

Foveal Crack Sign: An OCT Sign Preceding Macular Hole After Vitrectomy for Rhegmatogenous Retinal Detachment



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• **PURPOSE:** To describe an optical coherence tomography (OCT) sign preceding macular hole (MH) formation after pars plana vitrectomy (PPV) for rhegmatogenous retinal detachment (RRD).

• **DESIGN:** Retrospective observational case series.

• **METHODS:** Patients who underwent PPV for RRD at Osaka Rosai Hospital between January 2014 and December 2017 were examined. First, the medical records of the patients who had secondary MH after RRD repair were examined, and their sequential changes of the OCT images until MH formation were evaluated. Second, the OCT findings and the medical records of all patients who underwent PPV for RRD were evaluated based on the findings of the cases of secondary MH.

• **RESULTS:** Ten eyes of 10 patients who had secondary MH after PPV for RRD were enrolled. Before MH formation, all eyes had parafoveal epiretinal membrane (ERM) and a characteristic OCT sign that was termed a foveal crack sign (FCS), a hyperreflective vertical line in the foveola with a deformation of the fovea. FCS was found 255 ± 217 days after PPV for RRD, and MH developed 232 ± 171 days after FCS appearance. Furthermore, among 518 eyes that underwent PPV for RRD, FCS with parafoveal ERM was found in 3 eyes without succeeding MH after RRD repair. FCS of these 3 eyes were found 363 ± 4 days after PPV for RRD.

• **CONCLUSIONS:** In all cases of secondary MH formation after PPV for RRD, FCS with parafoveal ERM was found before MH formation. This sign may predict secondary MH formation caused by ERM traction. (Am J Ophthalmol 2020;218:192–198. © 2020 Elsevier Inc. All rights reserved.)

A SECONDARY MACULAR HOLE (MH) IS A POSTOPERATIVE complication of rhegmatogenous retinal detachment (RRD) surgery.^{1–9} Although MH formation is reported to be a rare complication after RRD repair,^{8–10} the complication should be noted because it can cause severe visual loss that would require an additional pars plana vitrectomy (PPV) to close the hole.¹¹ The onset time of this complication varied in previous reports, but the cases that underwent PPV for RRD tended to develop MH at a relatively late stage more than 1 year after RRD repair.^{5,7–9,12}

The pathogenesis of MH formation after PPV for RRD described in previous reports includes the association of epiretinal membrane (ERM), cystoid macular edema (CME), macula-off RRD, recurrent RRD, and high myopia.^{8,10,11,13,14} Recent reports using optical coherence tomography (OCT) have suggested that continuous tangential traction caused by ERM is the most considerable factor for MH formation after PPV for RRD.^{15–17} As opposed to an MH, ERM is a common postoperative complication of PPV for RRD, which occurs in the early stage after RRD repair.^{18,19} Taking into account the gaps of prevalence and onset time between these 2 complications, a clinical question arises as to which cases of patients with ERM after PPV for RRD should be monitored for MH formation in the long term.

The present study retrospectively examined sequential OCT images of eyes with MH after PPV for RRD. We report a novel characteristic OCT sign that precedes MH formation after PPV for RRD. OCT images of all patients who underwent PPV for RRD were further investigated, and we identified the progression of the cases with this sign.

SUBJECTS AND METHODS

THIS RETROSPECTIVE STUDY WAS CONDUCTED IN ACCORDANCE with the tenets of the Declaration of Helsinki and approved by the institutional review board of the Osaka Rosai Hospital. Written informed consent was obtained from all patients.

First, the sequential changes of OCT findings in all patients who developed an MH after primary PPV for RRD at Osaka Rosai Hospital between January 2014 and December 2017 were retrospectively investigated. The

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OCT findings were examined for the presence of a sign that could precede MH formation after PPV for RRD. Additionally, the clinical characteristics of these patients were collected from the medical records. Exclusion criteria were history of intraocular surgery, except for cataract surgery; history of trauma; combined or simultaneous MH with primary RRD; tractional RD; proliferative vitreoretinopathy; presence of any other retinal disease, except for ERM, which could affect the status of the macula; and a follow-up period less than 6 months.

Second, the OCT findings and the medical records of all patients who underwent primary PPV for RRD during the same period were also investigated. Exclusion criteria were the same as above. The natural course of a certain OCT finding which developed after PPV for RRD was examined.

