



Acute macular edema and serous detachment on the first day after phacoemulsification surgery: A case report

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ABSTRACT

Purpose: To report a case of an acute macular edema with serous retinal detachment on the first day after uncomplicated phacoemulsification surgery with the use of a standard dose of intracameral cefuroxime at the end of the surgery.

Observations: A 46-year-old man underwent a technically uneventful right eye phacoemulsification surgery using a standard dose (1mg/0.1mL) of cefuroxime solution injected into the anterior chamber at the end of the surgery. Serous macular edema and detachment were in our case observed on the first post-operative day. Without surgical intervention fast clinical recovery was observed and best corrected visual acuity improved to the final visual outcome of 1.0, which was satisfactory 10 days after surgery.

Conclusions and Importance: Acute serous macular detachment and edema should be considered in cases of poor visual acuity in the early postoperative period. The role of a standard dose of cefuroxime toxicity should be more widely explored and discussed.

1. Introduction

Cataract surgery is a commonly worldwide performed surgical procedure in elderly people.¹ Cataract surgery, same as other surgery procedures carries the risk of potential intraoperative and postoperative complications. One of them is well-known pseudophakic cystoid macular edema (CME) which is the most common cause of decreased vision following cataract surgery.^{2,3} The pathophysiology still remains unclear and the cause of cystoid macular edema is multifactorial. Different reports describe the influence of various causative factors in its development such as history of uveitis, history of diabetes mellitus, complicated cataract surgery, inflammation and vascular instability or vitreomacular traction and light toxicity.⁴⁻⁶ It is supposed that the main role is played by an inflammatory process that results in the creation of a physiological barrier between blood-aqueous liquid and/or blood-retina barrier. It is believed that any surgical manipulation in the anterior chamber may lead to the release of arachidonic acid from uveal tissue, the production of leukotrienes through the lipoxygenase pathway or prostaglandins (PG) through cyclooxygenase (COX) pathway.⁷ In addition to the manipulation within the anterior segment of an eye, substance used during the procedure may also have potential adverse impact on the

development of postoperative macular edema. In Europe cefuroxime sodium is a broad-spectrum second-generation cephalosporin antibiotic which is used to prevent postoperative endophthalmitis.⁸ Based on the analysis of the findings of the European Society of Cataract & Refractive Surgeons (ESCRS) multicenter study the use of intracameral cefuroxime in the concentration of 1 mg/0.1 mL at the end of surgery reduced the occurrence of postoperative endophthalmitis.⁸ In Europe, cefuroxime is available for intracameral injection as Aprokam and Ximaract.⁹ Intracameral injection of a standard dose of cefuroxime (0.1mL of 10mg/mL solution) has been reported to reduce the risk of postoperative endophthalmitis after cataract surgery.^{10,11} Despite the use of perioperative antibiotic prophylaxis and modern techniques of phacoemulsification which have reduced surgical injuries to the eye, there may occur many postoperative vision-threatening complications. One of them, as mentioned before, is macular edema (ME) which still remains an important cause of lower postoperative visual acuity than expected. In order to make the diagnosis of CME, there are required postoperative deterioration of vision and visualized CME on funduscopy, fluorescein angiography (AF), or optical coherence tomography (OCT).¹² ME usually occurs after 6–8 weeks after surgery¹³; according to the other authors about 4–6 weeks after surgery¹⁴ or 4–12 weeks after surgery,¹⁵ and

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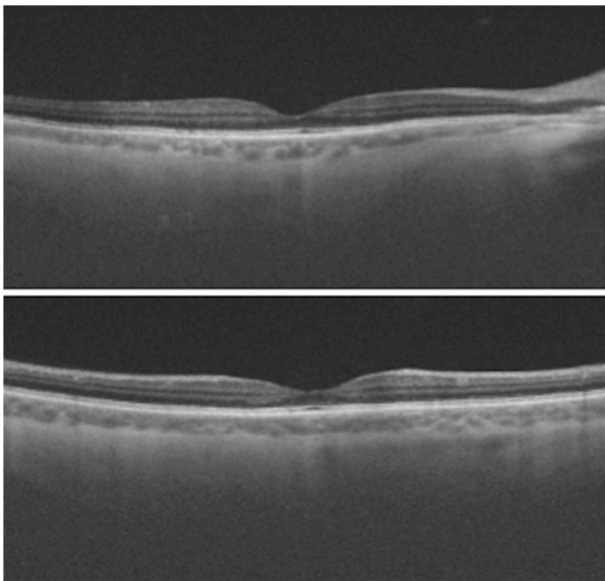


Fig. 1. Swept Source Optical Coherence Tomography (SS-OCT). The retinal SS-OCT image of the right eye showed normal macular morphology. The vitreous humour adhered to the retina.

it has been reported in the literature in 0.2%–2% of surgical eyes.^{3,12,16} Acute macular edema with retinal detachment after cataract surgery is a very rare complication after uncomplicated phacoemulsification surgery. We would like to report an acute serous macular edema and detachment on the first day after uncomplicated phacoemulsification with the use of a standard dose of cefuroxime (1mg/0.1mL) that was manifested by visual acuity impairment and was detected by OCT on the first postoperative day.

