INTRAVITREAL GAS INJECTION WITH LASER PHOTOCOAGULATION FOR HIGHLY MYOPIC FOVEOSCHISIS

Technique and Outcome

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Purpose: To evaluate the effects of gas tamponade combined with laser photocoagulation without vitrectomy in patients with highly myopic foveoschisis.

Methods: This retrospective noncomparative case series included 30 eyes of 23 patients with highly myopic foveoschisis who were treated by intravitreal injection of 0.5 to 0.7 mL C_3F_8 combined with laser photocoagulation 1 week later, and remained in the face-down position for 3 weeks. The patients were followed up for at least 6 months after the treatment. The refractive status, best-corrected visual acuity, and anatomical parameters of retina observed with the optical coherence tomography before and after the treatment were recorded.

Results: The mean age of the 23 patients (6 men and 17 women) was 50.4 ± 15.1 years. The average follow-up duration was 20.8 ± 20.6 months. At the final follow-up, 23 eyes (76.7%) completely (17 eyes) or partially (6 eyes) resolved. Seventeen eyes had complete data of optical coherence tomography parameters, the mean central foveal thickness decreased significantly from 505.24 ± 466.22 μm to 186.41 ± 95.36 μm (P = 0.01), and the mean maximal macular thickness from 687.88 ± 397.00 μm to 313.65 ± 83.07 μm (P = 0.001). The mean final logarithm of the minimum angle of resolution best-corrected visual acuity (Snellen equivalent) of the 30 eyes ranged from 1.6 (20/800) to 0.2 (20/32), showing a slight improvement from 0.91 ± 0.44 (20/163) preoperatively to 0.90 ± 0.39 (20/160) postoperatively (P = 0.87).

Conclusion: C_3F_8 tamponade combined with laser photocoagulation could be an alternative treatment for highly myopic foveoschisis.

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Highly myopic foveoschisis (MF), the splitting within the neurosensory layer of the retina at the macular area in patients with high myopia and posterior staphyloma, is a major cause of visual impairment in highly myopic eyes.[1,2] The prevalence of MF in myopic eyes with posterior staphyloma was reported to be 14.7% to 20%.[3–5] The development of MF was thought to be related to the complex force of vitreoretinal adhesion and the outward force of staphyloma.[2] If left untreated, severe central vision loss and complications such as macular hole (MH), epiretinal membranes, and retinal detachment can occur subsequently. Particularly, foveal detachment developed in 34.5% to 72% of patients with MF,[1,6,7] and has been noted as a predictive factor of poor visual prognosis.[1]

Surgical treatment including a pars plana vitrectomy with or without internal limiting membrane (ILM) peeling followed by intraocular tamponade and postoperative face-down positioning has been reported to be an effective approach in the management of MF.[1,6–9] Pervious studies have also suggested that surgical intervention may improve anatomical and functional outcomes when foveoschisis is associated with foveal detachment.[6,8] However, a high risk of developing postoperative full-thickness MH and retinal detachment was observed.[10–12] Peeling the ILM off the fovea could induce a break of the thinned central foveal tissue and anatomical changes of the macula such as dimpling or damage of the inner retina.[12] The rates of the MH after ILM peeling was reported to be 16.7%

and 20.8%, respectively.[10,11] Previous studies used perfluoropropane (C_3F_8) tamponade alone to treat retinal detachment associated with MH in patients with high myopia, with a reattachment rate of approximately 60% to 70%.[13,14] The efficacy of this less invasive method was subsequently reported in the treatment of MF with foveal detachment.[15,16] This study reports a modified combined therapy, that is, an intravitreal gas injection combined with macular laser photocoagulation one week later, to improve the anatomical and visual outcomes for patients with MF.

