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Research Article

Acute Transient Macular Oedema After Uneventful Cataract Surgery

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Abstract

Purpose: To analyze case reports of 17 patients who had acute transient macular edema appearing straight after uncomplicated cataract surgery.

Methods: Working with literature and retrospective observational case series reviewing clinical and imaging data from 17 patients (17 eyes) with acute transient macular edema.

Results: In literature several cases of acute macular hole development after cataract surgery (complicated and uncomplicated) are described. Also, there are reports of macular odema development several weeks after uncomplicated phacoemulsification due to pseudophakic cystoid macular oedema (Irvine-Gass syndrome) or due to vitreomacular traction syndrome. We observed a series of transient acute macular oedema with 3.8% incidence occurring in the initial days after uncomplicated phacoemulsification with IOL implantation that had no signs of vitreomacular traction or acute inflammation. Men suffer frequently compared to women (14:3). Systemic hypertension prevailed among these patients (15 from 17). Optical coherence tomography (OCT) was performed on patients complaining of blurred vision and signs of macular edema by ophthalmoscopy. By OCT high and often extensive neuroepithelium and local pigment epithelium detachments were observed on the first day after uneventful cataract phacoemulsification with intraocular lens implantation in 17 patients with quiet postoperative condition of the eye. The oedema resolved on the 3rd to 6th day by standard phaco accompanying pharmacological treatment. In most cases posterior vitreous cortex was adjacent to the retina except in 3 patients with posterior vitreous detachment (PVD) in the macular area. Costen and colleagues (2007) have reported the same striking appearance of maculopathy, designated by the authors "A-sign" maculopathy because of A-shaped pattern on OCT images in 3 patients after routine cataract surgery. Yaman., *et al*. (2008) and Panagiotidis., *et al*. (2010) also reported similar findings after uncomplicated cataract surgery. We compared our findings with the 3 papers mentioned above, as well as with typical pseudophakic cystoid macular edema (CME or Irvine-Gass syndrome) and vitreomacular traction syndrome. We also discussed possible etiopathogenesis of these cases in terms of morphology of the macula region.

Conclusion: This article may improve our understanding of mechanisms of interstitial fluid flow in the eye tissues.

Keywords: *Macula; Pseudophakic Cystoid Macular Edema (CME); Cataract Phacoemulsification; Irvine-Gass Syndrome; Vitreomacular Traction Syndrome (VMT); Optical Coherence Tomography (OCT)*

Introduction

In 2014 - 2015 we observed unusual cases of transient macular oedema in 17 patients after routine cataract surgery with peri-operative topical usage of non-steroid, steroid anti-inflammatory drugs and antibiotics. Anterior segment of the eye was clear and calm but patients complained of blurred vision. On OCT there were neuroepithelium detachment with local pigment epithelium detachment that resolved in 3 - 6 days on standard anti-inflammatory treatment. Patients stayed in the hospital until full recovery. Recently we found similar cases reported by Coasten and colleagues [1] and therefore encourages us to publish our cases.

Purpose of the Study

To analyze 17 cases of acute transient macular oedema (ATMO) after uneventful phacoemulsification with an intraocular lens (IOL) implantation, to compare them with similar conditions and to discuss it's etiopathogenetic pathways.

Methods

Literature overview, retrospective analysis of medical documentations of 17 cases including the age, sex, presence of associating diseases and drug treatment, length of the eye, keratometry, intraocular pressure (IOP) and OCT image of the macular region made by RT-Vue-100 (Optovue®, USA).

Results

The average age of patients was 68,24 ± 9,71 years (50 - 82 years). The men to women ratio were 14:3. The phacoemulsification with IOL implantation (Acrysof IQ, Alcon®, USA) was performed under a combination of topical and subtenon anesthesia through a 2,4 mm incision. Cataract density was mainly about 2 - 3 degree but patient N 13 was with soft posterior subcapsular cataract and patient N 3 with mature hard 4 degree cataract. All operations were carried out by the same trained surgeon on the "Millenium" machine (Baush&Lomb®, USA) by the "cross" method on the Burst mode with a maximum ultrasound power of 40%, vacuum 250 mm Hg and with the velocity of passive irrigation of balanced salt solution about 90 sm^3/min. All IOLs were implanted in the capsule bag. From the beginning of 2014 until the end of 2015 there were 449 phacoemulsifications performed by the same surgeon. Thus, the incidence of occurred acute transient macular oedema (ATMO) was 3.8%.

