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Original Article

Photoreceptor Disruption Related to Persistent Submacular Fluid after Successful Scleral Buckle Surgery

Se Joon Woo[1*], Kyoung Min Lee[2*], Hum Chung[2], Kyu Hyung Park[1]

[1]Department of Ophthalmology, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Korea
[2]Department of Ophthalmology, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea

Purpose: To investigate serial changes in photoreceptor status and associated visual outcome in patients with persistent submacular fluid after successful scleral buckle surgery for macula-off rhegmatogenous retinal detachment.
Methods: This was a prospective observational case series including 76 consecutive patients who underwent successful scleral buckle surgery for macula-off rhegmatogenous retinal detachment with symptom duration ≤90 days at a single tertiary hospital. Optical coherence tomography (OCT) and visual acuity examination were performed at one month and three months postoperatively and at three-month intervals until the submacular fluid disappeared. Main outcome measures were postoperative photoreceptor status on OCT and visual acuity.
Results: Forty-two patients (55.3%) showed persistent submacular fluid at postoperative one month. Of 42 patients with persistent submacular fluid, three (7.1%) showed photoreceptor disruption on OCT. None of the 34 patients without persistent submacular fluid showed photoreceptor disruption. Two patients (4.8%) had progressive photoreceptor disruption, and one patient (2.4%) had early photoreceptor disruption. All three patients showed photoreceptor reappearance and limited visual restoration after absorption of submacular fluid. Final visual acuities were significantly worse in these three patients (20 / 1000, 20 / 133, and 20 / 133) compared to those of the other patients (mean, 20 / 30) with persistent submacular fluid and intact photoreceptors.
Conclusions: Even after successful scleral buckle surgery for rhegmatogenous retinal detachment, photoreceptor disruption can occur related to persistent submacular fluid and may be a cause of poor visual outcome.

Key Words: Optical coherence tomography, Photoreceptor cells, Retinal detachment, Sclera buckling, Subretinal fluid

With recent advances in optical coherence tomography (OCT), subclinical submacular fluid can be detected after successful scleral buckle surgery [1]. In recent reports, about one-half (47% to 55%) of patients who underwent successful scleral buckle surgery for macula-off rhegmatogenous retinal detachment had persistent submacular fluid at one month postoperative [2-4]. Previously, we suggested that persistent submacular fluid after successful retinal detachment repair was associated with delayed visual recovery but had no influence on the final visual outcome [2]. Despite a high anatomical success rate, variable visual outcomes have been a problem after rhegmatogenous retinal detachment repair [5]. Several studies using high-resolution spectral-domain OCT demonstrated that poor surgical outcome after successful surgery was associated with disrupted photoreceptor status [6,7]. Photoreceptor status on OCT has been known to be an important prognostic factor of visual outcome in many retinal diseases, such as epiretinal membrane [8], central serous choroioretinopathy [9], and retinal detachment [6,7,10]. Persistent submacular fluid after retinal detachment surgery is also capable of causing harmful effects on photoreceptors due to blockage of the normal diffusion of oxygen and nutrients [11,12]. However, to our knowledge, serial changes in photoreceptors on OCT in association with persistent submacular fluid after successful scleral buckle surgery have not

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Corresponding Author: Kyu Hyung Park, MD, PhD. Department of Ophthalmology, Seoul National University Bundang Hospital, #300 Gumi-dong, Bundang-gu, Seongnam 463-707, Korea. Tel: 82-31-787-7373, Fax: 82-31-787-4057, E-mail: jiani4@snu.ac.kr

[*] These two authors equally contributed to this article.
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been previously studied.

The purpose of this study was to investigate serial changes in photoreceptor status in patients with persistent submacular fluid who underwent successful scleral buckle surgery for rhegmatogenous retinal detachment and to report the incidence and characteristics of photoreceptor disruption attributable to persistent submacular fluid.

Materials and Methods

This was a prospective observational case series including patients who underwent successful scleral buckle surgery for macula-off rhegmatogenous retinal detachment by two retinal surgeons (SJW and KHP) at Seoul National University Bundang Hospital between May 2003 and July 2008. We followed-up patients with OCT after surgery at one month and three months and at regular three-month intervals thereafter until the submacular fluid disappeared. Patients provided informed consent prior to surgery, and the study protocol was approved by the Institutional Review Board of Seoul National University Bundang Hospital.