Materials and Methods

Twenty-three patients (30 eyes) who received the combined therapy for MF were recruited between January 2008 and January 2014 in this retrospective study. The inclusion criteria were as follows: the decrease in visual function caused by foveoschisis in recent months, more than −6 diopters (D) of spherical equivalent or an axial length of ≥26 mm; and the presence of inner and/or outer retinal schisis in the posterior pole. Exclusion criteria were eyes with preoperative MH, myopic choroidal neovascularization, diffuse macular chorioretinal atrophy, dense opacities of the optical media, or other retinal diseases that could affect the central vision, and those with a history of ocular trauma or vitreoretinal surgery. The study was approved by the ethics committee of Zhongshan Ophthalmic Center and was performed in accordance with the Tenets of the World Medical Association's Declaration of Helsinki. Written informed consent was obtained from all participants.

Preoperatively, the baseline data including age, sex, eye affected, duration of disease, and lens status were obtained. Comprehensive eye examinations including measurement of refractive error, best-

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corrected visual acuity (BCVA) by Snellen chart, axial length by A-scan ultrasonography, intraocular pressure, fundus examination, dilated fundus photography, and standard 6- or 10-mm optical coherence tomography (OCT) (Spectralis HRA OCT; Heidelberg Engineering Inc, Heidelberg, Germany; or Stratus OCT; Carl Zeiss Meditec, Dublin, CA) of the macula were performed. Optical coherence tomography was performed to record the vitreoretinal interface status, central foveal thickness (CFT), and maximal macular thickness (MMT). The CFT was defined as the largest vertical distance measured manually between the retinal pigment epithelium and the inner retinal surface at the foveal area, and the MMT was the largest vertical distance between the retinal pigment epithelium and the inner border of retina within the perifoveal area (circle with 6-mm radius centered at the fovea).

The surgery was performed by one experienced retinal specialist (X.Z.). C_3F_8 gas was withdrawn from the container using a sterile 0.22-μm filter. After proper disinfection using povidone iodine and anterior chamber paracentesis, intravitreal injection of 66% C_3F_8 (0.5–0.7 mL) was performed through the sclera at the 3.5 mm posterior to the limbus between the 10 and 2 o'clock meridians using a 30-gauge needle.

Postoperatively, all patients maintained a face-down position for 3 weeks. One week after surgery, "C" type laser photocoagulation was performed on the temporal side of the foveal avascular zone (more than 1/2 papillary diameter (PD) temporal to the fovea) using a 532-nm green laser (OcuLight GL; IRIS Medical Corp, Mountain View, CA) (spot size 100 μm, laser power 100–150 mW, duration of exposure 100 ms). The photocoagulation was titrated to a light gray burn (Grade 1), then two or three rows of laser burns (applied 2 spot diameter apart, about 10–20 spots) at the same intensity were pattern scanned. Thereafter, they were followed up every 2 months to 3 months. Optical coherence tomography was repeated every 3 months after the procedure. The postoperative assessment included BCVA, intraocular pressure, and OCT measurement.

Anatomical success after the combined treatment was defined as a complete reattachment of the retina in the foveal area observed with OCT. A partial anatomical success was defined as persistent foveal schisis with decreased foveal thickness equal to or more than 50%. Anatomical failure was defined as either the foveal thickness decreased less than 50% or an increase in the schisis area. A repeated injection was performed if OCT showed anatomical failure at 1 month postoperatively, or recurrence of foveoschisis during follow-up. Vitrectomy would be performed if

the retinal detachment or MH occurred during follow-up.

Statistical Analysis

The BCVA in Snellen value was converted to the logarithm of the minimum angle of resolution (logMAR) for statistical analysis. Baseline and follow-up data were compared using Student t-test. The results were presented as the mean ± SD. A P value of <0.05 was considered significant. Analyses were performed using the Stata Statistical Software, Release 8.0 (StataCorp, College Station, TX).