Three patients had bilateral compensated primary open angle glaucoma at different stages (patients № 2, 12 and 15), and one underwent trabeculectomy a year ago (№ 15). There were three patients with mild and high myopia (№ 1, 7 and 14).

The most common associated disease was systemic arterial hypertension - 15 of 17 cases. Also, the permanent form of atrial fibrillation was mentioned (patients № 2 and 4). Implanted sinus pacemakers were observed in 3 patients (№ 2, 10 and 16). Patients № 10 and 16 suffered from coronary heart disease and underwent vessel's stenting. Beside cardiovascular diseases there were patients with nephrolithiasis and hydronephrosis (cases № 10, 14, 17), cirrhosis of the liver (case № 7) and rheumatoid arthritis (cases № 4 and 16).

Three patients suffered from diabetes mellitus: two were insulin-dependent (№ 6 and 7) and one (№ 11) took hypoglycemic drugs orally. None of them had signs of diabetic retinopathy. Among patients on regular antihypertensive medications there were patients on diuretics (№ 1, 11) and ß-blockers (№ 8, 11 and 12). Antiplatelet drugs ("Cardiomagnil") were taken by two patients (№ 8 and № 16).

Patient №3 with mature cataract was in the interval between chemotherapy courses for breast cancer with metastases.

The second eye was pseudophakic in 5 patients.

The mean uncorrected visual acuity before surgery by the Sivcev table was 0.11 ± 0,11 (log MAR +1.0) and corrected 0.21 ± 0.18 (log MAR +0.7). In spite of the presence of macular oedema, the mean corrected visual acuity on the first day after surgery was 0.31 ± 0,20 (log MAR +0.5). When macular oedema resolved, the mean uncorrected visual acuity was 0.48 ± 0.28 (log MAR +0.3) and the best corrected visual acuity was 0.82 ± 0.16 (log MAR +0.1).

IOP before surgery was 21.18 ± 2.38 mm Hg. On the first day after surgery, IOP was within the normal values and was 19.5 ± 3.2 mm Hg at patients' discharge.

The mean length of the eye was 23.93 ± 1.23 mm (22.45 - 26.2 mm), the mean keratometry along two main meridians was 43.41 ± 1.41 D (40.1 - 45.5 D).

Postoperative inflammatory reaction was minimal: one male patient (№ 1) had +1 cell reaction in the anterior chamber's aqueous humor on the first day after surgery. All patients received medical treatment: instillations of non-steroidal anti-inflammatory drugs (Indocollyre 0,1%), dexamethasone 0.1% and ciprofloxacin 0.4% 4 times a day, and subconjunctival injections of dexamethasone 0.3 ml 0.4% № 2-5.

A high detachment of neuroepithelium in the macular region was observed on OCT in majority of cases on the first day after surgery due to liquid accumulation in the outer nuclear layer and under the photoreceptor layer. Local pigment epithelium detachment was also detected. This typical swelling resolved in 3 - 6 days. The OCT image of patient № 1 on the first and third day after uncomplicated phacoemulsification with IOL implantation is presented in figure 1. On the third day after surgery the detachment of neuroepithelium had almost resorbed, with only a tiny detachment of the photoreceptor's layer left, which disappeared on the fourth day.