Inclusion criteria were as follows: patients who underwent successful scleral buckle surgery for macula-off rhegmatogenous retinal detachment; symptom duration <90 days; and a complete follow-up with OCT. Successful scleral buckle surgery was defined as a significant decrease in the amount of subretinal fluid within one week after surgery, complete closure of retinal tear ducts, and no demonstrable subretinal fluid on postoperative indirect ophthalmoscopy.

Exclusion criteria were as follows: need for a second operation (scleral buckle surgery or vitrectomy) due to surgical failure or recurrence; prior retinal surgery including vitrectomy; combined tractional and rhegmatogenous retinal detachment; presence of uveitis; presence of tractional membrane on macula, i.e., epiretinal membrane; and patients who could not remember the symptom onset.

During the study period, 183 consecutive patients underwent scleral buckle surgery for primary rhegmatogenous retinal detachment and served as candidates for this study. We excluded 47 patients for macula-on rhegmatogenous retinal detachment, 39 patients for reoperation for recurred retinal detachment or epiretinal membrane, 11 patients for incomplete follow-up with OCT, 6 patients for symptom duration of more than 90 days, 3 patients for epiretinal membrane preoperatively and one patient with presumed chronic retinal detachment who could not remember the symptom onset. Seventy-six patients completed follow-up with OCT and were ultimately included in our study.

The main measurement outcome was serial postoperative changes in photoreceptor on OCT and visual acuities.

Preoperative data were obtained including age, sex, symptom duration, best-corrected visual acuity (BCVA), and anterior and posterior segment findings. Postoperative data included postoperative BCVA, presence of persistent sub-

Table 1. Clinical characteristics of patients with and without persistent submacular fluid one-month after successful scleral buckle surgery for macula-off rhegmatogenous retinal detachment

Clinical characteristic	Persistent submacular fluid group (n = 42)				No submacular fluid group (n = 34)
	Intact PR	Progressive PR disruption		Early PR disruption	Intact PR
	(n = 39)	Case 1	Case 2	Case 3	(n = 34)
Age (yr)	39 ± 29 (12-73)	48	58	47	41 ± 20 (8-80)
Male:female	20:19	F	F	F	18:16
Symptom duration (day)	12 ± 17 (1-90)	1	30	3	11 ± 15 (1-60)
Follow-up period (mon)	20 ± 12 (3-51)	21	21	54	14 ± 7 (1-29)
High myopia	35.9%	No	Moderate myopia (AL, 25.6mm)	No	38.2%
Buckle type	Segmental, 37 Encircling, 2	Segmental	Segmental	Segmental	Segmental, 23 Encircling, 11
External subretinal fluid drainage	3 (7.7%)	No	No	No	6 (17.6%)
Type of persistent submacular fluid one-month after surgery	Diffuse, 28 (71.8%) Focal, 11 (28.2%)	Diffuse	Diffuse	Diffuse	-
Height of submacular fluid on one-month OCT (μm)	129 ± 126	206	440*	63	0
Duration before disappearance of submacular fluid (mon)	8.6 ± 4.5 (1-18)	18*	15*	9	1
Preoperative BCVA (logMAR)	1.16 ± 0.77	2.30*	1.22	2.0*	1.25 ± 0.74
Final BCVA (logMAR)	0.18 ± 0.19	1.70*	0.82*	0.82*	0.36 ± 0.38

Continuous values are expressed as mean ± standard deviation.
High myopia was diagnosed when the axial length was >26.5 mm or myopic spherical equivalent was -6.00 diopters or more.
PR = photoreceptor; AL = axial length; OCT = optical coherence tomography; BCVA = best-corrected visual acuity; logMAR = logarithm of the minimum angle of resolution.
*$p < 0.001$ using one-sample t-test (comparison with the intact photoreceptor group).

macular fluid, and photoreceptor status on OCT. We used Stratus OCT (Carl Zeiss, Dublin, CA, USA) for time-domain OCT and Spectralis OCT (Heidelberg Engineering, Heidelberg, Germany) and Cirrus high-definition OCT (Carl Zeiss) for spectral-domain (SD)-OCT. Because of its recent introduction, SD-OCT was performed only in two cases with progressive photoreceptor disruption (cases 1 and 2).