1.1. Case report

A 46-year-old male patient was admitted to Chair and Clinical Department of Ophthalmology, School of Medicine with the Division of Dentistry in Zabrze, Medical University of Silesia in Katowice for standard procedure of cataract surgery. He had no significant medical or drug history, diabetic, uveitis as well as no previous retinal disease in both eyes. The patient presented in the case report is relatively young for the cataract occurrence. This is because the patient has had a right eye blunt injury in the past. The patient did not come to an ophthalmological examination directly after the eye injury several years ago in the past (lack of medical documentation). A few years after the right eye injury, when his vision began to deteriorate, he came to an ophthalmologist for examination. Then he was diagnosed with cataract in his right eye. On admission the preoperative best corrected visual acuity was (BCVA): right eye (cc -1.0Dcyl axis 175°) 0.1; left eye (cc +0.25Dsph -0.75Dcyl axis 175°) 1.0; intraocular pressure (IOP) in both eyes was 16 mmHg. Axial length in the right eye 23.19mm; in the left eye 22.83mm measured by IOL Master (Carl Zeiss Meditec, Inc, Dublin, California, USA). Corneal endothelial cell density of the right eye was 2240/mm² and 2221/mm² of the left eye. Fundus examination of the right eye was unremarkable. He also had preoperative normal retinal morphology by swept source OCT (DRI SS-OCT Triton, Topcon) (Fig. 1) documented before cataract surgery. Preoperative pupil dilation was achieved with 1% tropicamide and 10% neosynephrine eye drops. Standard 2.6mm phacoemulsification procedure with acrylic posterior chamber intraocular lens (PCIOL) implantation into the lens capsule was performed under topical anesthesia (proxymethacaine 0.5%) by an experienced surgeon. The surgery was uneventful. A standard dose of 1mg/0.1mL intracameral cefuroxime (Aprokam) was administered into anterior chamber at the end of the surgery. On examination on the first

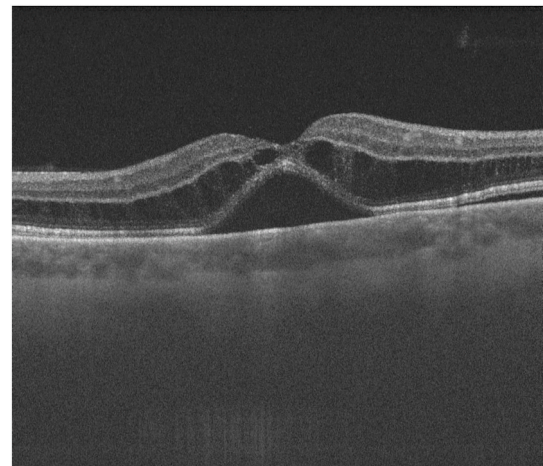


Fig. 2. SS-OCT scan of the right eye on the first postoperative day. The retinal SS-OCT image revealed a serous macular detachment with subretinal fluid mainly within the foveal area accompanied by macular edema. The fluid accumulation especially in the outer nuclear layer. The central macular retinal thickness increased to 697 μ m.

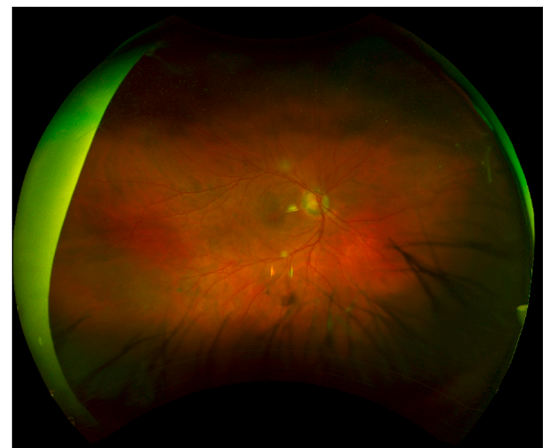


Fig. 3. The scanning laser ophthalmoscopy photograph of the right eye on the first postoperative day. The image revealed no peripheral retinal abnormalities.