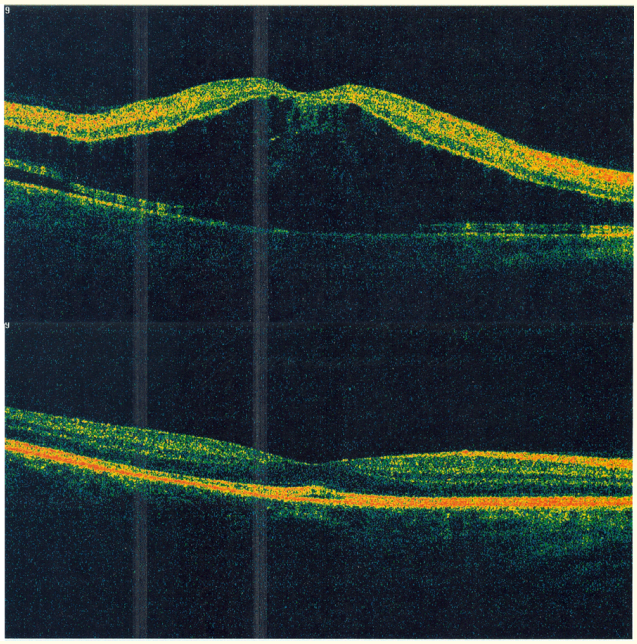

Figure 1: *OCT image OD of case 1 on the 1st day after surgery (top) and on the 3rd day (below).*

Changes that were observed on OCT between the second and fifth day in case № 3 are represented in the figure 2.

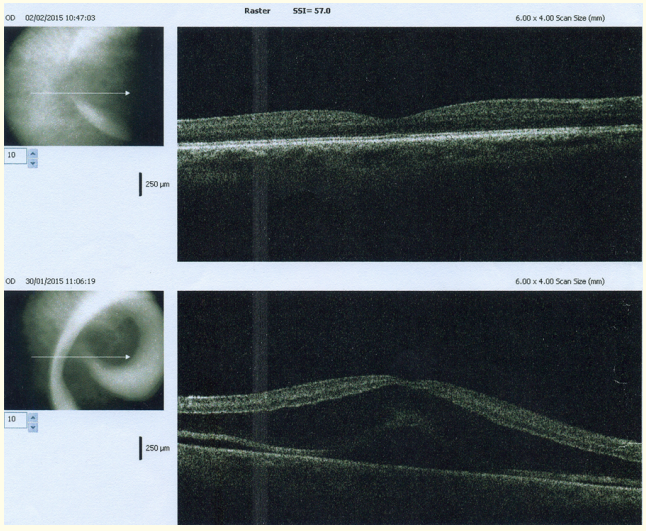

Figure 2: *OCT OD of case 3 on the 2nd (below) - 5th (top) days.*

"A-pattern" of retinoschisis described by Coasten., *et al*. (2007) was mentioned only in case №5 which also had a posterior vitreous detachment (PVD) see (Figure 3).

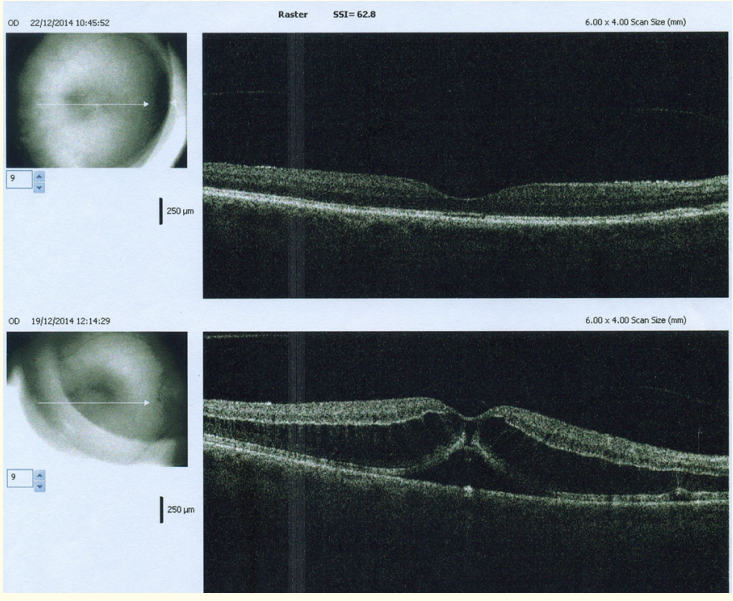

Figure 3: *Dynamic on OCT OD of case 5: 3rd day (below) and 6th day (top), "A-sign", PVD.*

There is interstitial swelling of the outer retinal layers resulting in partial or total neuroepithelium detachment in the majority of cases. On OCT images in the fovea region above the detached bodies of photoreceptors, there are low-differentiated shapeless structures that in some cases had radial direction and could represent Henle fibers or swelled Muller cell' bodies and processes locating in radial direction on the frontal plane [2].