Results

Baseline Characteristics

We recruited 30 eyes of 23 patients (6 men and 17 women) in this study, whose baseline characteristics were summarized in Table 1. The mean age was 50.4 ± 15.1 years (range, 26–76 years). The mean axial length was 28.85 ± 1.43 mm (range, 26.06–33.00 mm), and the mean spherical equivalent of 27 eyes (the other three eyes were pseudophakic) was −14.47 ± 5.53 D (range, −7.25 to −30.5 D). The average follow-up period was 20.8 ± 20.6 months (range, 6–67 months). Preoperative OCT showed that 16 eyes had foveal detachment and 3 eyes had epiretinal membrane with vitreomacular traction. All patients presented choroid–retinal degeneration of the macula with posterior staphyloma. None has predominant peripheral retinal degeneration.

Anatomical Outcome

One month after the combined treatment, 25 eyes responded well with decreased height and/or area of the foveal schisis. Thereafter, the CFT decreased gradually in these subjects.

At the final follow-up (average 20.7 ± 22.6 months), 23 eyes (76.7%) resolved after single or repeated gas injections. Seventeen eyes (56.7%) of those showed the foveoschisis resolved completely, and these cases were considered to be anatomical success. A partial success with decreased foveal thickness was achieved in six eyes (20.0%). Twelve cases received a second injection of C_3F_8 one month after the initial treatment.

Seventeen eyes had complete data of OCT parameters, the mean CFT decreased significantly from 505.24 ± 466.22 μm to 186.41 ± 95.36 μm ($P = 0.01$; paired t-test), and the mean MMT from 687.88 ± 397.00 μm to 313.65 ± 83.07 μm ($P = 0.001$). For the cases obtaining anatomical success or partial success, the mean CFT decreased significantly from 567.36 ± 493.01 μm to 171.43 ± 90.84 μm ($P = 0.006$), and the mean MMT from 744.14 ± 417.38 μm to 303.86 ± 83.62 μm ($P = 0.002$).

In two cases with an initially good response, recurrence of foveoschisis occurred 2 months after the first injection. In 4 cases, increase in the height of the schisis was noted during follow-up. Vitrectomy with ILM peeling and silicone oil tamponade was performed for one case with MH retinal detachment. The postoperative OCT showed successful foveal reattachment.

Visual Acuity Outcome

At baseline, the logMAR BCVA (Snellen equivalent) ranged from 1.6 (20/800) to 0.3 (20/40), and in 19 eyes, the logMAR BCVA were worse than 0.6 (20/80). The mean final logMAR BCVA (Snellen equivalent) of the 30 eyes ranged from 1.6 (20/800) to 0.2 (20/32), showing a slight improvement from 0.91 ± 0.44 (20/163) preoperatively to 0.90 ± 0.39 (20/160) postoperatively ($P = 0.87$). For the cases with complete or partial MF resolution, the logMAR BCVA improved from 1.00 ± 0.44 (20/200) to 0.92 ± 0.40 (20/167) ($P = 0.37$). Vision acuity improved by two or more than two lines of Snellen visual acuity in 6 cases, and remained the same in 14 cases.

Complications

The intraocular pressure after the treatment was within the normal range in all cases. No patient complained of visual symptom of scotoma after treatment. One eye developed a peripheral retinal tear 6 months after the procedure, and then received retinal photocoagulation. One eye showed a full-thickness MH along with retinal detachment 5 months after the treatment. Vitrectomy with ILM peeling and silicone oil tamponade was then performed.

Discussion

This retrospective noncomparative case series included 30 eyes of 23 patients with MF, demonstrating that intravitreal C_3F_8 injection combined with laser photocoagulation can yield an accepted outcome. After a follow-up of at least 6 months, the foveoschisis of 23 eyes completely or partially resolved with improved or stable visual acuity, obtaining an effective rate of 76.7%.