postoperative day, the patient complained about painless visual acuity deterioration in his right eye and central scotoma. Right eye (RE): best corrected visual acuity (BCVA) was 0.02. Intraocular pressure was within normal limits (15 mmHg). Corneal endothelial cell density of the right eye was 2161/mm². On the slit lamp examination, the anterior segment of the eye was clear with clear anterior chamber and no signs of remarkable inflammation or abnormality in the vitreous. A dilated fundus examination showed diffuse macular edema. There were no cotton wool spots or retinal haemorrhages. The SS-OCT and fluorescein angiography (AF) were performed on the same day. Retinal SS-OCT scan revealed a serous macular detachment with subretinal fluid mainly within the foveal area accompanied by macular edema, with the fluid accumulation especially in the outer nuclear layer (Fig. 2). The central macular retinal thickness increased to 697 μ m. In the choroid there wasn't found any significant abnormalities. The subfoveal choroidal thickness was 220 μ m. The vitreous humour adhered to the retina. There wasn't observed posterior vitreous detachment in the SS-OCT image. The scanning laser ophthalmoscopy was performed and revealed no peripheral retinal abnormalities. (Fig. 3). B-scan ultrasonography revealed correct outline of the eyeball with no signs of scleritis or choroidal infiltration. Fluorescein angiography of the right eye on the first postoperative day: on early phase a non-fluorescent zone is visible