Foveal photoreceptor status was evaluated using OCT after pupillary dilation. On Stratus OCT, a "normalize and align" mode was adopted for foveal inspection. The hyperreflective band indicating the photoreceptor inner and outer segment (IS-OS) junction was inspected [7]. The disappearance of the IS-OS junction on OCT and severe thinning of the retina in the fovea were regarded as photoreceptor disruption [9]. We also measured the height of persistent submacular fluid with OCT using a caliper in "retinal thickness analysis mode" which was described in a previous report [2]. On Cirrus OCT, a 5 line raster scan mode was used. Two cross-hair scans centered on the fovea were obtained using Spectralis OCT. On one-month OCT, we classified the types of persistent submacular fluid as diffuse and focal. A focal type indicates that the subretinal fluid is confined in the fovea and the photoreceptors in the perifovea are adherent to the retinal pigment epithelium on both horizontal and vertical scans of OCT. We defined the diffuse type of submacular fluid when submacular fluid extends over the fovea and its margin could not be observed on horizontal or vertical scans of OCT.

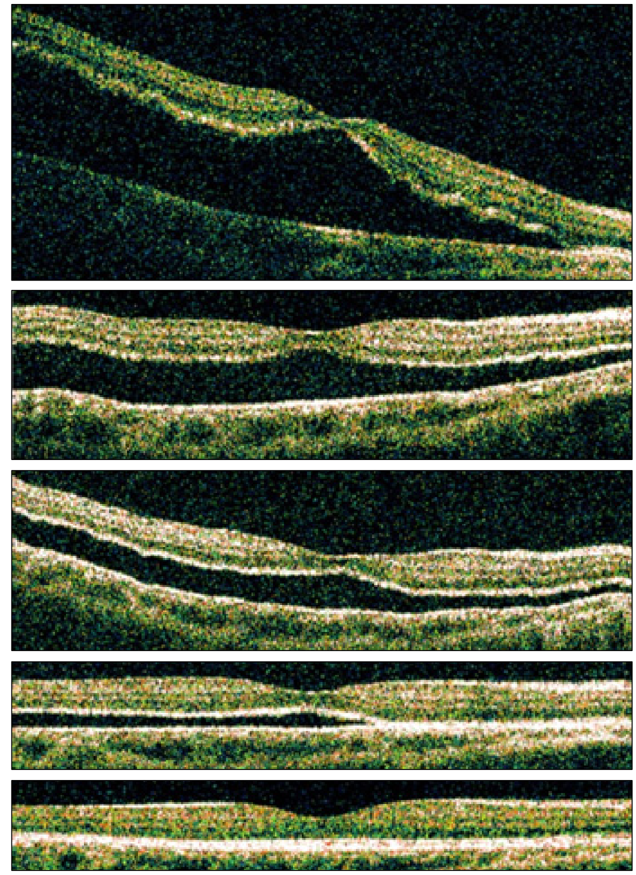

Fig. 1. Serial changes of typical time-domain optical coherence tomography (horizontal scans) in a case with persistent submacular fluid after successful scleral buckle surgery for rhegmatogenous retinal detachment. The images were obtained preoperatively and at 1, 3, 6, and 9 months postoperatively, from top to bottom. There were no signs of photoreceptor disruption throughout the follow-up periods.

Results

Of 76 patients, 42 (55.3%) had persistent submacular fluid at one month after successful repair. Of 42 patients with persistent submacular fluid, three (7.1%) had photoreceptor disruption on postoperative OCT. Two patients (4.8%, cases 1 and 2) showed progressive photoreceptor disruption, and one patient (2.4%, case 3) showed early photoreceptor disruption. None (0%) of the 34 patients without persistent submacular fluid had photoreceptor disruption on OCT at postoperative one month.

The clinical characteristics of patients are shown in Table 1. Three patients (cases 1-3) with photoreceptor disruption showed a diffuse type of persistent submacular fluid and significantly worse final visual acuities than the intact photoreceptor group. Delayed absorption of submacular fluid (18 and 15 months) was encountered in cases 1 and 2. Myopia and large height of submacular fluid were associated with case 2. Fig. 1 depicts the OCT images of intact foveal photoreceptors of typical patients with the diffuse type of persistent submacular fluid after successful scleral buckle surgery. The photoreceptor IS-OS junction was intact and showed no disruption throughout the follow-up periods. Fig. 2A and 2B show the progressive photoreceptor disruption on serial postoperative OCT in cases 1 and 2. In both cases, the photoreceptors in the fovea showed linear elimination in parallel with gradual deterioration of BCVA while the amount of subretinal fluid decreased with time. The earliest sign of progressive photoreceptor disruption was a notch in the photoreceptor IS-OS junction on OCT at one month, as shown in Fig. 3A and 3D.

