Anaphylactic Shock Following Cataract Surgery: A Documented Intracameral Cefuroxime Allergy

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Intracameral cefuroxime is recommended at the end of cataract surgery, since it has been shown to substantially reduce the rate of postoperative endophthalmitis, a severe postoperative infectious complication [1]. Intracameral cefuroxime is well tolerated, with few adverse events reported [1]. The development of topical anaesthesia means that more and more cataract surgeries are performed in outpatient centers [2], with fewer and fewer ophthalmologists considering the presence of an anesthetist to be necessary [3].

We report a case of documented life-threatening immediate hypersensitivity reaction to cefuroxime after cataract surgery.

An 81-year-old woman with no history of food or drug allergy underwent phacoemulsification and intraocular lens implantation in both eyes under topical anesthesia (3-week interval between procedures). The substances administered during the interventions were as follows: Minims oxybuprocaine hydrochloride 0.4% eye drops; Isobetadine (polyvidone iodine) 5% eye irrigation solution; intracameral Mydrane (tropicamide 0.04 mg/0.2 mL); phenylephrine chlorhydrate 0.62 mg/0.2 mL; lidocaine chlorhydrate 2 mg/0.2 mL; Healon EndoCoat, a viscoelastic device containing sodium hyaluronate; intracameral Aprokam (cefuroxime 1 mg/0.1 mL); and Maxitrol eye drops and ointment (dexamethasone 1 mg/mL; neomycin sulfate 3500 IU/mL; polymyxin B sulfate 6000 IU/mL). The intervention on the right eye was completed without complications. Three weeks later, the same procedure was repeated on the left eye. At the end of the intervention, the patient lost consciousness. Her blood pressure and heart rate were 40/20 mmHg and 140 bpm, respectively. Immediate management by the anesthetist comprised intravascular filling, intravenous epinephrine, and orotracheal intubation. The patient was then admitted to the intensive care unit. Within a few minutes she had developed erythematous macules on the limbs and swelling of the lips and eyelids. Refractory hypotension was treated with intravenous norepinephrine and epinephrine for 21 hours. Serum tryptase was elevated at 31.1 µg/L (normal value, <14 µg/L) at that time. Basal serum tryptase measured 16 weeks later was normal (6.6 µg/L). Anaphylactic shock due to a substance received during the cataract surgery was suspected. Two days later, the patient had fully recovered and was discharged with a well-tolerated 7-day course of amoxicillin/clavulanic acid for suspected respiratory infection. No ocular sequelae have been reported to date.

Four months later, after obtaining the patient’s informed consent, we performed diagnostic skin prick tests (SPTs) on the forearm, as previously described [4] and with some modifications, in a day hospital near the intensive care unit and under close medical supervision. We tested the medications used during surgery, namely, cefuroxime (5 mg/mL in 0.9% saline), a panel of cephalosporin derivatives (ie, cefazolin, ceftriaxone, cefepime) at 100 mg/mL in saline (concentration already used in more than 50 patients in our center without skin irritation), and latex (ALK-Abello BV). All the compounds were tested at the same time. Ten minutes after the SPTs, the patient developed malaise, dyspnea, palmar pruritus, labial edema, and erythema of the right arm. Blood pressure fell to 80/40 mmHg (150/80 mmHg before the tests). Intravascular filling, intravenous epinephrine, corticosteroids, and oral antihistamine were administered immediately, and the patient’s condition improved quickly. SPT results were positive for cefuroxime (15×15 mm wheal reaction), ceftriaxone (9×8 mm), and cefepime (10×11 mm) and negative for all other drugs. Histamine (ALK-Abello BV, 10 mg/mL, 6×5 mm) was used as a positive control and saline solution as a negative control. In vitro assays for specific IgE antibodies to penicilloyl G, penicilloyl V, amoxicilloyl, ampicilloyl, cefaclor, and latex (ImmunoCAP Specific IgE, Thermo Fisher Scientific) were performed according to the manufacturer’s instructions. The results were all negative (<0.1 kU/L).

The patient experienced 2 severe anaphylactic reactions: one after cataract surgery and another (less severe) after SPTs. SPTs provided convincing evidence that cefuroxime was the causal agent of the anaphylactic shock following surgery. SPTs also identified cross-sensitization to other cephalosporins with the same R1 side chain [5]. As the antibiotics were tested at the same time, cross-reactive cephalosporins may have also contributed to the systemic reaction following SPTs.

