Anaphylactic shock following cataract surgery: a documented intracameral cefuroxime allergy

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Intracameral cefuroxime administration is recommended at the end of cataract surgery, since this has been shown to reduce substantially the rate of postoperative endophthalmitis, a dramatic postoperative infectious complication[1]. Intracameral cefuroxime is well tolerated with few reported adverse events [1]. With development of topical anesthesia, more and more cataract surgeries are performed in ambulatory centres [2], while it seems that fewer and fewer ophtalmologists consider 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, without history of previous food or drug allergy, underwent phacoemulsification and intraocular lens implantation of both eyes under topical anesthesia at a 3-weeks interval. Substances administered during the interventions included: Minims oxybuprocaine hydrochloride® 0.4% eye drops, Iso-betadine® (polyvidone iodine) 5% eye irrigation solution, intracameralMydrane® (tropicamide 0.04mg / 0.2mL, phenylephrine chlorhydrate 0.62mg / 0.2mL, lidocaine chlorhydrate 2mg / 0.2mL), HealonEndoCoat®, a viscoelastic device containing sodium hyaluronate, intracameralAprokam® (cefuroxime 1mg / 0.1mL), Maxitrol® eye drops and ointment (dexamethasone 1 mg/mL, neomycin sulphate 3500 UI/mL, polymyxin B sulfate 6000 UI/mL). The intervention on the right eye completed without complication. Three weeks later, the same procedure was repeated on the left eye. At the end of the intervention, the patient lost consciousness. Blood pressure and heart rate were measured at 40/20 mmHg and 140 beats per minute, respectively. She was immediately managed by the anesthetist by intravascular filling, intravenous adrenaline, and orotracheal intubation. She was then admitted to the intensive care unit. Erythematous macules on the

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limbs and swelling of the lips and eyelids appeared within a few minutes. Refractory hypotension was treated with intravenous norepinephrine and adrenaline for 21 hours. Serum tryptase was elevated at 31.1 µg/L (normal value < 14 µg/L) at that time. Her basal serum tryptase measured 16 weeks later was normal (6.6 µg/L). An 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 a suspected respiratory infection. So far, there has been no ocular sequel.

Four months later, after obtaining patient's informed consent, we performed diagnostic skin prick-tests (SPT), as previously described [4] with some modifications,on the forearm, in day hospital near intensive care unit and under close medical supervision. We tested the medications used during surgery, cefuroxime (concentration of 5 mg/mL in 0.9% saline), a panel of cephalosporin derivatives (i.e. cefazolin, ceftriaxone, cefepime) at a concentration of 100 mg/mL in saline (concentration already used in more than 50 patients in our centre without skin irritation), as well as latex (ALK-Abello BV). All the compounds were tested at the same time. Ten minutes after SPT, malaise, dyspnea, palmar pruritus, oedema of the lips and erythema of the right arm appeared. The blood pressure fell to 80/40 mmHg (150/80 before the test).Intravascular filling, intravenous adrenalin, glucocorticoids and oral antihistamine were immediately administered and the patient's condition improved quickly. SPT were positive for cefuroxime (15x15 mm wheal reaction), ceftriaxone (9x8 mm) and cefepime (10x11 mm) and negative for all other molecules, with a positive histamine control (ALK-Abello BV) 10 mg/ml at 6x5 mm and negative control with sodium chloride. In vitro assays for specific IgE antibodies to penicilloyl G, penicilloyl V, amoxicilloyl, ampicilloyl, cefaclor and latex(ImmunoCAP® Specific IgE, Thermo Fisher Scientific, Uppsala, Sweden) performed according to the manufacturer's instruction were all negative (≤ 0.1 kU/L).

Our patient developed two severe anaphylactic reactions: one severe after a cataract surgery and one less severe after SPT. SPT provided convincing evidence that cefuroxime was the causal agent of the anaphylactic shock following the surgery. SPT also identified cross-sensitization to other cephalosporins with the same R1 lateral chain[5]. As the antibiotics

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were tested at the same time, cross-reactive cephalosporins may also have contributed to the systemic reaction following SPT.

This report demonstrates that anaphylactic reactions may happen for drugs injected into the anterior chamber of the eye. Interestingly, the first intracameral cefuroxime administration did not trigger allergic manifestations. Since our patient had never received cefuroxime before, we hypothesize that sensitization occurred during the first procedure. In normal conditions, the blood–aqueous barrier restricts entry of inflammatory and immune cells into the eye and separate the anterior chamber from the blood flow [6]. However, as this barrier is ruptured during cataract surgeries [6], this allowed cefuroxime exposure to immune cells, leading to sensitization and anaphylactic reaction during the first and second surgery, respectively.