SD-OCT findings (Fig. 3B and 3E) showed disappearance of the photoreceptor inner and outer segments. The external limiting membrane was intact and in contact with the persistent submacular fluid in cases 1, 2, and 3. Inner retinal structures showed no abnormalities. The SD-OCT of case 1 after disappearance of persistent submacular fluid revealed a partial restoration of the foveal photoreceptor layer (Fig. 3C). In case 2, although parts of the photoreceptor signals had been restored, diffuse photoreceptor atrophy and retinal pigment epithelium degeneration were observed (Fig. 3F).

Case 3 revealed early photoreceptor disruption shown as a defect in the photoreceptor layer at postoperative one month (Fig. 2C). As the submacular fluid decreased during the follow-up, the defect in the photoreceptor IS-OS junction was gradually reduced. On the final examination with OCT (54 months post-surgery), the photoreceptor IS-OS junction in the fovea was completely restored and visual acuity had slightly improved to 20 / 133.

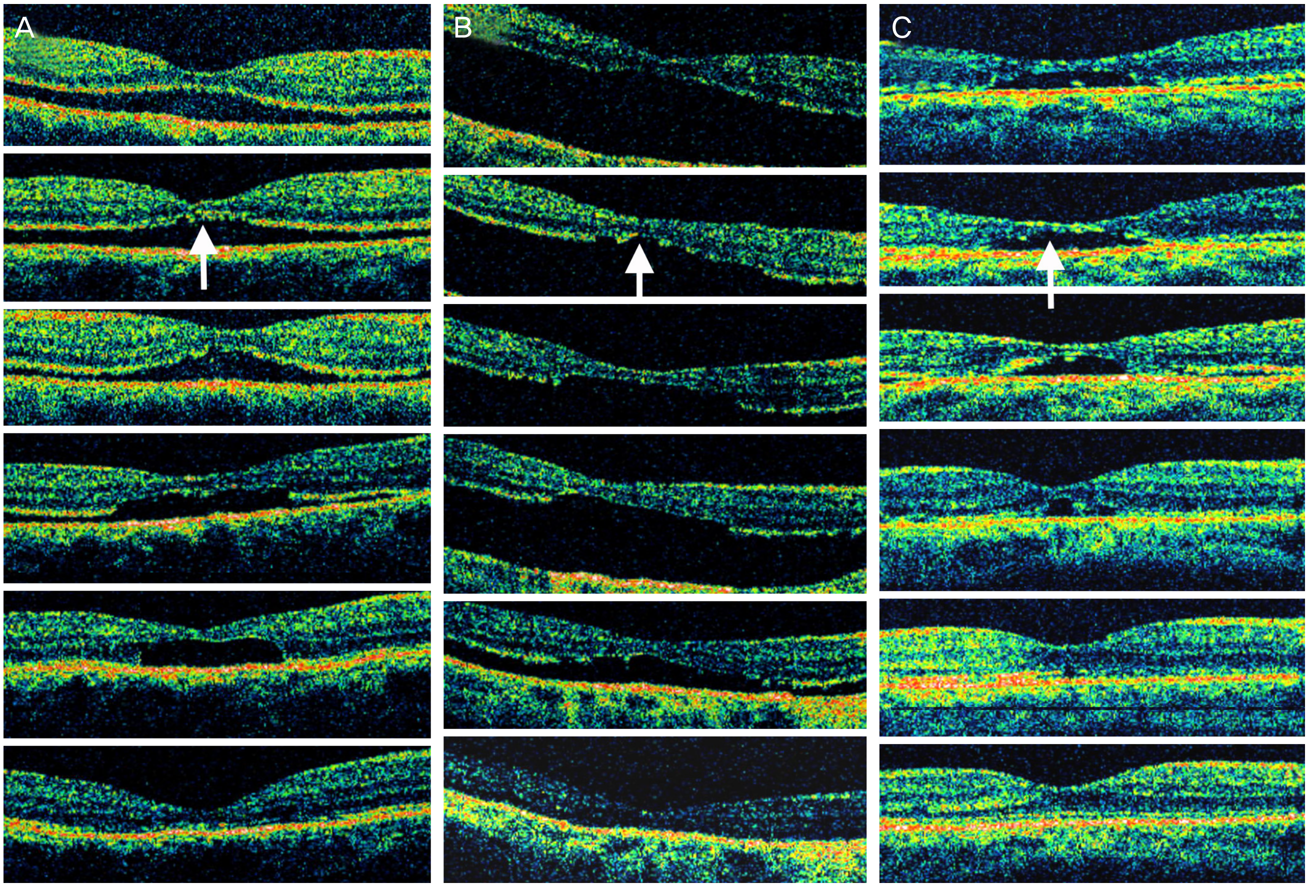

Fig. 2. Optical coherence tomography findings (horizontal scans) of cases 1-3 (A-C). Arrows indicate the disrupted photoreceptor inner and outer segment line. (A) Case 1 at 1, 3, 6, 9, 12, and 18 months postoperatively, from top to bottom. Best-corrected visual acuities (BCVAs) were 20 / 40, 20 / 67, 20 / 333, 20 / 500, 20 / 1,000, and 20 / 1,000 at the respective follow-up periods. (B) Case 2 at 1, 3, 6, 9, 12, and 15 months postoperatively. BCVAs were 20 / 1,000, 20 / 250, 20 / 333, 20 / 333, 20 / 500, and 20 / 133. In cases 1 and 2, the foveal photoreceptor inner and outer segment disappeared progressively, while the amount of submacular fluid gradually decreased. (C) Case 3 at 1, 2, 3, 6, 9, and 54 months postoperatively. BCVAs were 20 / 333, 20 / 333, 20 / 200, 20 / 250, 20 / 250, and 20 / 133, respectively. The photoreceptor inner and outer segment junction line in the fovea disappeared initially and reappeared as the submacular fluid was absorbed.

