

# Cefuroxime-induced anaphylaxis with prominent central nervous system manifestations: A case report

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Jianqing Gu<sup>1,\*</sup>, Shuang Liu<sup>2,\*</sup>  and Yuxiang Zhi<sup>1</sup>

## Abstract

Cefuroxime is a second-generation cephalosporin antibiotic that causes immediate hypersensitivity reactions, ranging from mild urticaria to severe anaphylactic shock. Anaphylactic reactions typically involve multiple systems, most notably, the skin and the respiratory and cardiovascular systems. Here, we report the unusual case of a patient who presented with oral cefuroxime-induced anaphylaxis with prominent neurologic manifestations. To identify the drug responsible for the anaphylaxis, we performed skin tests. Based on positive skin-prick test results, the diagnosis of cefuroxime-induced anaphylaxis was confirmed. Therefore, we suggest that clinicians should consider the possibility of a drug-induced anaphylactic reaction when neurologic but not cutaneous symptoms are present. The skin-prick test is a safe and useful diagnostic tool to confirm this kind of immediate drug hypersensitivity.

## Keywords

Cefuroxime, anaphylaxis, neurologic, skin-prick test, drug hypersensitivity, cephalosporin antibiotic

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<sup>1</sup>Department of Allergy, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Wangfujing, Beijing, China

<sup>2</sup>Institute of Clinical Medicine, Peking Union Medical College, Chinese Academy of Medical Sciences, Beijing, China

\*Jianqing Gu and Shuang Liu contributed equally to this manuscript.

### Corresponding author:

Yuxiang Zhi, Department of Allergy, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, #1 Shuaifuyuan, Wangfujing, Beijing, 100730, China.  
Email: [yuxiang\\_zhi@126.com](mailto:yuxiang_zhi@126.com)



## Introduction

Cephalosporins are commonly prescribed antibiotics that can cause mild to severe immediate hypersensitivity reactions. Anaphylaxis is the most severe and dangerous reaction, because it usually involves multiple systems, especially the skin, and the respiratory and cardiovascular systems. Here, we report the unusual case of a patient with oral cefuroxime-induced anaphylaxis with prominent neurologic manifestations. The structure of cefuroxime is shown in Figure 1.

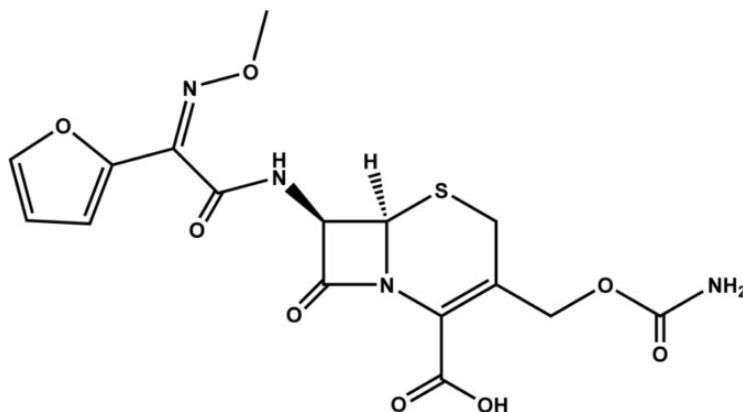
## Case report

Written informed consent was obtained from the patient to publish this case report, and the study was approved by the Ethics Committee of Peking Union Medical College Hospital and the Chinese Academy of Medical Sciences.

A 60-year-old woman was referred to the Department of Allergy at the Peking Union Medical College Hospital following an episode of convulsion and loss of consciousness 3 weeks before the referral. Because of a sore throat and cough, she had taken one tablet of cefuroxime (0.25 g) 10 minutes after breakfast (a steamed bun, millet

congee, and brined vegetables) at 7 a.m. Two to 3 minutes later, she experienced a burning sensation in her esophagus, which was not relieved by drinking water. Ten minutes later, she became dizzy, with loss of consciousness. Syncope and carpopedal spasm ensued, and her blood pressure fell to 45/10 mmHg. She recovered 30 minutes later after receiving shock treatment (0.5 mg epinephrine intramuscularly, 5 mg dexamethasone intravenously, and rehydration therapy) in the emergency department of a local hospital. The attack was not accompanied by fever, rash, cough, chest tightness, nausea, or abdominal pain. The patient's medical history was unremarkable and did not include food or drug allergies or epilepsy. A neurological physical examination at the local hospital, electrocardiography, electroencephalography, cranial computed tomography, and magnetic resonance imaging all revealed no notable findings.

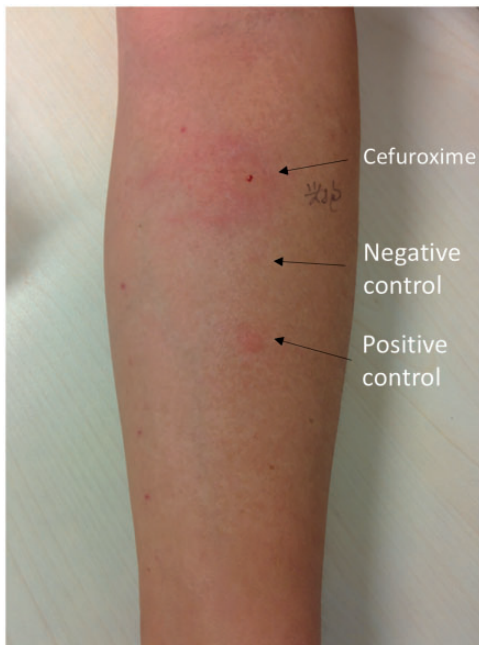
Routine blood test results at our hospital revealed elevated red blood cell counts ( $5.17 \times 10^{12}/L$ ), hemoglobin levels (154 g/L), and procalcitonin levels (0.31%) and a decreased red cell distribution width (37.8 fL). The total immunoglobulin E (T-IgE) level was high (106.0 kU/L), whereas IgE levels produced in response to



