPAT) [2] and no dose adjustment in the patient with renal impairment or hemodialysis [1]. In additional, owing to a good penetration into various organs, this antimicrobial agent has been approved lots of indication such as lower respiratory tract, bloodstream, urinary tract, intra-abdominal tract, and central nervous system infections [1,3].Even ceftriaxone has developed for clinical use with favorable tolerability since 1980, the major adverse drug reactions, quite low, but was noted consistency. The previous study of ceftriaxone use over a 10-year period as OPAT service reported 51 events including rash, bone marrow suppression (leukopenia, thrombocytopenia or anemia), hepatic transminitis, acute kidney injury, and also anaphylaxis [2]. This report showed anaphylactic reactions caused selectively by ceftriaxone in patient was tolerable to piperacillin and imipenem use.

CASE REPORT

An 89-year-old female patient, who had been an end-stage renal disease with regular stable twice a week hemodialysis, was admitted due to 2-day fever preceding hospitalization. She also had hypertension and anemia. Her medication regimen before hospitalization included metoprolol, nifedipine, furosemide, hydralazine, calcium carbonate, folic acid, and ferrous sulfate. According to urine analysis, it showed pyuria with white blood cell 30-50 cells/mL. The physician suspected urinary tract infection and catheter-related infection in hemodialysis patients treated unintentionally with intravenous piperacillin/tazobactam and vancomycin even she had been documented allergic to ceftriaxone-related anaphylactic shock and respiratory depression since 9 months ago. At that time, she had sepsis treated with ceftriaxone as empirical therapy. The anaphylaxis

due to ceftriaxone was categorized as probable ADR based on the Naranjo's algorithm.

On the third day after starting empirical therapy without drug allergic reaction, Gram-negative bacilli (GNB) was detected in blood culture. By then, vancomycin was discontinued and piperacillin/tazobactam was changed to imipenem for more spectrum coverage GNB pathogens. Considering a good clinical symptom on day 5th and documented testing reported *Enterobacter cloacae* sensitive to all third-generation cephalosporins, carbapenems, fluoroquinolones, and aminoglycosides. The patient was accidentally started intravenous ceftriaxone (2 g once daily by infusion over a period of 30-min).

During 5 min after administration of ceftriaxone, she developed nausea, vomiting, and hypotension (60/40 mmHg) without any skin rash or bronchospasm. Ceftriaxone was stopped due to suspected anaphylactic shock and the appropriate adverse drug management with antihistamine and systemic corticosteroids were started immediately. Her unfavorable symptoms got well shortly and she received ciprofloxacin instead of ceftriaxone for *E. cloacae* septicemia treatment. The causality assessment by the Naranjo's algorithm revealed as definite ADR. The following blood culture set was negative and no anaphylactic reaction was noticed. She could discharge and returned to follow-up at outpatient hemodialysis clinic. Subsequently, she had sepsis several times treated by ampicillin, cloxacillin, piperacillin/tazobactam, and imipenem without any serious events.

DISCUSSION

Anaphylaxis is a rapid onset and the most serious drug allergy classified as Ig-E mediated immune response. This phenomenon is associated with hemodynamic disturbance in which can cause sudden death. The spectrum of Type I immediate reaction represents as wide range severity from urticaria, angioedema to a sudden constriction of airway and anaphylactic shock [4]. In general, this reaction is cautious to repeat causing medications or suspected drug that has similar chemical structure. Especially, β-lactam anti-infective agents such as penicillins, cephalosporins, and carbapenems have been frequently reported as allergens [5].