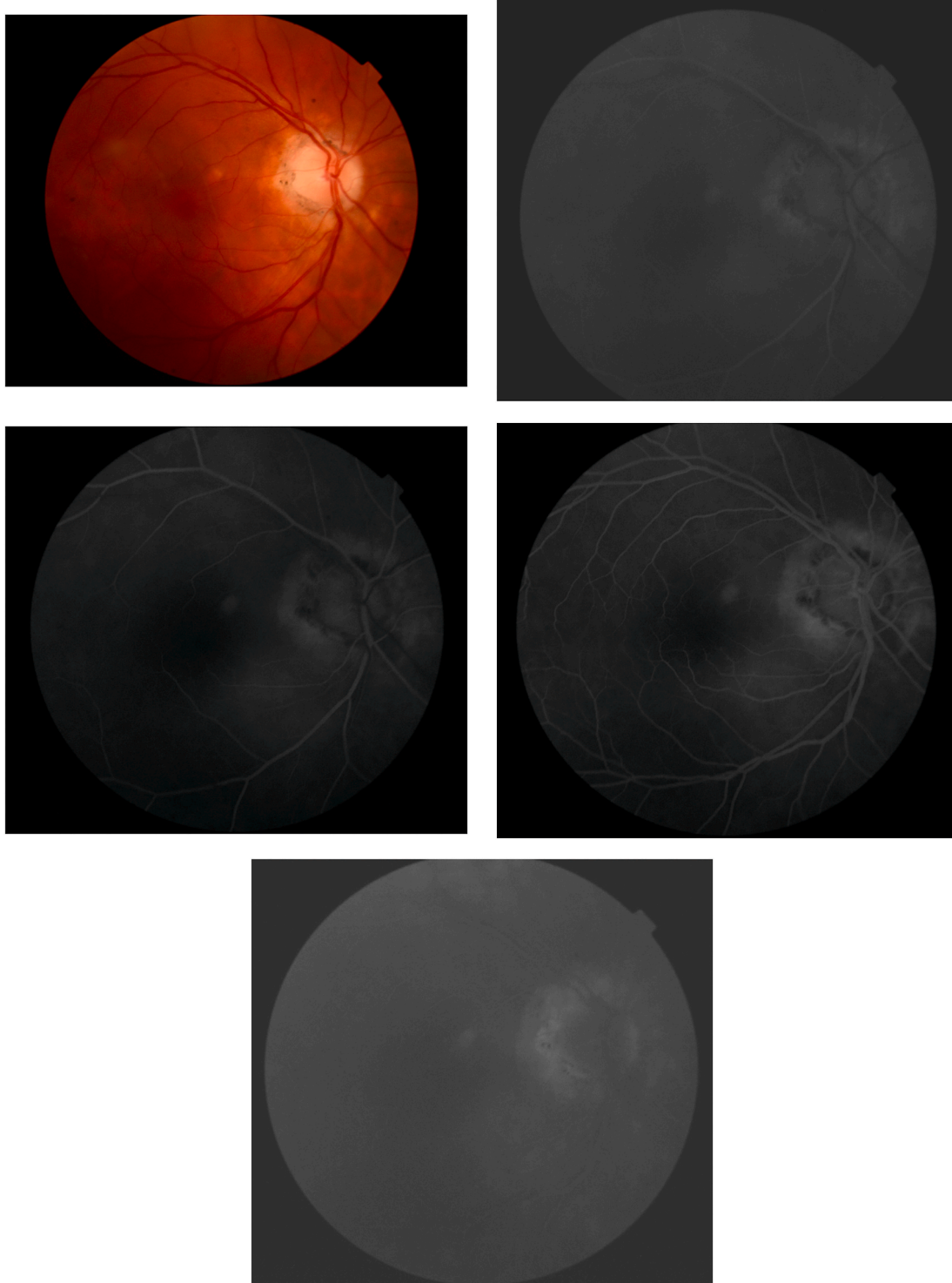


Fig. 4. a. The color fundus photography of the right eye on the first postoperative day. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.). b–e. Fluorescein angiography of the right eye on the first postoperative day demonstrated: on early phase a non-fluorescent zone is visible adjacent to the optic disc. Outside it is surrounded by an irregularly fluorescent band. In late phase a diffusing fluorescein from the periphery of the non-fluorescent zone is reaching the disk. Numerous, diffuse, non-fluorescent spots corresponding to RPE formation within and in the borders of peripapillary atrophy were noted. The hyperfluorescent spot of the approximate size of 400–500 μm located parafoveally in the upper nasal region of the macula was visible from early phases and presented diffuse borders in late phases. Foveal avascular zone did not reveal noticeable changes.

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of the approximate size of 400–500 μm located parafoveally in the upper nasal region of the macula was visible from early phases and presented diffuse borders in late phases. Foveal avascular zone did not reveal noticeable changes (Fig. 4). At the same day, the patient was treated with: nimesulide (0.100g), acetazolamide (0.250g), pentoxifylline

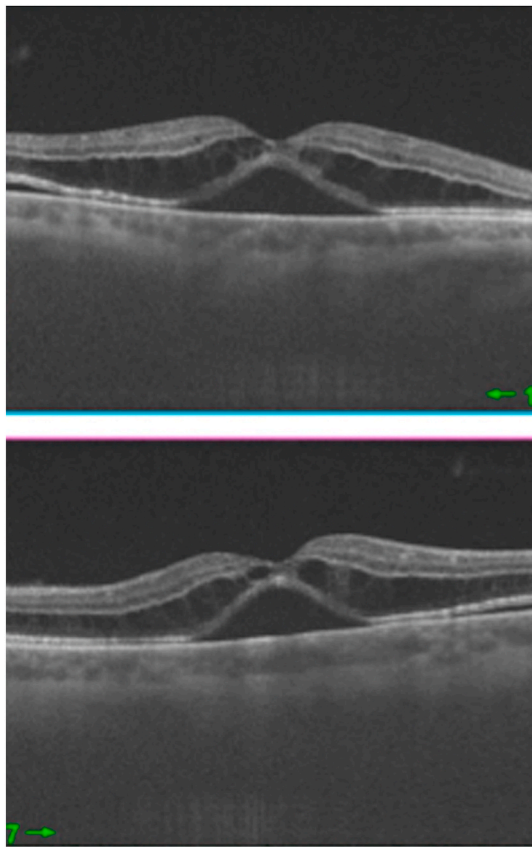


Fig. 5. SS-OCT scan of the right eye on the second postoperative day. The retinal SS-OCT image revealed a serous macular detachment and edema with partial reabsorption of subretinal fluid with some persistent intraretinal and subretinal spaces. The central macular retinal thickness decreased to 537 μm . There weren't observed any vitreomacular tractions and PVD.

(0.100g), pantoprazole (PPI - proton pump inhibitor) (0.020g) and with topical drops 0.1% dexamethasone and levofloxacin 7 times a day, bromphenacum 2 times a day and 1% tropicamide 5 times a day. On the second postoperative day the BCVA improved to 0.1. The SS-OCT was performed on the second postoperative day. Retinal SS-OCT scan revealed a serous macular detachment and edema (Fig. 5). The central macular retinal thickness decreased to 537 μm . There wasn't found any vitreomacular traction and there wasn't observed posterior vitreous detachment (PVD) in the SS-OCT image as well. The patient was discharged home on the third day after surgery with BCVA OD 0.3 with appropriate recommendations: in the right eye topical drops 0.1% dexamethasone and levofloxacin 7 times a day, bromphenacum 2 times a day and 1% tropicamide 5 times a day until the follow up examination in 7 day. He reported to the Hospital for a follow-up 7 days after hospital discharge. On examination 10 days after cataract surgery procedure, visual acuity in the right eye increased up to 0.8. Intraocular pressure was 15 mmHg. The anterior segment of the right eye was calm and stable with transparent optical media, clear anterior chamber and proper centration of the intraocular lens. The fundus image of the right eye was normal (Fig. 6). The macular retina was scanned in the same area. The central retinal thickness returned to the normal range-it was 189 μm . The macular edema and subretinal fluid were fully absorbed. There wasn't observed posterior vitreous detachment, but the floaters appeared in the back of the vitreous adjacent to the retina (Fig. 7). In the following 24 months the BCVA in the right eye was 1.0, no recurrence of macular detachment or edema were observed. (Fig. 8).