**Figure 1.** Structure of cefuroxime.

specific allergens were all  $<0.35$  kUa/L. The allergens sIgE d1 (*Dermatophagoides pteronyssinus*), d2 (*Dermatophagoides farinae*), f4 (wheat), f14 (soybean), f23 (crab), f24 (shrimp), m6 (*Alternaria alternata*), w6 (Mugwort), and wx7 (*Chrysanthemum leucanthemum*, *Taraxacum vulgare*, *Plantago lanceolata*, *Chenopodium album*, and *Solidago virgaurea*) were tested using testing kits (ImmunoCAP; Thermo Fisher Scientific/Phadia, Uppsala, Sweden).

The skin-prick tests for routine food allergen groups (over 40 allergens) was performed 1 week later, and the results were negative. However, a skin-prick test for diluted cefuroxime produced a  $13 \times 10$  mm wheal, a  $40 \times 30$  mm flare, and pruritus at the injection site (Figure 2), but no systemic symptoms such as rash, nasal itching, sneezing, coughing, or chest tightness. Cefuroxime-induced anaphylaxis was therefore diagnosed.



**Figure 2.** Skin-prick test results.

The results of the diluted cefuroxime skin-prick test (15 minutes after skin-prick test) are shown. This test was performed 1 day after the skin-prick tests for the food allergen groups.

## Discussion

Anaphylaxis is a severe, potentially life-threatening hypersensitivity reaction involving multiple systems. It is caused by the sudden release of mast cells and basophil mediators into the systemic circulation.<sup>1</sup> A recent study found that the lifetime prevalence of anaphylaxis varies from 0.02% to 5%.<sup>2</sup> Recorded hospitalization rates for anaphylaxis are increasing, although it is unclear whether this increase is real or simply the result of better identification.<sup>2</sup> While anaphylaxis may involve any organ, cutaneous involvement occurs most frequently, accounting for  $>90\%$  of all anaphylaxis patient cases.<sup>3</sup> Respiratory involvement occurs with the second-most frequency; its symptoms include dyspnea, wheeze, upper airway angioedema and rhinitis. Cardiovascular involvement (hypotension, shock, cardiac arrest) and central nervous involvement (impaired consciousness, seizures, spasms, involuntary voiding and defecating) appear to be more common in severe anaphylactic reactions.<sup>4</sup>

In our patient, the lack of classic cutaneous manifestations made it difficult to diagnose anaphylaxis. Differential diagnoses for convulsions with unclear causes include anaphylaxis, central nervous system diseases, and medication side effects. Our patient experienced persistent gastrointestinal discomfort (a burning sensation in the esophagus), beginning almost immediately after exposure to the likely allergen, and her blood pressure fell to 45/10 mmHg. In accordance with the 2011 World Allergy Organization (WAO) guidelines, these reactions are consistent with anaphylaxis.<sup>5</sup>

Drugs are believed to be the most common cause of anaphylaxis in adults. Beta-lactams are the second most frequent cause of anaphylaxis, reportedly accounting for 14.3% of all drug-induced anaphylaxis reactions.<sup>6</sup> Cephalosporins are the most frequently prescribed class of antibiotics, and they can trigger hypersensitivity reactions to varying degrees and with various severities and multi-systemic involvement. An integral diagnosis and treatment protocol for cephalosporin was proposed by Del Carpio-Orantes et al.<sup>7</sup>

The WAO recommends a clinical diagnosis of anaphylaxis when characteristic signs and symptoms occur shortly after exposure to a known or likely trigger.<sup>8</sup> Laboratory tests are usually not helpful in diagnosing anaphylaxis at patient presentation.<sup>8</sup> Diagnoses of drug hypersensitivity reactions are based on the patient's medical history and on clinical manifestations, using *in vivo* and, if possible, *in vitro* tests.<sup>9</sup> Compilation of a patient's clinical history requires careful collection of information and evaluation of factors such as symptomatology, chronology, other medications taken, and the medical background.<sup>10</sup> In our case, the patient became hypersensitive to cefuroxime after several courses of treatment, which further supports the diagnosis of IgE-mediated hypersensitivity.

Specific allergic diagnostic tests should be performed 4–6 weeks and 6–12 months after the complete resolution of clinical symptoms because false negatives may occur.<sup>10</sup> The chosen test should depend on suspected pathomechanisms: the skin-prick test and intradermal test for an IgE-dependent mechanism, and patch tests and/or a late-reading intradermal test for a T-cell-dependent mechanism.<sup>10</sup> Specific IgE assays are not recommended because they are less sensitive and less readily available than skin tests.<sup>11</sup> A medically supervised graded challenge/provocation test is the gold standard to identify the source of

drug hypersensitivity reactions,<sup>10</sup> and it is sometimes necessary to confirm and evaluate the recurrence risk.<sup>12</sup>

## Conclusion

Although anaphylaxis typically involves multiple systems, the patient in our case presented with cefuroxime-induced anaphylaxis with prominent neurologic symptoms. Thus, we suggest that clinicians consider the possibility of a drug-induced anaphylactic reaction when neurologic but not cutaneous symptoms are present.

## Author contributions

Jianqing Gu, Shuang Liu, and Yuxiang Zhi conceptualized the manuscript. Jianqing Gu acquired data and interpreted the results. Shuang Liu wrote the manuscript. Jianqing Gu and Yuxiang Zhi critically revised the manuscript. All authors read and approved the final manuscript.

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## Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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## ORCID iD

Shuang Liu  <http://orcid.org/0000-0003-2099-5140>

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