Patient №6 had hard drusen and depigmentation in the macula region observed ophthalmoscopically but on OCT there are only pigment movement in the complex pigment epithelium - Bruch's membrane - chorocapillaries (RPE-BM-CH) (Figure 4). It is interesting to note that none of the patients had structures with high optical density such as large drusen or neovascular membranes.

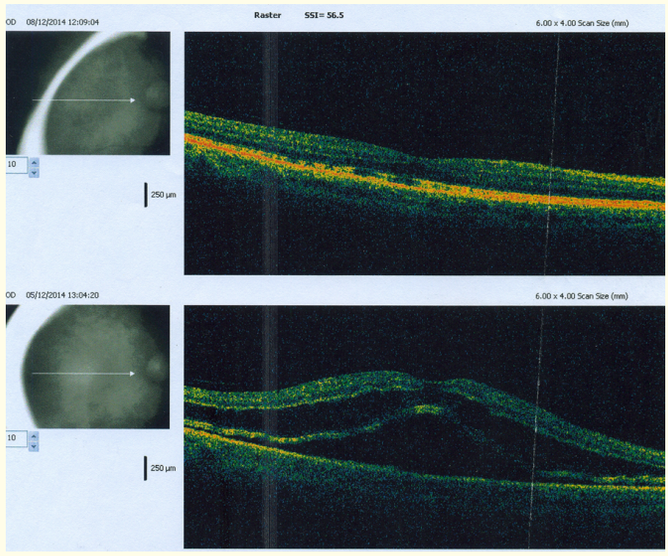

Figure 4: *OCT OD dynamics of case 6 on the 2nd (below) - 5th (top) days.*

On figure 5 and 7 there are OCT images of patient №7 and №14 that are similar to those observed in pseudophakic cystoid macular oedema with cysts in the outer plexiform and nuclear layers (Irvine-Gass syndrome).

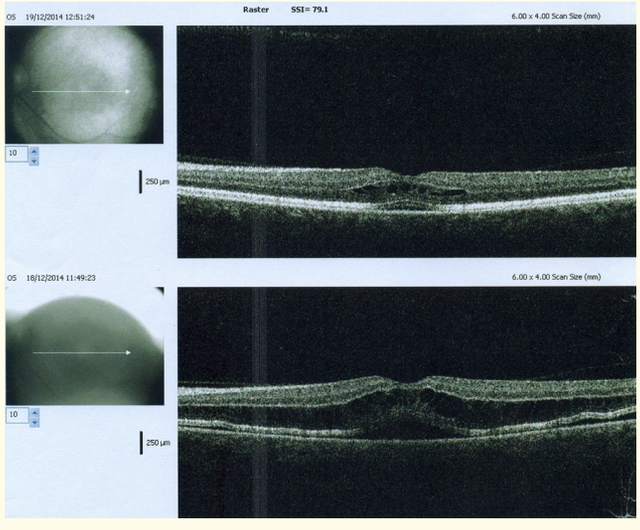

Figure 5: *OCT OS dynamics of case 7 on the 3rd (below) - 4th (top) days, no PVD.*

The lowest detachment of neuroepithelium on the first day was observed in patient №8, and one of the highest in patient № 9 (772 mkm). Nevertheless, enlargement of the outer nuclear layer, appearance of optical voids in the outer plexiform layers and detachment of photoreceptors with or without pigment epithelium, in some cases local and in some cases throughout the whole macula region was seen.

On OCT image of patient № 12 (Figure 6) amid moderate neuroepithelium detachment of Henle fiber layer is detected shifting upward together with photoreceptors and locating on the sides of foveal pit as radially oriented beams, between the outer plexiform and nuclear layers and is limited by the round cysts in the outer nuclear layer.