2. Discussion and conclusions

Cystoid macular edema (CME) is a primary cause of reduced vision after cataract surgery. Positive preoperative medical history - uveitis in the past or the presence of diabetes mellitus with diabetic retinopathy as well as intraoperative complications - can raise the risk of CME after surgery.^{17,18} In Europe, after 2007, when, the European Society of Cataract and Refractive Surgeons (ESCRS) conducted the first randomized controlled trial and observed a five-fold decrease in the incidence of postsurgical endophthalmitis with the use of intracameral cefuroxime, we observed the increased adoption of the routine use of intracameral cefuroxime as prophylaxis from 30% in 2007 to nearly 50% in 2014. Concentration of 1mg/0.1mL has been shown to be safe and efficacious.^{8,19} In the presented case, the patient had no retinopathy, hypertension, diabetic or uveitis history. Our case illustrates that in the absence of vascular or inflammatory causes (such as retinopathy or uveitis in previous history), a standard dose of cefuroxime may be associated with serous macular detachment and CME that may already occurs on the first day after surgery. The etiology of CME is not fully understood. Gulikilik et al. have described potential mechanisms which may lead to the occurrence of macular edema after cataract surgery.¹³ Toxicity of cefuroxime may also cause acute serous macular edema and macular detachment. In the literature, there are 19 intracameral preparations reported to be commonly used during cataract surgery where the cefuroxime is listed as the second highest free radical concentrations.²⁰ We had also taken into consideration the differentiation with the toxic anterior segment syndrome (TASS) which is a rare, acute and severe intraocular inflammation. It usually takes place within 12–48 hours after the anterior segment surgery. The patient had no increased intraocular pressure, no diffuse corneal edema, no hypopyon and no photophobia, which allowed for an exclusion of TASS. Hypotonous maculopathy is another complication that may occur after phacoemulsification and should be included in the differential diagnosis of ME. In the presented case, the patient had an intraocular pressure within normal limits, therefore, hypotonous maculopathy was excluded. Retinal vein occlusion is as well a potential cause of macular edema that was excluded in presence in our case. The other potential cause of ME is a vitreomacular traction. In their prospective study, Gulikilik et al. demonstrated that complete posterior vitreous detachment (PVD) may have a protective effect against CME development.¹³ In the presented case report the SS-OCT imaging was performed and there were no observed PVD and vitreomacular tractions which could have a potential impact on the observed ME. The surgery was performed by an experienced surgeon in a short time without any intraoperative complications. On the other hand, Copete et al. in their prospective cohort study revealed that previous PVD or vitreoretinal contact did not seem to be a risk factor for pseudophakic cystoid macular edema (PCME), however, the only variable risk factor associated with PCME was identification of a nonsurgical epiretinal membrane (ERM) on preoperative SS-OCT. According to the authors, this may indicate that the development of CME may be influenced by other factors besides status of the vitreoretinal interface.²¹ Recently the American authors reported the case of acute macular edema with serous retinal detachment after cataract surgery with standard intracameral cefuroxime prophylaxis in a vitrectomized eye.²²

In the literature there are several reports of early serous retinal detachment (RD) and CME following the use of intracameral injection of cefuroxime sodium in a high dose (40–62.5mg/mL).^{23,24} Wong et al. reported transient macular edema of intracameral injection of cefuroxime at a dose of 9mg/0.1mL associated with diminished visual acuity in 6 of 13 exposed eyes.²⁵ Other authors also reported early serous macular detachment after intracameral injection of cefuroxime at a dose of 2mg/0.1mL after phacoemulsification surgery.¹⁵ Delyfer et al. also reported 6 cases that received a dose of 10 mg/0.1 mL into the anterior chamber at the end of the phacoemulsification by mistake.²³ Similar complications on the first postoperative day were observed by Kontos



Fig. 6. a. The scanning laser ophthalmoscopy of the right eye on the tenth postoperative day. The color photography revealed no peripheral retinal abnormalities. b. The autofluorescence image of the right eye. There are abnormalities in two spots in interpapilomacular area, one of them clearly corresponds to the FA images. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