This report demonstrates that anaphylactic reactions can be induced by drugs injected into the anterior chamber of the eye. Interestingly, the first intracameral cefuroxime injection did not trigger allergic manifestations. Since the patient had never received cefuroxime before, we hypothesize that sensitization occurred during the first procedure. Under normal conditions, the blood–aqueous barrier restricts entry of inflammatory and immune cells into the eye and separates the anterior chamber from the bloodstream [6]. However, as this barrier is ruptured during cataract surgery [6], immune cells could be exposed to cefuroxime, leading to sensitization in the first procedure and anaphylactic reaction in the second.

Our findings should make clinicians aware that perioperative anaphylactic reactions may not always be predictable and can occur during surgery under topical anesthesia. The presence of an anesthetist is useful for management of such life-threatening complications.
To our knowledge, 3 cases of anaphylactic reactions to intracameral administration of cefuroxime during cataract surgery have been reported to date [7-9] (Table). The results of allergy testing were not available in 2 of the cases. The role of cefuroxime allergy was based only on a history of penicillin allergy [7,8], although there is usually no cross-reactivity between penicillin and cefuroxime because of different R1 side chains [5]. Moreover, other drugs administered during cataract surgery might also have triggered the systemic reactions. In the third case, the patient had a history of anaphylactic reaction after intravenous and oral administration of cefuroxime [9]. The patient was referred to an allergist, who confirmed ß-lactam allergy, although the details of the allergy tests were not reported [9]. Our report emphasizes the need to accurately identify the causal agent involved in the development of anaphylactic reactions after cataract surgery and to explore potential cross-sensitization by performing appropriate allergy tests in order to propose accurate avoidance measures. These tests should be performed under close medical supervision, given the risk of severe anaphylactic reactions, as reported here and elsewhere [10]. If systemic reactions occur after administration of a small quantity of antibiotics to the eye, SPTs should be performed more cautiously at higher dilutions.

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**Conflicts of Interest**

The authors declare that they have no conflicts of interest.

<table>
<thead>
<tr>
<th>Author, year</th>
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<th>Previous known allergy</th>
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<tbody>
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<tr>
<td>Present case</td>
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<td>Second</td>
<td>Hypotension, skin rash, lips and eyelids swelling, loss of consciousness</td>
<td>Recovery</td>
<td>Yes</td>
<td>Yes (skin prick tests)</td>
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**References**

DRESS Syndrome Induced by a Gadolinium-Based Contrast Agent in a 13-Year-Old Boy

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Drug rash with eosinophilia and systemic symptoms (DRESS) syndrome is characterized by a combination of high fever, maculopapular rash, lymphadenopathy, eosinophilia with atypical circulating lymphocytes, reactivation of human herpesvirus (HHV), and multiorgan involvement [1]. It is an uncommon, life-threatening syndrome that appears 2 to 8 weeks after the intake of the eliciting drug. Initially described with aromatic antiepileptic drugs, DRESS syndrome can be induced by many other agents [2]. We report the case of a patient who developed DRESS syndrome associated with several drugs, one of which was a gadolinium-based contrast agent (GBCA).

A 13-year-old boy was admitted to the hospital with suspected pyelonephritis. Blood culture was positive for Staphylococcus aureus, and treatment with intravenous cefotaxime and vancomycin was subsequently prescribed. Analgesia was added with metamizole, paracetamol, and dexketoprofen owing to intense back pain. The following day, left paravertebral pyomyositis was confirmed by magnetic resonance imaging (MRI) with the GBCA gadobutrol.

After 23 days of treatment and 22 days after the MRI, the patient developed fever and pruriginous maculopapular rash affecting the face and trunk. This worsened after each dose of cefotaxime, which was replaced by meropenem. Seven days later, the patient had only mild symptoms and was discharged with oral rifampicin and cloxacillin. A few hours later, the patient was readmitted with fever (39ºC) and aggravation of the rash (which had spread in a cephalocaudal manner), facial edema, and painful occipital lymphadenopathies.

Laboratory studies revealed a leukocyte count of 21 370/µL with 8.3% eosinophils (1770/µL), increasing 5 days later to 22 270/µL with 15.9% eosinophils (3530/µL). We also recorded abnormal liver enzymes and renal function profile...