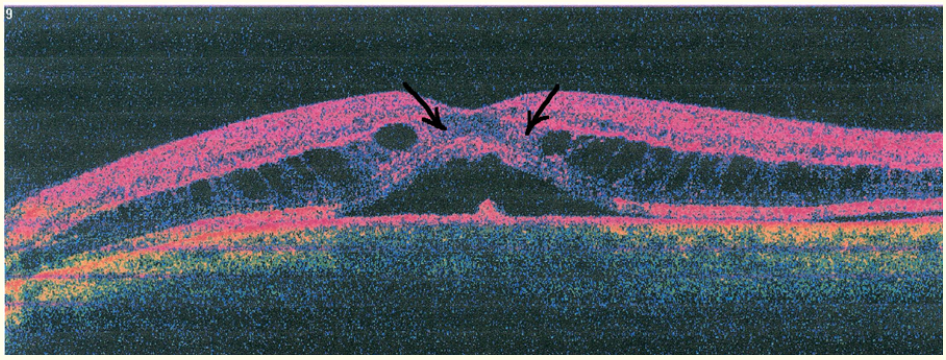

Figure 6: *OCT image OS of case 12 on the 2nd day visualizing elevated Henle's fiber layer (arrows).*

The OCT image of patient № 14 with high myopia on the second day after surgery is represented in the figure 7. Worthy of note is the small size of the cysts in the outer nuclear layer. Complete resorption of edema was observed on the third day after surgery.

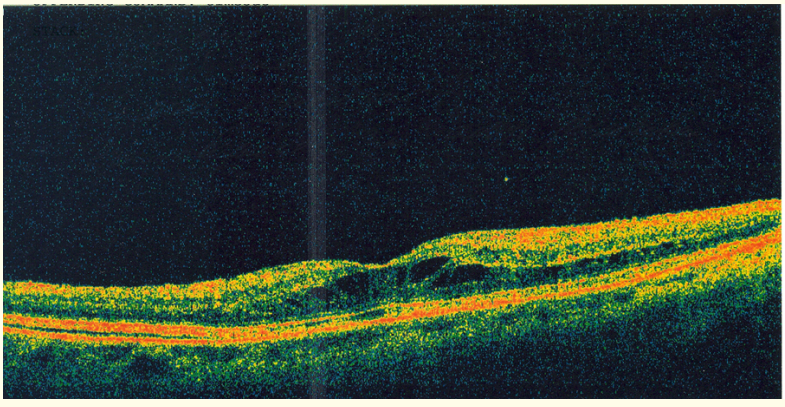

Figure 7: *OCT image OD of case 14 with high myopia on the 2nd day.*

There was no PVD in the macula region in 9 cases. Sometimes the posterior hyaloid was elevated on the sides of the detached neuroepithelium but lay down again after resorption of oedema. In spite of high neuroepithelium detachment, the foveal pit remained in all cases,

which meant that the structure of the inner retina layers that normally may suffer from vitreous traction was saved during the observed condition.

In patient № 15 with surgically treated stage III- and- IOP normalized glaucoma, resolution of oedema was detected on the sixth day (Figure 8).

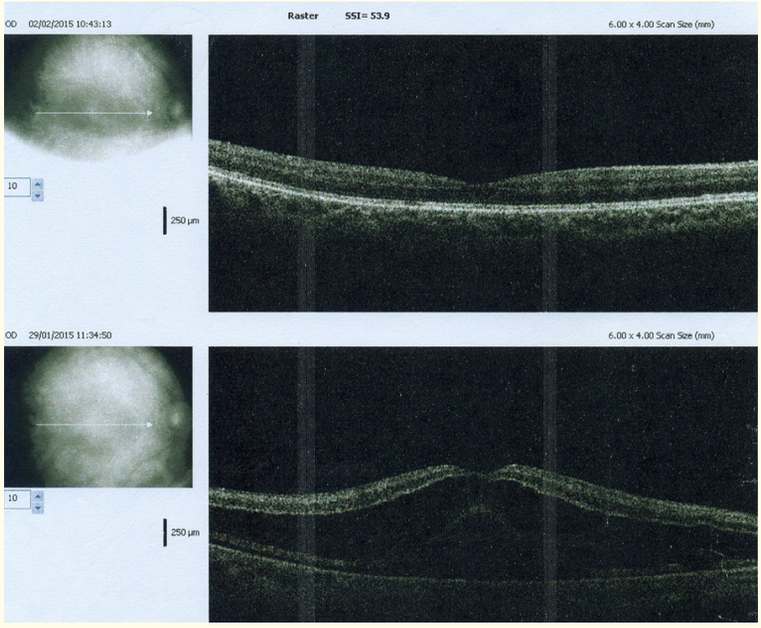

Figure 8: *OCT OD dynamics of case 15 on the 2nd (below) - 6th (top) days, POAG.*

On OCT images of patient № 16 (Figure 9) and patient № 17 (Figure 10), beside the neuroepithelium detachment, epiretinal fibrosis was detected which had not changed after resorption of oedema. Patient № 17 had complete resolution on 4^{th} - 5^{th} day.