This report should also increase the awareness thatperioperative anaphylactic reactions are sometimes not predictable and can occur during surgeries under topical anaesthesia. The presence of an anesthetist is useful to manage such life threatening complications.

To our knowledge,3 cases of anaphylactic reactions to intracameral administration of cefuroxime during cataract surgery have so far been reported[7-9] (Table 1).In two previously published cases, the result of allergic tests were not available. The role of cefuroxime allergy was only based on 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 surgeries might also have triggered the systemic reactions. In the third case, there was a history of anaphylactic reactions after intravenous and oral cefuroxime administration [9]. The patient was addressed to an allergist that confirmed beta-lactam allergy, but the details of the allergic tests were not reported [9]. Our report emphasises 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 allergic tests, in order to propose accurate eviction measures. These tests should be performed under close medical supervision, given the risk of severe anaphylactic reactions, as in our case and as previously reported [10]. If systemic reactions

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occurred after administration of small quantity of antibiotics in the eye, SPT should be made with more precautions at higher dilutions.

Declaration of conflicts of interest

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References

1. Barry P, Cordovés L, Gardner S. Guidelines for Prevention and Treatment of Endophthalmitis following Cataract Surgery: Data, Dilemmas and Conclusions. European Society of Cataract and Refractive Surgeons, Dublin, Ireland. 2013. http://www.escrs.org/endophthalmitis/guidelines/ENGLISH_2018_updated.pdf. Accessed January 30, 2021.
2. Stagg BC, Talwar N, Mattox C, Lee PP, Stein JD. Trends in Use of Ambulatory Surgery Centers for Cataract Surgery in the United States, 2001-2014. JAMA Ophthalmol. 2018;136:53-60.
3. Chandradeva K, Nangalia V, Hugkulstone CE. Role of the anaesthetist during cataract surgery under local anaesthesia in the UK: a national survey. Br J Anaesth. 2010;104:577-81.
4. 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.
5. Romano A, Gaeta F, Valluzzi RL, Maggioletti M, Zaffiro A, Caruso C, et al. IgE-mediated hypersensitivity to cephalosporins: Cross-reactivity and tolerability of alternative cephalosporins. J Allergy Clin Immunol. 2015;136:685-91 e3.
6. Liu Y, Luo L, He M, Liu X. Disorders of the blood-aqueous barrier after phacoemulsification in diabetic patients. Eye. 2004;18:900-4.
7. Villada JR, Vicente U, Javaloy J, Alió JL. Severe anaphylactic reaction after intracameral antibiotic administration during cataract surgery. J Cataract Refract Surg. 2005;31:620-1.
8. Moisseiev E, Levinger E. Anaphylactic reaction following intracameral cefuroxime injection during cataract surgery. J Cataract Refract Surg. 2013;39:1432-4.
9. Kędziora W, Żarnowski T. [Anaphylactic shock due to Aprokam application to the anterior chamber during cataract surgery – case report] Wstrząs anafilaktyczny po podaniu Aprokamu do komory przedniej podczas operacji zaćmy – opis przypadku. Klin Oczna. 2016;118:298-300.
10. Fernandes RA, Regateiro FS, Pita J, Ribeiro C, Carrapatoso I, Todo-Bom A, et al. Severe Anaphylaxis With Cardiac Arrest Caused by Prick Test With Cefuroxime. J Investig Allergol Clin Immunol. 2018;28:426-8.

Table 1. Cases reported of anaphylactic reactions following intracameral cefuroxime administration.

Author, year	Age (years)	Previous known allergy	First/ second surgery	Manifestations	Endpoint	Anesthetist present in operating theatre	Allergic confirmation
Villada et al, 2005 [7]	68	Ampicillin	Second (first: no antibiotic used)	Hypotension, dyspnea, eyelid swelling	Recovery	Yes	Not available
Moisseiev et al, 2013 [8]	64	Penicillin	Not specified	Hypotension, dyspnea, skin rash, tongue swelling, vomiting, lethargy	Recovery	No	Not available
Kędziora et al, 2016 [9]	Not reported	Cefuroxime	Not specified	Hypotension, dyspnea, breathing arrest, skin rash, agitation, unconsciousness	Recovery	Yes	Yes (tests not specified)
Our case	81	None	Second	Hypotension, skin rash, lips and eyelids swelling, unconsiousness	Recovery	Yes	Yes (skin prick-tests)