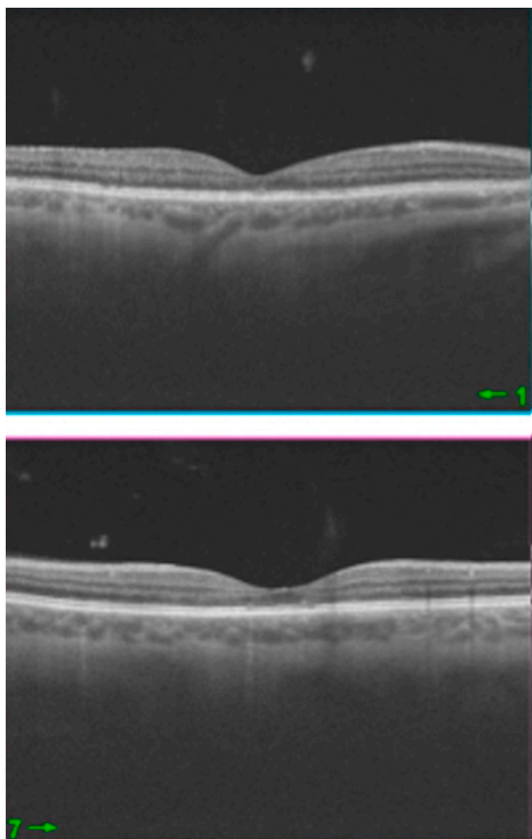


Fig. 7. SS-OCT scan of the right eye on the tenth postoperative day. The retinal SS-OCT image revealed a complete reabsorption of intraretinal and subretinal fluid (the central macular retinal thickness: 189 μm). There wasn't observed PVD. The floaters appeared in the back of the vitreous adjacent to the retina. There is an RPE abnormality in interpapillomacular area.

et al. with the use of a standard dose (62.5 mg/mL) of subconjunctival injection of cefuroxime.²⁶ Gimenez-de-la Linde et al. in their work described the occurrence of ME in the immediate postoperative period with temporary deterioration of visual acuity after administration of an excessive volume of cefuroxime into the anterior chamber of an eye at the end of surgery.²⁷ On the other hand, there are several reports in which the authors observed the occurrence of serous RD and ME after the intracameral injection of a standard dose of cefuroxime. The retinal toxicity, which occurred on the second postoperative day after use of a standard dose of intracameral cefuroxime administrated at the end of the surgery, was observed by Faure et al.²⁸ In our case report we postulate that an intracameral injection of a standard dose of cefuroxime resulted in the macular changes which closely resemble those recently reported by Xiao et al. in China.²⁹ A similar case report was described by Longo et al.¹⁴ Svetozarskiy et al. also reported a similar complication at the patient on the first postoperative day after cataract phacoemulsification with 1 mg intracameral cefuroxime injected.³⁰ Aslankurt et al. experienced the same problem as we report. In 8 patients who underwent uneventful phacoemulsification with the use of 1 mg/0.1 mL of cefuroxime during surgery, they revealed a serous macular detachment with intraretinal fluid accumulation.³¹ Similar to our case report Le Du et al. reported six patients with macular edema predominantly in the outer retinal layers associated with serous retinal detachment after cataract surgery with a standard dose of intracameral cefuroxime injection. Authors based this strong suspicion of retinal toxicity on clinical, pharmacokinetic, tomographic and retinographic criteria.³² We can notice that not only dilution errors of cefuroxime may induce adverse effects but also the method of injection of cefuroxime in the course of phacoemulsification. In the study performed by Zuo et al., there were 20