The visual outcomes of patients with and without photoreceptor disruption are compared in Fig. 4, which suggests that the visual acuities were associated with the status of photoreceptors in cases 1-3. Final BCVAs were significantly worse in these three patients (20 / 1000 in case 1, 20 / 133 in case 2, and 20 / 133 in case 3) than those (mean, 20 / 30) of the other patients with intact photoreceptors and persistent submacular fluid ($p < 0.001$ by one-sample t-test). All of the patients with persistent submacular fluid and intact photoreceptors had final visual acuities better than or equal to 20 / 67.

Discussion

The present study revealed that, even after successful scleral buckle surgery for rhegmatogenous retinal detachment, some patients showed photoreceptor disruption due to persistent submacular fluid. The photoreceptor disruption was associated with visual loss and was the main cause of poor visual outcome after successful surgery. Even after the disrupted photoreceptor layer reappeared on OCT, the visual acuities showed limited restoration. Photoreceptor disruption at one month OCT can be a poor prognostic sign in patients with persistent submacular fluid after successful scleral buckling surgery. Despite a meticulous and exhaustive search in Medline, we could not find any reports addressing progressive or early photoreceptor disruption related to persistent submacular fluid after successful scleral buckle surgery. Photoreceptor disruption was reported only in detached retinas before repair or was analyzed without regard to persistent submacular fluid [6,7,13].

Central serous chorioretinopathy (CSC) has a common anatomic alteration with persistent submacular fluid after retinal detachment surgery in that the neurosensory retina is detached from the underlying retinal pigment epithelium and eyes in both conditions and can maintain tolerable vision for a substantial period of time. The photoreceptor changes in CSC were reported to be an elongation of the outer segments of photoreceptors, while disruptions of photoreceptors do not occur before retinal reattachment [9]. Our results show that the photoreceptor disruption which infrequently develops in