- **DATA COLLECTION:** Patients underwent comprehensive ophthalmic examinations at least before and 1, 3, and 6 months after PPV for RRD. Most patients were followed for 12 months or more at the clinicians' discretion. Examinations included measurement of best-corrected visual acuity, measurement of intraocular pressure, slit-lamp biomicroscopy, fundus photography, and spectral-domain OCT (Cirrus HD-OCT; Carl Zeiss Meditec, Dublin, California) or swept-source OCT (DRI-OCT; Topcon Medical Systems, Tokyo, Japan). A swept-source OCT biometer (intraocular lens Master 500 or 700; Carl Zeiss Meditec) was used to measure the axial length of all patients before RRD surgery. Clinical data, including patient age, sex, axial length, macular status at initial surgery, best-corrected visual acuity at each visit, surgical procedure of each PPV, presence of any postoperative OCT findings, onset time of the OCT findings, and MH size were reviewed from medical records. Continuous variables were expressed as mean \pm standard deviation.

Horizontal and vertical B-scan cross-sectional images were acquired in each OCT examination. All OCT images obtained before and after surgery were evaluated by 3 masked investigators (T.I., Y.I., H.N.). In this evaluation, ERM was defined as hyperreflective lines on the retina accompanied by deformation of the foveal pit, and parafoveal ERM as ERM without covering the umbo. An MH was defined as a full-thickness anatomic defect in the fovea. The minimum foveal thickness (MFT) was measured manually between the vitreoretinal interface and the retinal pigment epithelium at the thinnest point of the foveola, and the diameter of the MH was measured at the narrowest hole point in the mid-retina by using the OCT caliper function as previously reported.^{20,21}

- **SURGICAL PROCEDURE:** Twenty-five gauge PPV (Constellation Vision System; Alcon Laboratories, Inc., Fort Worth, Texas) with a wide-angle viewing system (Resight; Carl Zeiss Meditec) was performed in all patients with RRD. Phacoemulsification and intraocular lens im-

plantation were performed simultaneously at the surgeons' discretion. A core vitrectomy and peripheral vitreous shaving under scleral indentation were performed using a vitreous cutter. Triamcinolone acetonide was used to clarify the vitreous gel and posterior vitreous membrane as needed. Internal limiting membrane (ILM) peeling using Brilliant Blue G stain (Sigma-Aldrich, St. Louis, Missouri) was performed at the surgeons' discretion. Diathermic coagulation was performed around all retinal breaks. As much subretinal fluid as possible was then drained from the pre-existing retinal break or the break created by drainage retinotomy. After fluid-air exchange, endophotocoagulation around all retinal breaks was performed. If needed, a long-acting gas (sulfur hexafluoride or octafluoropropane) or silicon oil was injected into the vitreous cavity.

The cases which developed MH after PPV for RRD underwent additional PPV to close the hole. Removal of the residual vitreous, ERM, and ILM were performed. After fluid-air exchange, sulfur hexafluoride was injected into the vitreous cavity as a case-dependent treatment.

RESULTS

TEN EYES THAT DEVELOPED AN MH AFTER PPV FOR RRD WERE enrolled in this study. Figure 1 shows the sequential morphological changes of the representative case (Figure 1, Case 5) up to MH formation after PPV for RRD. Before MH formation, a hyperreflective vertical line in the foveola with a deformation of the fovea was found (Figure 1, D). The authors named this OCT finding the *foveal crack sign* (FCS). Table 1 summarizes the OCT findings in the 10 patients up to the MH formation. Swept-source OCT was used in 8 patients (80%). Regardless of the type of OCT, FCS was observed as a hyperreflective line at the umbo in all cases (Figure 2), and parafoveal ERM had developed by the time FCS appeared in all cases. This sign was found 255 ± 217 days after PPV for RRD, and the mean interval from FCS appearance to MH diagnosis was 232 ± 171 days. The OCT images between FCS appearance and MH formation could be obtained in 3 of 10 eyes (Table 1, Cases 2, 5, and 6), and the MFT decreased before MH formation in all 3 cases. The mean diameter of an MH was $135 \pm 34 \mu\text{m}$.

Characteristics of these patients are shown in Table 2. The mean age at the time of RRD diagnosis was 57.9 ± 8.9 years old, and 7 of the 10 patients (70%) were men. The mean axial length was 25.8 ± 1.2 mm. All eyes had macula-on RRD and underwent PPV for RRD without ILM peeling. Retinal reattachment was achieved with primary surgery, and the MH was closed with an additional surgery in all cases.