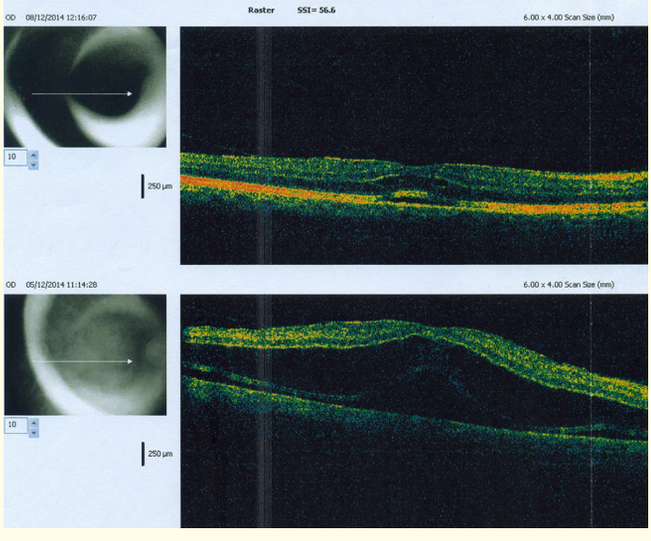

Figure 9: *OCT OD dynamics of case 16 on the 2nd (below) and 5th (top) days, ERM.*

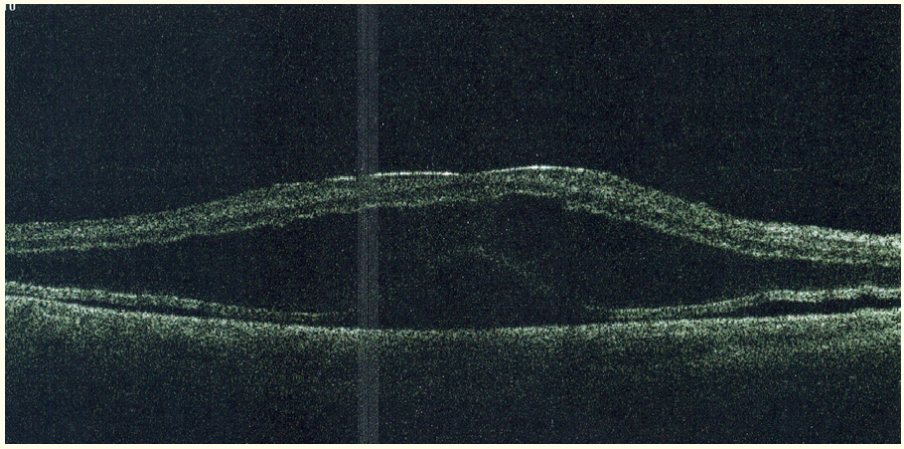

Figure 10: *OCT image OD of case 17 on the 1st day, SRD and ERM.*

Thus, in the majority of the images there are cavities in the outer nuclear layer which merge and split inner and outer nuclear layers. Also, there is detachment of the photoreceptor layer and the pigment epithelium but the order of this process is unknown. Complete anatomical recovery of the macular region on OCT usually occurs on the forth day (3 - 6 days) after surgery. Associated glaucoma, diabetes mellitus, treatment with diuretics influenced little on the area and height of the oedema.

Discussion

Coasten and colleagues in 2007 described similar cases. Their incidence was not mentioned. Patients were two women and a man of age 72, 59 and 66 years, respectively. Authors mention that all three patients had no sign of PVD but on OCT image of the second patient almost total PVD is shown except for the foveal region where contact with the internal limiting membrane is observed (http://nature.com/articles/6702587). British colleagues did not determine the cause of the oedema but assumed that vitreomacular traction could be the reason in the described cases [1].