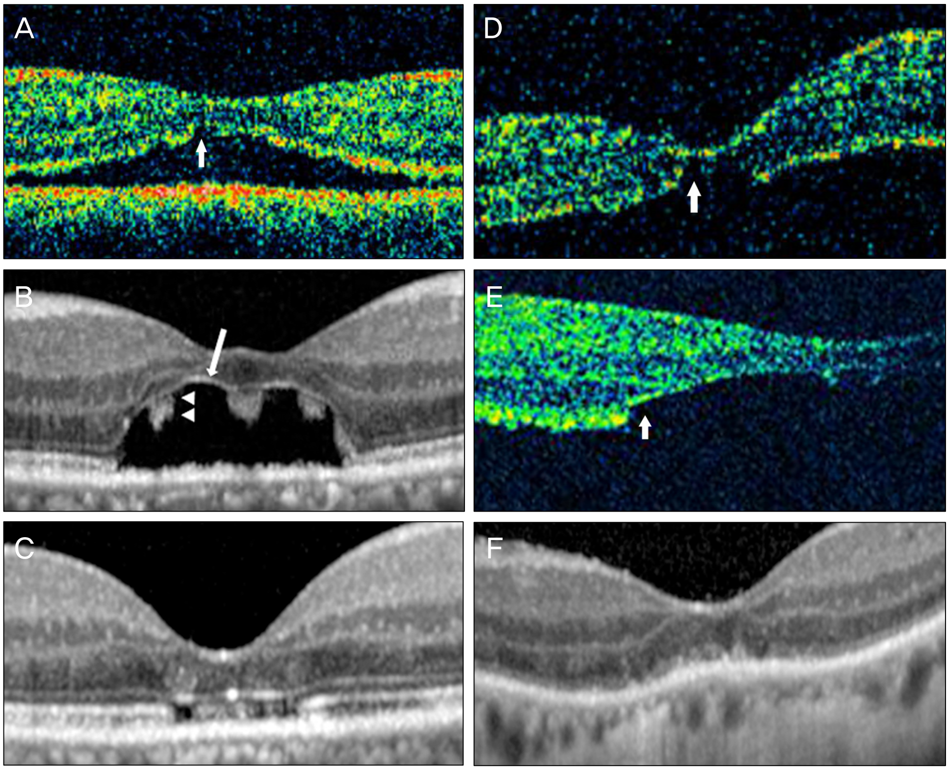

Fig. 3. Optical coherence tomography (OCT) findings of fovea in cases 1 (A-C) and 2 (D-F). Early signs of progressive photoreceptor disruption (a focal defect in inner and outer segment junction layer) on Stratus OCT (vertical scans) are indicated with arrows in A (case 1) and D (case 2) at postoperative one month. Spectral-domain OCT findings (horizontal scans) of case 1 at 12 (B, Spectralis OCT) and 21 (C, Spectralis OCT) months and case 2 at 9 (E, Cirrus OCT) and 21 (F, Spectralis OCT) months show disruption and partial restoration of the photoreceptor layer on the fovea. Long arrows indicate the external limiting membrane, and arrowheads indicate the inner and outer segments of photoreceptors.

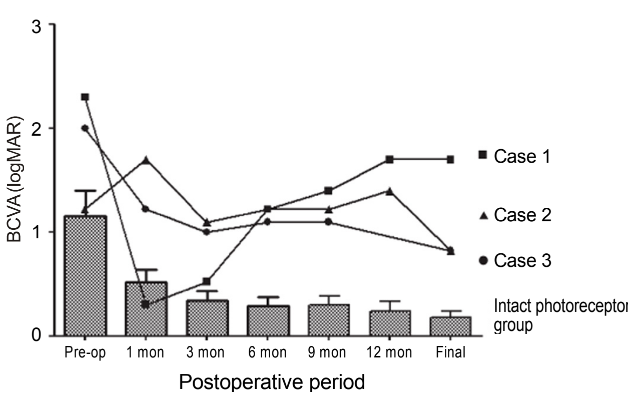

Fig. 4. Serial changes of best-corrected visual acuity (BCVA) in patients with persistent submacular fluid detected on optical coherence tomography one month after successful scleral buckle surgery for macula-off rhegmatogenous retinal detachment. The error bars indicate 95% confidence intervals of BCVA in the intact photoreceptor group (n = 39). Cases 1 and 2 showed progressive photoreceptor disruption postoperatively and case 3 showed early disruption. The final BCVAs of the three cases were significantly worse than those of the intact photoreceptor group ($p < 0.001$ by one-sample *t*-test). logMAR = logarithm of the minimum angle of resolution; pre-op = preoperative.

the persistent submacular fluid after retinal detachment surgery was essentially different from the photoreceptor changes in CSC. Therefore, the two anatomically similar conditions may be different in terms of the photoreceptor environment and the mechanism of photoreceptor damage.

Interestingly, if we had not studied the early postoperative OCT images and had used only the final follow-up OCT images, we would not have noticed the photoreceptor disruption during the absorption of submacular fluid and would not have discovered the reason for poor visual outcome in three of the cases. From our results, we can hypothesize that the photoreceptor disruption and foveal thinning of reported cases [6,7], especially those with chronic retinal detachment, had experienced a similar process of photoreceptor degeneration as in our study cases. We hypothesize that persistent submacular fluid after surgery in clinically attached retinas might mimic a state of chronic retinal detachment and could result in photoreceptor disruption in rare occasions.