Several studies suggested that the separation of retinal layers in MF may be due to inward traction caused in part by a progressive ectasia of the sclera and the relative resistance to a stretch of the inner

Table 1. Patient Characteristics and Treatment Outcome of 30 Eyes Receiving Intravitreal C$_3$F$_8$ Injection Combined With Laser Photocoagulation for Therapy of MF

No.	Age/Sex	Eye Affected	Refraction (D)	Lens Status	Axial Length (mm)	Macular Anomaly	Number of Injection	Anatomical results	LogMAR BCVA (Snellen Equivalent)		CFT (µm)		MMT (µm)	
									Preoperative	Postoperative	Preoperative	Postoperative	Preoperative	Postoperative
1	76/M	OD	—	Pseudophakic	29.43	FD, EM	2	Partial	1.4 (20/500)	0.7 (20/100)	969	407	1,085	470
2	40/F	OD	−11.75	Phakic	29.42	No	1	Failure	0.5 (20/63)	0.9 (20/160)	199	226	488	341
3-1	36/F	OD	−29.75	Phakic	32.03	No	2	Partial	1.3 (20/400)	0.7 (20/100)	369	170	387	245
3-2	36/F	OS	−30.5	Phakic	29.77	No	1	Success	0.7 (20/100)	0.7 (20/100)	209	174	289	259
4	56/F	OS	−12	Phakic	28.26	FD, EM	2	Success	1.3 (20/400)	1.6 (20/800)	973	147	1,027	261
5	28/M	OS	−18	Phakic	30.02	No	1	Success	0.7 (20/100)	0.8 (20/125)	134	110	473	294
6	60/F	OS	−15.5	Phakic	29.73	No	2	Failure	0.5 (20/63)	1.5 (20/632)				
7-1	67/M	OD	−7.75	Phakic	28.62	No	1	Success	1.6 (20/800)	1.6 (20/800)	1789	155	1789	187
7-2	67/M	OD	−7.75	Phakic	28.62	FD	2	Success	0.9 (20/160)	0.8 (20/125)	1,137	308	1,210	444
8	41/F	OD	−9.75	Phakic	27.62	No	1	Success	1 (20/200)	0.7 (20/100)	240	202	423	311
9	72/F	OD	—	Pseudophakic	29.45	No	1	Success	1 (20/200)	0.9 (20/160)	57	39	583	191
10	43/F	OD	−15	Phakic	28.29	FD	1	Partial	1.5 (20/632)	0.7 (20/100)	304	146	488	258
11-1	51/M	OS	−12.75	Phakic	29.45	No	1	Success	1 (20/200)	1 (20/200)	439	134	693	331
11-2	51/M	OD	−11.25	Phakic	28.92	FD	1	Success	0.4 (20/50)	0.5 (20/63)	560	146	802	310
12-1	44/F	OS	−18.5	Phakic	27.04	No	1	Failure	1.1 (20/250)	1.1 (20/250)	148	174	390	293
12-2	44/F	OD	−12.25	Phakic	27.93	No	1	Failure	0.4 (20/50)	0.4 (20/50)	299	369	398	444
13	47/F	OD	−7.25	Phakic	26.06	FD	2	Success	0.5 (20/63)	0.7 (20/100)	645	176	808	387
14	65/F	OS	−18	Phakic	29.88	EM	2	Partial	1.2 (20/320)	1.2 (20/320)	118	86	361	306
15	26/F	OS	−15	Phakic	29.73	FD	1	Success	1.3 (20/400)	1 (20/200)				
16-1	53/F	OS	−17	Phakic	26.98	FD	2	Partial	0.5 (20/63)	1.3 (20/400)				
16-2	53/F	OD	−17.25	Phakic	27.72	FD	1	Success	1.1 (20/250)	1.3 (20/400)				
17	53/F	OD	−10.75	Phakic	27.62	FD	1	Success	1.6 (20/800)	0.5 (20/63)				
18	33/F	OD	−10.5	Phakic	27.40	FD	2	Success	0.3 (20/40)	0.3 (20/40)				
19	36/F	OS	−14	Phakic	29.04	No	1	Success	0.4 (20/50)	1 (20/200)				
20	76/F	OD	—	Pseudophakic	33	FD	2	Failure	0.5 (20/63)	0.4 (20/50)				
21-1	37/M	OS	−12	Phakic	27.95	FD	1	Failure	0.3 (20/40)	0.9 (20/160)				
21-2	37/M	OD	−11	Phakic	27.65	FD	1	Failure	1.2 (20/320)	0.7 (20/100)				
22-1	53/F	OS	−14.75	Phakic	29.43	FD	2	Partial	1.3 (20/400)	1.3 (20/400)				
22-2	53/F	OD	−14.5	Phakic	29.12	FD	2	Success	1.6 (20/800)	1.6 (20/800)				
23	67/M	OD	−16.25	Phakic	29.36	No	1	Success	0.3 (20/40)	0.2 (20/32)				