patients who had acute macular edema and extensive posterior serous neurosensory RD after uneventful phacoemulsification with the use of the correct dilution of a standard dose of cefuroxime (1 mg/0.1 mL).³³ The authors suggest that it may have been caused by transient retinal pigment epithelium sodium-potassium pump dysfunction. The pump function of retinal pigment epithelium (RPE) membrane proteins is to regulate the amount and composition of subretinal and outer retinal fluid and to maintain the adhesion between the neural retina and RPE.^{34,35} Andreev et al. suggested that serous detachment of retinal pigment and sensory epithelia that occurred at the described case report in the first day after uncomplicated cataract phacoemulsification may be caused by a toxic reaction to a standard dose of intracameral cefuroxime administrated.³⁶ In our case report and in the two cases reported by Xiao et al., the visual impairment was detected earlier than the one reported by Faure et al.,²⁸ however we suppose that the retinal toxicity in these cases may have been caused by cefuroxime toxicity although it was a use of a standard intracameral dose. Of course, one may argue that the retinal changes may represent post-operative CME (Irvine-Gass Syndrome), nonetheless this is highly unlikely due to the timing of the acute macular edema and detachment on the first postoperative day. The Irvine-Gass syndrome usually appears 4–12 weeks after surgery and in most symptomatic eyes spontaneously improve from 3 to 12 months; nevertheless, it can occur even several months after cataract surgery and it might be associated with inflammation medium, vitreomacular traction, intraoperative complications or the type of surgery.³⁷ On the first postoperative day we performed the fluorescein angiography and optical coherence tomography. The result of the examination does not affirm consistent with Irvine-Gass syndrome. In the literature, there are other similar studies in which the authors describe the case of a patient who had serous RD after uneventful phacoemulsification with the use of a standard dose of intracameral cefuroxime (1mg/0.1mL).³⁶ In our case report, AF did not reveal pathological vascular activity and hemoretinal barriers disruption compared to other reports.^{28,36} Faure et al. observed in the electroretinogram (ERG) results of the patient that cefuroxime was toxic to retina and may cause the Müller cell function, however the retinal physiopathology of the toxicity remains unclear.²⁸ In the ERG recording, they observed that cefuroxime toxicity affected the entire retina, and not only the macula area. In their study, they did not show a reduced b-wave in opposition to the ERG findings in humans with a scotopic b-wave reduction which could have resulted from massive dose of cefuroxime used in the study by Delyfer et al.²³ There was a similar study in rabbits performed by Shahar et al. in which the electrophysiological study revealed retinal dysfunction in the high dose group (10mg/0.1mL) and no retinal toxicity in the low dose group (1mg/0.1mL).³⁸ In contrast to the previous reports, Sakarya and Sakarya reported in their study 6 cases with cefuroxime at a dose of 3mg/0.1mL injected into the anterior chamber without adverse reactions or inflammatory reactions.³⁹ Contrary to our case report and reports by other authors mentioned above, we know that there are numerous reports describing no complications after phacoemulsification with the use of a standard dose of cefuroxime at the end of the surgery in which the thickness of the retina in the macula region was not changed. Citing the prospective randomized double-masked clinical study performed by Gupta et al. no revealed evidence of increased macular thickness secondary to the use of intracameral cefuroxime and supported the safety of a use 1mg of intracameral cefuroxime in uneventful cataract surgery.¹¹ Their results are in line with those performed by Montan et al. in which no statistically significant effect of intracameral cefuroxime on post-operative visual acuity was found.¹⁹ First-line treatment of CME after cataract surgery should be topical nonsteroidal anti-inflammatory drugs and corticosteroids. Thus, combination of pharmacotherapy have been reported to be safe and effective in the preventing macular edema and ocular inflammations after surgery.^{40,41} In the presented case report, topical anti-inflammatory treatment was applied as a routine therapy after phacoemulsification with additional oral drugs supplementation and revealed recovery at 10 days after surgery with fully absorbed