It is unclear why photoreceptor disruption developed in only three of the cases and what the mechanism is behind this finding. The clinical characteristics and surgical procedures were not different from the other cases except that these three cases were female. There are several possible explanations for this finding. First, the large amount and long duration of persistent submacular fluid may be a part of causative factors for progressive photoreceptor disruption, as the submacular fluid was of a diffuse type and was not completely absorbed before postoperative 12 months in cases 1 and 2. A previous study using an animal retinal detachment model showed that subretinal fluid interferes with normal diffusion of oxygen and nutrients from the retinal pigment epithelium to photoreceptors and thus could induce photoreceptor degeneration [12]. Moreover, the high concentration of degradative enzymes in the subretinal fluid might have resulted in something more than simple diffusion-blockage in rhegmatogenous retinal detachment [14,15]. Second, in the three cases, there might have been additional defects in structural factors in the subretinal space which could not be detected with SD-OCT, i.e., connections between photoreceptor and retinal pigment epithelium or interphotoreceptor matrix [16]. Third, although we found no systemic abnormalities in those three patients, there might have been some minor problems in anti-apoptotic or protective mechanisms in the photoreceptors. An animal experiment [17] also suggested that the apoptotic signaling pathway plays a crucial role in the photoreceptor cell loss in retinal detachment.

In the final follow-up OCT images in cases 1-3, the photoreceptor IS-OS junction signals reappeared. However, it is unclear whether the photoreceptors were newly regenerated or redistributed from the perifoveal areas. Despite the reappearance of the photoreceptor layer, cases 2 and 3 had poor visual outcomes which might be associated with early photoreceptor injury. The photoreceptor reappearance might have a correlation with the functional restoration as all three patients experienced limited improvement in vision after reappearance of the photoreceptor layer. Wakabayashi et al. [7] recently reported that, among 11 eyes with photoreceptor IS/OS junction disruption which was found 10 months after surgical repair of retinal detachment, 7 (64%) showed restoration of the photoreceptor IS/OS junction on SD-OCT. However, as the authors did not perform OCT in the early postoperative periods, they could not evaluate the association between photoreceptor disruption and persistent submacular fluid.

It is noteworthy that, in the three cases, only the photoreceptors in the fovea disappeared and the photoreceptors in the perifovea were intact throughout the follow-up periods, although subretinal fluid was also present in the perifoveal areas. This indicates that the photoreceptors in the fovea are more likely to be damaged by subretinal fluid than those in the perifovea. The fovea is the region of maximum acuity, and there is a massive peak of cone distribution at the fovea, approximately 100 times the peripheral density [18]. The structural and physiologic characteristics of the fovea may explain the photoreceptor disruption.

Until now, there has been no proven method to remove subretinal fluid or to stop the progression of photoreceptor disruption in cases that show early photoreceptor defects. Vitrectomy and gas tamponade with or without scleral buckle removal might be helpful in removing the submacular fluid and could halt progressive visual deterioration. To support the effects of these therapeutic options on persistent submacular fluid and photoreceptor integrity, however, a greater number of patients and clinical trials are needed. It is fortunate that this detrimental phenomenon occurred only in a very small proportion of surgical cases.

There are several limitations in our study. First, we did not perform SD-OCT in all patients or in all follow-up periods. If we had analyzed immediate photoreceptor status with high-resolution SD-OCT, signs of photoreceptor disruption might have been found earlier than one month after surgery. Second, preoperative OCT was not performed in our study. Early photoreceptor disruption in case 3 might have developed preoperatively. In order to determine the exact time of the initiation of photoreceptor disruption, preoperative SD-OCT is necessary. Third, we did not perform serial OCT on patients without persistent submacular fluid. Therefore, we did not completely rule out delayed photoreceptor changes in patients without persistent submacular fluid.

In conclusion, photoreceptor disruption might occur in relation to persistent submacular fluid even after successful scleral buckle surgery for rhegmatogenous retinal detachment and can be a cause of poor visual outcome. When persistent submacular fluid is present and an early sign of photoreceptor disruption such as focal defects in the IS-OS junction layer is found on postoperative OCT, the clinician should anticipate the possibility of visual deterioration.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Acknowledgements

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