EM, macular epiretinal membrane; FD, foveal detachment.

retinal layers and the retinal vessels.[2] Wu et al[17] in a cross-sectional study observed 124 eyes and found that axial length of greater than 31 mm, chorioretinal atrophy, and vitreoretinal interface factors were independently and significantly associated with the presence of MF in highly myopic eyes. Among the interface factors, the presence of vitreomacular traction, vitreoschisis, the presence of epiretinal membranes, or traction of the ILM on the retinal vessels in a posterior staphyloma could contribute to the development and persistence of the retinoschisis. Longitudinal studies of case series of patients with MF suggest that it is a slowly progressive condition leading to severe central visual loss in untreated cases.[1,3,18] Treatment of MF has progressively evolved over the years: macular and equatorial buckling, internal tamponade, scleral buckling with a macular plombe, vitrectomy with a macular buckle, vitrectomy and gas tamponade with or without ILM peeling, and vitrectomy with limited ILM peeling (nonpeeling of residual epifoveolar ILM).[2] Currently, the vitrectomy with gas tamponade seems to be the most favored of all the surgical options available. However, vitrectomy on patients with high myopia could be hazardous, carrying the risk of inducing MH formation and retinal nerve fiber layer defects.

Benhamou et al[3] noted the absence of preretinal structures in 17 of 21 eyes with MF, and observed that foveal detachment often did not resolve after complete vitrectomy. They concluded that vitreomacular traction was not responsible for the initial development of MF. In this study, we found that only three eyes had severe vitreomacular traction, whereas the others showed only little or no vitreomacular traction. This finding seems to reinforce the conclusion above that the vitreomacular traction may not be the essential factor for MF to occur. In highly myopic eyes, especially those with MF, the vitreous usually liquefied and split into layers, the posterior hyaloid membrane usually separated from the vitreous cortex, and the ILMs were thinner, and tended to fragment.[19] Besides, anatomical success and visual improvement are not always achieved in vitrectomy.[2,16] All the above indicate that vitrectomy is not the necessary prerequisite for the resolution of MF. Thus, Ikuno et al[9] suggested the idea of treating foveal detachments without dense membranes by producing a posterior vitreous detachment with gas injection. Presumably, the expansile gas bubble could stretch the vitreous and cause a posterior vitreous detachment, thus releasing vitreoretinal traction, allowing the retina to reattach. Recent studies have revealed that gas tamponade with C_3F_8 could result in faster MF resolution and better improvement of visual acuity.[20,21] However, there is limited litera-

ture on intravitreal gas injection for the treatment of MF without vitrectomy.[15,16]

Of the 30 cases receiving treatment in this study, 12 eyes showed anatomical reattachment after single injection, and another 5 eyes obtained anatomical success after repeated injection. A partial success with decreased foveal thickness was achieved in six eyes. Thus, our experience with this case series suggests that this less invasive treatment could be effective in 76.7% subjects with MF, and the anatomical success after combined treatment is often achieved after a prolonged period and repeated gas injections. Given that the vitrectomy is usually complicated and hazardous in highly myopic eyes, this simple and low-cost procedure is suitable for many hospitals, especially those which lack technology and equipment.

In 2013, Wu et al[16] reported 10 cases of foveal detachment associated with MF, and the foveoschisis resolved in 70% of the cases after intraocular C_3F_8 tamponade, which is similar to the results from our study. This study showed that combined therapy with macular focal photocoagulation improved the resolution rate. We speculated that the adhesive effect by the laser burns and the therapeutic stimulation of viable retinal pigment epithelium cells by the laser treatment could help to promote the resolution of the foveoschisis. In each patient, a test burn was used to titrate the appropriate power, so as to maximize the reduction of the damage to neurosensory retina.