"A-sign" OCT image pattern described by Coasten MTJ., *et al*. may be explained by the structure of Muller cells that form a carcass in the macula region. The horizontal bar of the A sign probably is part of this carcass contributing to the outer limiting membrane. A side bars are sometimes wavy, sometimes compact and straight. This was, noted on OCT images, go up from the detached photoreceptor layer in the fovea, form an inverted trapezoid, and highly likely represent Henle fibers layer [2-4]. This is located in tight connection with the Muller cells in the parafovea region. Using immunohistochemistry and OCT Matet., *et al*. in 2015 detected a Z-like location of the Muller cells' processes in the sagittal plane: oblique path in the outer plexiform layer together with Henle fibers and vertical path in the inner retinal layers forming bonds with axons of the cones [5].

In 2008 Yaman., *et al*. conducted a prospective study with 59 patients (59 eyes) who underwent cataract surgery. Macular swelling on the first day after surgery was detected in 2 patients (3.3%) and it's resorption occured over a week. Patients had a total PVD after resorption and no sign of leakage on fluorescent angiography. Authors considered that the cause in the described cases was a vitreo-macular traction [6].

In 2010 Panagiotidis., *et al*. retrospectively described five cases of acute macular swelling on the first day after routine cataract surgery which also resolved spontaneously in ten days due to PVD as the authors assumed [7]. Traction genesis of swelling was also suggested, but the authors noted common pathogenesis with a pseudophakic cystoid macular oedema. "A-sign" pattern was mentioned in 2 cases. The incidence of those cases was 1:600 but authors mentioned that it should in fact be higher. One patient with a structural changes in the pigment epithelium complained on metamorphopsia even after oedema resorption as well as the two patients described by Coasten., *et al* [1].

Idiopathic traction macular syndrome (TMC) described in 1967 by Jaffe [8] and in 1970 by Reese and colleagues [9] is characterized by partial detachment of the posterior hyaloid because of its tight adhesion to the inner limiting membrane and results in changed foveal contour. This condition may spontaneously resolve in 10% of cases without a macular hole formation but only as a result of complete PVD [10-12]. There are rare cases of macular holes occurring on the first day after uncomplicated cataract surgery described in the literature [13,14]. Also, there are conditions documented when after a routine cataract surgery vitreo-macular adhesion and traction resulted in cystoid macular oedema (CME) development refractive to anti-inflammatory drug treatment and resolved only after vitrectomy [15,16].

The involvement of the vitreomacular adhesion in the pathogenesis of the observed cases is doubtful considering the intact foveal pit amid the high neuroepithelium detachment and the absence of PVD after resorption in most cases. The volume of the extracted lens is several times lower than the IOL, so there should be changes in the structure of the vitreous body under the action of anterior-posterior forces which could be involved in the pathogenesis of the macular holes [14]. But only in 3.8% of our cases and 3.3% of Yaman., *et al*. [6] cases transient changes of the macular region were observed. Moreover, several prospective researchers measuring by the OCT thickness of the macular region, before and after phacoemulsification, have found only minimal enlargement in the macula in early and late terms after surgery [17-19] and in 3.2% of cases of cystoid macular oedema [19].

We noted that the OCT images at certain stages are similar to that in cystoid macular oedema with still unknown etiology. But Irvine-Gass syndrome occurs between 4 to 6 weeks after cataract surgery. It is characterized by leakage of the dye on fundus angiography through parafoveal capillaries at late stages of the investigation and by the appearance of cysts in the outer plexiform and nuclear layers on OCT. The risk factors of its appearance are: age, male gender, uveitis, diabetes mellitus, duration of the surgery, rupture of the anterior hyaloid and, loss of the vitreous body [20,21]. In the era of small incision surgery, incidence of this condition decreased and is about 1.17%. The additional risk factors are: epiretinal fibrosis, history of vitreoretinal surgery and branch retinal thrombosis. It was noted that high myopia, dry age related maculodystrophy and the usage of prostaglandin analogues do not increase the incidence of pseudophakic cystoid macular oedema [22].