Among β-lactams, only the penicillin derivatives induced allergy has been well-studied. The penicilloyl determinant is a major antigenic component due to about 95% of hapten-bound penicillin. The remaining degraded penicillin to some derivatives these are also classified as haptens. Unfortunately, cephalosporins have more degraded immunogenic forms and have not been clearly defined what are the exact determinants [6]. However, according to the shared core structure among β-lactam antibiotics, might be acting as moiety to occur cross allergy. Romano *et al*. evaluated the potential of using penicillins, and carbapenems in subjects with cephalosporin induced immediate reactions. Among the 98 participants with positive skin test for cephalosporin, about 25% of them showed positive skin results to penicillins, 2% to imipenem/cilastatin, and 1% to meropenem. Moreover, a positive reaction to cephalosporins with similar side-chain structures to those of penicillins was an increasing 3-fold risk of cross-reactivity [7]. Specifically, cross allergy between cephalosporins, Romano *et al*. reported that 3 patients with 3rd generation cephalosporin Type I allergy had been reactivated by the different agents in the same group (i.e., ceftriaxone, ceftazidime or cefotaxime) [8].

Previously, very few Type I selective hypersensitivity to ceftriaxone have been reported in the literatures. The first documentation by Romano presented a 68 year-old man who had developed urticaria, dyspnea, and severe hypotension after intramuscular ceftriaxone within 15 min-administration. This patient was the only positive result to prick testing with ceftriaxone, whereas the specific Ig-E plasma assay (penicilloyl G, penicilloyl V, ampicilloyl, moxicilloyl, cefuroxime, cefaclor, cefalexin, cefotaxime, and cefatrizine) and oral challenges with penicillin V (1,000,000 IU), ampicillin (1 g), cephalexin (500 mg), cefaclor (500 mg), and cefixime (400 mg) were negative [9]. Another case was a 71-year-old man with ceftriaxone-induced generalized urticaria, wheezing, and dropped blood pressure. 2 years later, he was rechallenged with oral amoxicillin, cefaclor, cefpodoxime, cefuroxime, intravenous cefotaxime, ceftazidime, cefepime, aztreonam, cefpirome, cefazolin, and ceftriaxone. Challenges were positive only to ceftriaxone, with an anaphylactic reaction after the fourth injections at doses 50 mg [10]. Currently, our report is the third case of selectively immediate ceftriaxone reaction, but this is the first case in which selective immediate hypersensitivity to ceftriaxone and confirmed by unintentional use (imipenem and piperacillin) and multiple course of ampicillin, cloxacillin, imipenem, and piperacillin has been documented in the latter.

In contrast to previous two case reports, the authors cannot exclude the other β-lactam recognized as allergenicity because this case had no rechallenge with the skin test, oral, and intravenous desensitization. However, intradermal with ceftriaxone or other β-lactam antibiotics might be warranted due to previously reported fatal anaphylactic case [11] and the present 89 years old-case might not be tolerable to provoke serious reactions. Owing to very few case reports, the documented case of allergy to selective medication among β-lactam has to be confirmed in the further study.

Fortunately, this case could safely rechallenge ampicillin, cloxacillin, imipenem, and piperacillin/tazobactam without any hypersensitivity. The authors could not explain a mechanism of allergy clearly, but there are some literatures indicated that the immediate hypersensitivity to cephalosporin might be specified by the whole chemical structure and no cross allergy within cephalosporins [12-16]. Although, the authors could not exclude the cross allergy among cephalosporins because she had no previous use. Especially, the cross-reactivity ceftriaxone with an identical side chain at 7-position on cephem ring (i.e., cefpodoxime, cefotaxime, cefpirome, and cefepime) might be possible because this chemical structure seems to be an important contributor to hypersensitivity [7,17-19].

CONCLUSION

Ceftriaxone-induced Ig-E mediated allergy is not quite low and this is also a serious condition to cause death. This case had obviously ceftriaxone allergy and some β-lactam antibiotics can be used because she experienced such medications without allergy. However, the rechallenge of another β-lactam

do not routinely reintroduced because the serious effect might occur. The different antimicrobial class, such as polymixins, fluoroquinolones, or fosfomycin might be the preferred options. If unavoidable the rechallenging has occurred, desensitizing protocol for β-lactam and the closely monitor during reintroduction needed to be promptly.