Despite the good anatomical results, we found no statistically significant improvement in BCVA after treatment. The poor preoperative visual acuity was perhaps correlated with a poor visual prognosis. In this study, 16 eyes had MF with foveal detachment before treatment, and the preoperative logMAR BCVA of 19 eyes were worse than 0.6 (Snellen equivalent 20/80). These complicated conditions may hinder further visual recovery. There are several limitations to this study, which include its retrospective design, small sample size, and lack of a control group. The missing of the OCT parameters in 12 cases was not favorable for the accurate analysis of the anatomical outcome. We were also unable to identify the underlying cause of anatomical failure, and which patients are better candidates for this low-cost and less invasive treatment.

In conclusion, we observed acceptable success rates using intravitreal expansible gas injection combined with laser photocoagulation in treating patients with MF. This simple, low-cost, and less invasive procedure may be considered as an alternative for vitrectomy in selected cases of MF. Repeated injection is also required in some patients who obtained a partial response or even no response. Long-term follow-up to
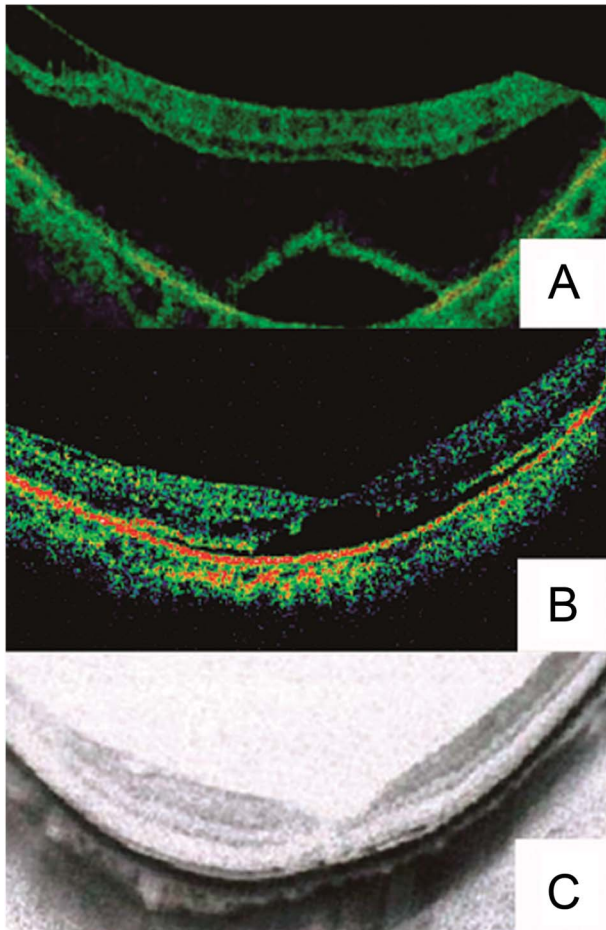
Fig. 1. Optical coherence tomography images taken preoperatively and postoperatively in the highly myopic patient (no. 17) undergoing intravitreal C_3F_8 injection combined with laser photocoagulation. **A.** Optical coherence tomography images revealed foveoschisis with foveal detachment, Snellen vision acuity 20/800. **B.** Postoperative 1-month follow-up: The OCT showed a partial resolution with decreased height and area of the foveal schisis. **C.** Postoperative final follow-up (47-month): The OCT showed a complete retinal reattachment and resolution of foveoschisis. The final Snellen vision acuity was 20/63.

Fig. 2. Optical coherence tomography images taken preoperatively and postoperatively in the highly myopic patient (no. 13) undergoing intravitreal C_3F_8 injection combined with laser photocoagulation. **A.** Optical coherence tomography images revealed foveoschisis with foveal detachment, Snellen vision acuity 20/63. **B.** Postoperative 1-month follow-up: The OCT showed a partial resolution with decreased area of the foveal schisis. **C.** Postoperative final follow-up (30-month): The OCT showed a complete retinal reattachment and resolution of foveoschisis. The final Snellen vision acuity was 20/100.

assess possible complications and recurrences are needed in the future work, as well as prospective comparative studies to identify the indications and visual outcomes of this treatment method for MF.