Gulkilik., *et al*. found that CME after uneventful phacoemulsification with IOL implantation is observed in the tenth week more frequently if there were signs of postoperative inflammation in the first days after surgery as cell reaction 2+ in the aqueous humor - 43.2% versus 11.5% in case of absence of the cell reaction. The presence of total PVD had a protective effect against CME development [23]. Many authors consider that the real incidence of CME after routine cataract surgery is not 0.1 - 2.5% [24,25], but 10 times higher and may reach 25.5% which is confirmed by investigations with the usage of fundus angiography [23,26]. Mentes., *et al*. detected that the incidence of CME found on angiography after phacoemulsification is about 9.1% which is comparable with its incidence after extracapsular methods of cataract extraction [27].

Unlike our cases, in CME there is a cystoid pattern on OCT images and subretinal fluid with the detachment of neurosensory retina is rarely observed [25].

Systemic cardiovascular and autoimmune diseases undoubtedly affect the level of microcirculation in all structures of the eye. A fluctuation of IOP during the operation and release of inflammatory mediators due to tissue injury leads to changed permeability of the capil-

laries. There are cases of occlusion of retinal microcirculation in the parafoveal region on the first day after cataract surgery in case of so-called paracentral middle maculopathy. This is characterized by permanent paracentral visual field defects and ischemic hyper reflexivity in the projection of deep capillary layer of the retina on OCT images [28].

Ioshin considers that pseudophakic CME is developed when velocity of capillary filtration exceeds the outflow rate of interstitial fluid from the retina through perivascular pathways despite the auto regulation mechanisms, and probably some autoimmune reactions to IOL play a role in this process [29].

The intracameral usage of cefuroxime is considered to be the cause of such conditions as we observed with serous retinal and pigment epithelium detachment [30,31]. The toxic effect of cefuroxime is thought to be the reason of structural changes of the macular region. But the goal of this paper is to pay attention to the similarity of OCT images of ATMO and CME at certain stages of the process. Avascularity of the foveal region makes it susceptible to any changes in the molecular or chemical compound of the intraocular and interstitial fluids. The fact that pseudophakic CME usually occurs 4 weeks after surgery and has an OCT image that resembles the resorption stage in ATMO suggests a late breakdown of some compensatory mechanisms normally providing homeostasis in this region.

The resorption of the intra- and subretinal fluid takes place simultaneously in the outer retinal layers and along an entire zone under detached photoreceptors, mainly due to the activity of the retinal pigment epithelium ion channels and pumps. All patients had a native vitreous body. Structural features of the vitreous body described by Worst (1975) and Makhacheva (2004), i.e. connection between the retrolental bursa and premacular bursa through the central channel, probably has an impact in the pathogenesis of ATMO [32]. It is obvious that traction and transudation closely relate to each other. The individual intolerance of cefuroxime revealed to us a part of the mechanism of resorption of the interstitial fluid that normally occurs in the posterior segment of the eye. There is no clear and complete understanding of fluid circulation in the posterior segment. It is known that one of the functions of the retinal pigment epithelium is ion-dependent water transport [33]. Muller cells also play a huge role in the maintenance of water-metabolic balance of the retina [34]. OCT images of ATMO should be differentiated with those of central serous chorioretinopathy and optic disc pit where also serous retinal detachment is observed.

The disadvantages of this study: it is retrospective, so OCT images were available only in the paper format. OCT scans were performed in linear regimes not in 3D which reduces the morphological details and its connection to the optic disc.

Conclusion

Many colleagues in the world observed similar cases of ATMO but due to self-resorption and absence of significant effects on visual acuity, this condition was not of clinical interest. We hope that this study may help investigators to understand the mechanisms underlying interstitial fluid circulation in the posterior segment of the eye. Further research is needed to reveal the fluid-tissue exchanges in the retina.

Authors' Contributions

Beisekeeva J.: Design, data and literature analysis, writing.

Bezrukov A.V.: Operations performance, data collection, discussion.

Kochergin S.A.: Editing, revision.

Samoylenko A.I: OCT interpretation, discussion.

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Authors have no financial or proprietary interest in any material or methods mentioned.

Conflicts of Interest

None declared.

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Volume 13 Issue 5 May 2022