REFERENCES

1. Lamb HM, Ormrod D, Scott LJ, Figgitt DP. Ceftriaxone: An update of its use in the management of community-acquired and nosocomial infections. Drugs 2002;62:1041-89.
2. Duncan CJ, Barr DA, Seaton RA. Outpatient parenteral antimicrobial therapy with ceftriaxone, a review. Int J Clin Pharm 2012;34:410-7.
3. Esposito S. Parenteral cephalosporin therapy in ambulatory care: Advantages and disadvantages. Drugs 2000;59 Suppl 3:19-28.
4. Lieberman PL. Recognition and first-line treatment of anaphylaxis. Am J Med 2014;127 1 Suppl: S6-11.
5. Blanca M, Romano A, Torres MJ, Férnandez J, Mayorga C, Rodriguez J, *et al.* Update on the evaluation of hypersensitivity reactions to betalactams. Allergy 2009;64:183-93.
6. Solensky R. Hypersensitivity reactions to beta-lactam antibiotics. Clin Rev Allergy Immunol 2003;24:201-20.
7. Romano A, Gaeta F, Valluzzi RL, Caruso C, Rumi G, Bousquet PJ. IgE-mediated hypersensitivity to cephalosporins: Cross-reactivity and tolerability of penicillins, monobactams, and carbapenems. J Allergy Clin Immunol 2010;126:994-9.
8. Romano A, Mayorga C, Torres MJ, Artesani MC, Suau R, Sánchez F, *et al.* Immediate allergic reactions to cephalosporins: Cross-reactivity and selective responses. J Allergy Clin Immunol 2000;106:1177-83.
9. Romano A, Piunti E, Di Fonso M, Viola M, Venuti A, Venemalm L. Selective immediate hypersensitivity to ceftriaxone. Allergy 2000;55:415-6.
10. Demoly P, Messaad D, Sahla H, Hillaire-Buys D, Bousquet J. Immediate hypersensitivity to ceftriaxone. Allergy 2000;55:418-9.
11. Riezzo I, Bello S, Neri M, Turillazzi E, Fineschi V. Ceftriaxone intradermal test-related fatal anaphylactic shock: A medico-legal nightmare. Allergy 2010;65:130-1.
12. Romano A, Viola M, Guéant-Rodriguez RM, Valluzzi RL, Guéant JL. Selective immediate hypersensitivity to cefodizime. Allergy 2005;60:1545-6.
13. Atanaskovic-Markovic M, Cirkovic Velickovic T, Gavrovic-Jankulovic M, Ivanovski P, Nestorovic B. A case of selective IgE-mediated hypersensitivity to ceftibuten. Allergy 2005;60:1454.
14. Gaig P, San Miguel MM, Enrique E, García-Ortega P. Selective Type-1 hypersensitivity to cefixime. Allergy 1999;54:901-2.
15. Romano A, Di Fonso M, Artesani MC, Viola M, Adesi FB, Venuti A. Selective immediate hypersensitivity to ceftazidime. Allergy 2001;56:84-5.
16. Moreno E, Dávila I, Laffond E, Macías E, Isidoro M, Ruiz A, *et al.* Selective immediate hypersensitivity to cefepime. J Investig Allergol Clin Immunol 2007;17:52-4.
17. Miranda A, Blanca M, Vega JM, Moreno F, Carmona MJ, García JJ, *et al.* Cross-reactivity between a penicillin and a cephalosporin with the same side chain. J Allergy Clin Immunol 1996;98:671-7.
18. Perez-Inestrosa E, Suau R, Montañez MI, Rodriguez R, Mayorga C, Torres MJ, *et al.* Cephalosporin chemical reactivity and its immunological implications. Curr Opin Allergy Clin Immunol 2005;5:323-30.
19. Pichichero ME. Use of selected cephalosporins in penicillin-allergic patients: A paradigm shift. Diagn Microbiol Infect Dis 2007;57 3 Suppl:13S-8.