Report of Cases

Patient No. 17

A 53-year-old woman with −10.75 D myopia in right eye presented with gradual decreased vision in the right eye that developed over about 6 months. During the preoperative evaluation, poor vision in the right eye was noted, with BCVA being 1.6 logMAR (Snellen equivalent 20/800) (Figure 1). The axial length was 27.62 mm in the right eye. Fundo-
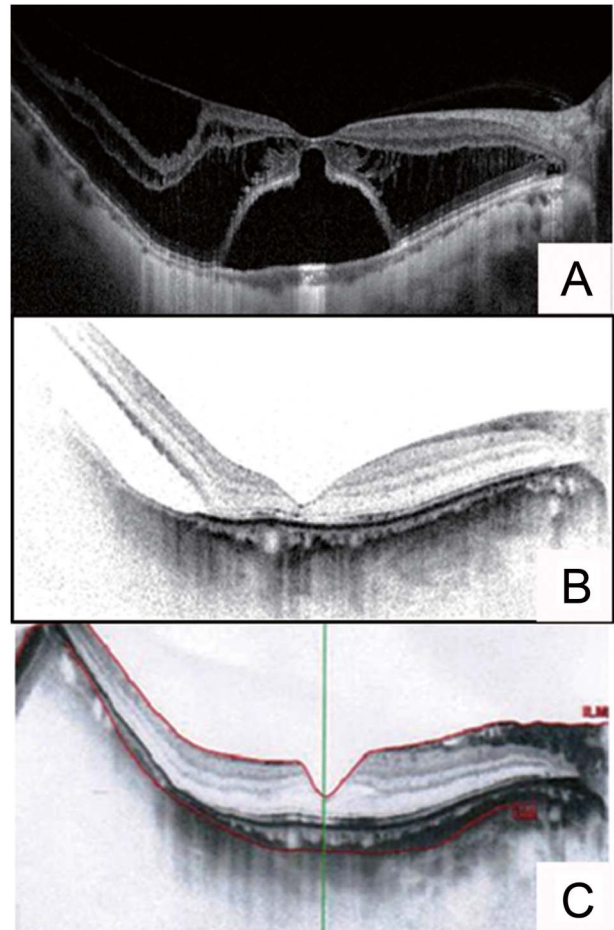
scopy revealed a tessellated fundus with diffuse atrophy, and OCT showed foveoschisis with foveal detachment (Figure 1A). One month after combined treatment, the patient responded well with decreased height and area of the foveal schisis (Figure 1B). Thereafter, the CFT decreased gradually. At the final follow-up (47 months later), the foveoschisis resolved completely (Figure 1C), and the final BCVA in right eye was 0.5 logMAR (Snellen equivalent 20/63).

Patient No. 13

A 47-year-old woman with −7.25 D myopia in right eye was referred to our clinic. She complained of decreased vision in the right eye, which had persisted for about 3 months before her initial visit to

our hospital (Figure 2). The patient's BCVA was 0.5 logMAR (Snellen equivalent 20/63), and her axial length was 26.06 mm in the right eye. Fundoscopy revealed a tessellated fundus with diffuse atrophy, and OCT showed foveoschisis with foveal detachment (Figure 2A). One month after combined treatment, the patient responded well with decreased area of the foveal schisis (Figure 2B). A repeated injection was performed because the fundus examinations showed no further improvement at 2 months postoperatively. At the final follow-up (30 months after the initial treatment), the retina had reattached (Figure 2C), and the final BCVA in right eye was 0.7 logMAR (Snellen equivalent 20/100).

Key words: myopic foveoschisis, perfluoropropane, gas tamponade, laser photocoagulation.

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