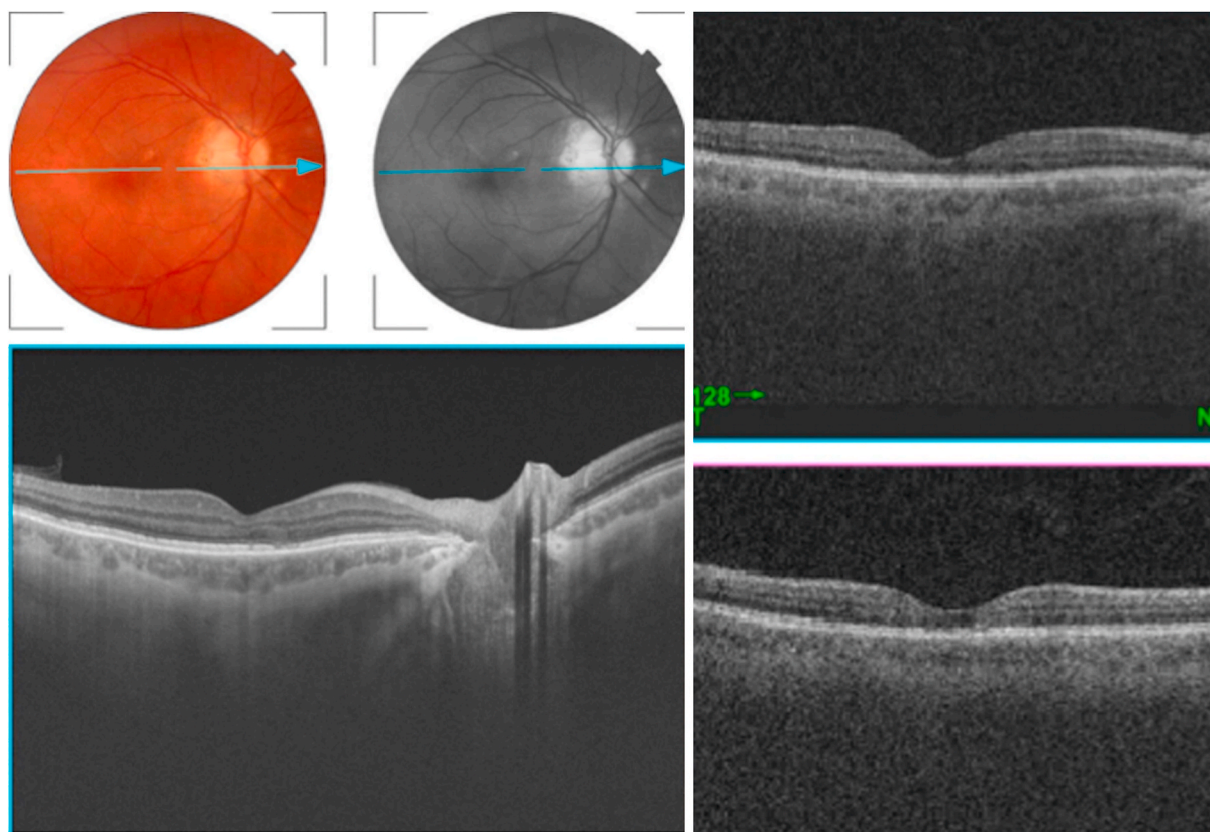


Fig. 8. a–b. SS-OCT scan of the right eye 24 months after cataract surgery. No recurrence of macular detachment or edema were observed (the central macular retinal thickness: 188 μm). There is an RPE abnormality in interpapilomacular area.

subretinal fluid on the SS-OCT scan and good visual acuity. Xiao et al. have applied the same topical treatment in their report and have obtained totally absorbed subretinal fluid 1 week after surgery.²⁹ The recovery time was shorter in our case report and those cases reported by other authors^{26,28,29} than the ones observed by the authors who used a high-dose injection of cefuroxime.²³ Routine anti-inflammatory treatment is a safe and effective therapy after phacoemulsification surgery that reduce the rate of the risk of postoperative ME and retinal detachment.

We would like to emphasize that the use of a standard dose of cefuroxime during the phacoemulsification may lead to the retinal toxicity, same as the use of a high dose of cefuroxime. However, in the presented case report, we cannot rule out a human mistake in preparing a solution on an operating block. The licensed intracameral cefuroxime is available as a sterile powder of 50 mg. The recommended dose for intracameral use is only 1 mg in 0.1 mL applied at the end of the surgery. The powder has to be dissolved in a 5 mL of sodium chloride 9 mg/mL (0.9%) solution prior to injection. The protocol for the sterile preparation in the operating room by the surgery nurse is clear, but due to inaccuracy between the amount of the powder in the vial and final intracameral dose (50 mg and 1 mg) could be the source of the dilution errors due to non-adherence to protocol or inadequate mixing of cefuroxime in the vial. Dilution errors could increase the dose of cefuroxime substantially above the recommended 1 mg dose, with potential clinical implications. To ensure accurate dosage administration the licensed intracameral cefuroxime should be provided in smaller dose to prevent dilution errors. Therefore, we cannot rule out human mistake as well as we have no direct evidence that the cause of acute macular edema was retinal toxicity caused by cefuroxime, although it seems to be very probable compared to the other authors' previous reports of cefuroxime-induced retinal toxicity. We also would like to draw the attention of surgeons to be aware and take into consideration the

possibility of the occurrence of this potential complication especially in patients with associated decreased visual acuity after uneventful phacoemulsification already on the first day after surgery. In our opinion it would be necessary to conduct more widely spread study with the use of OCT already on the first day after the surgery. This could exclude potential retinal toxicity of intracameral use of a standard dose of cefuroxime in cataract surgery.

2.1. Take away

1. Acute serous macular edema and detachment should be considered in cases of low visual acuity during the early postoperative period after uncomplicated phacoemulsification surgery. Surgeons should be aware of this potential postoperative complication.
2. Standard anti-inflammatory treatment is effective in such cases and allow to achieve a good functional visual acuity.

Declaration of competing interest

The following authors have no financial disclosures: EC-T, AN, EW.

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Not Applicable.

List of abbreviations

BCVA	best corrected visual acuity
CME	cystoid macular edema
PG	prostaglandins
COX	cyclooxygenase
ESCRS	European Society of Cataract & Refractive Surgeons

ME	macular edema
AF	fluorescein angiography
OCT	optical coherence tomography
IOP	intraocular pressure
PC-IOL	posterior chamber intraocular lens
RE	right eye
SS-OCT	swept source optical coherence tomography
PVD	posterior vitreous detachment
TASS	toxic anterior segment syndrome
PCME	pseudophakic cystoid macular edema
ERM	epiretinal membrane
RD	retinal detachment
RPE	retinal pigment epithelium
ERG	electroretinogram
PPI	proton pump inhibitor

Ethics approval and consent to participate

Not applicable.

Consent for publication

We obtained written consent from the patient to publish this report.

Availability of data and materials

All data and materials in this article are available.

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Authors' contributions

ECT was a major contributor to the drafting of the manuscript. ECT acquired the clinical data. AN analyzed and interpreted the patient's ophthalmologic data. AN and EW reviewed and edited the manuscript. All named authors take responsibility for the integrity of the work as a whole and have given their approval for this version to be published.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

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