Furthermore, 518 eyes that underwent primary PPV for RRD during the study period were evaluated. Among

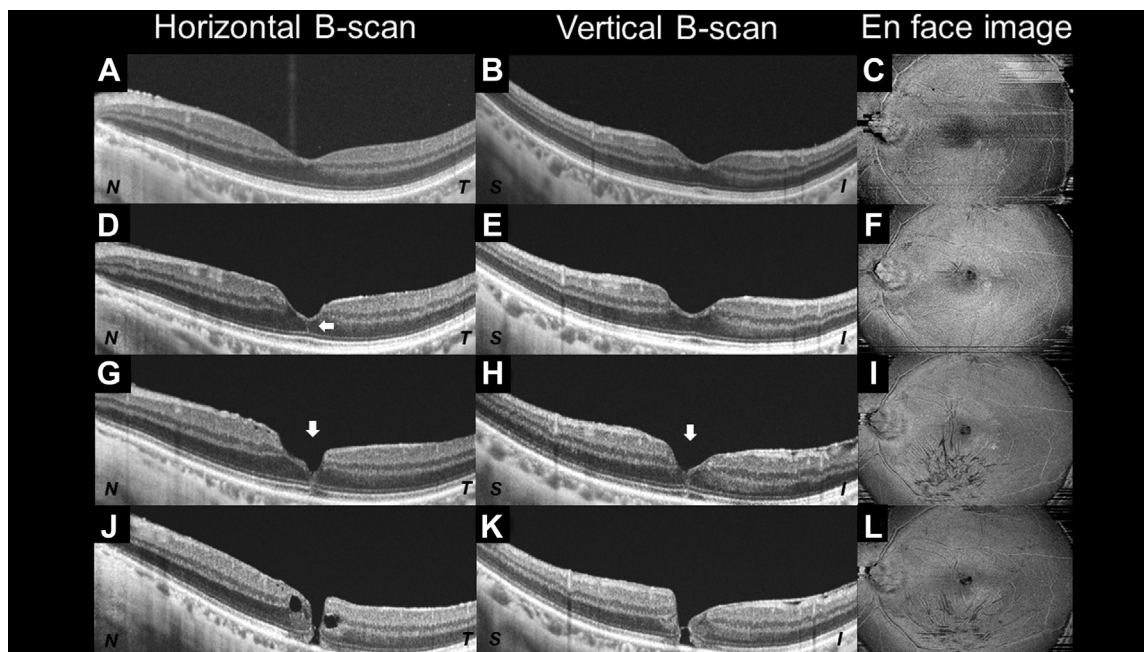


FIGURE 1. Swept-source optical coherence tomography images of Case 5 up to the macular hole formation after a vitrectomy for rhegmatogenous retinal detachment. (A-C) One week after rhegmatogenous retinal detachment repair. No abnormality was observed in the fovea. Visual acuity was 20/32. (D-F) Twelve months after rhegmatogenous retinal detachment repair, a hyperreflective vertical line (white arrow) appeared along with the progression of parafoveal epiretinal membrane. The authors named this finding a *foveal crack sign*. The hyperreflective vertical line was observed only in the inner retina, and the minimum foveal thickness was 181 μm . Visual acuity was 20/16. (G-I) Twenty-four months after the rhegmatogenous retinal detachment repair, the foveal crack sign became clear (white arrows) along with the further progression of the parafoveal epiretinal membrane. The hyperreflective vertical line extended to full thickness, and the foveal pit was deformed by the traction of the inferior epiretinal membrane. The minimum foveal thickness was 114 μm . Visual acuity was 20/20. (J-L) Thirty-three months after rhegmatogenous retinal detachment repair, a macular hole developed. Visual acuity deteriorated to 20/32. I = inferior; N = nasal; S = superior; T = temporal.

TABLE 1. OCT Findings Until MH Formation After a Vitrectomy for RRD

Case	OCT	Parafoveal ERM	Interval from RRD Surgery to FCS Appearance (Days)	Interval from FCS Appearance to MH Diagnosis (Days)	MFT at FCS Appearance (μm)	MFT at the Last Visit Before MH Formation (μm)	MH Size (μm)
1	SD	Present	208	61	137	NA ^a	89
2	SD	Present	45	114	134	116	112
3	SS	Present	363	147	180	NA ^a	147
4	SS	Present	365	86	179	NA ^a	126
5	SS	Present	371	623	181	114	158
6	SS	Present	28	434	161	124	95
7	SS	Present	182	189	172	NA ^a	190
8	SS	Present	32	129	111	NA ^a	148
9	SS	Present	175	189	116	NA ^a	180
10	SS	Present	778	350	165	NA ^a	103

ERM = epiretinal membrane; FCS = foveal crack sign; MFT = the minimum foveal thickness; MH = macular hole; NA = not available; OCT = optical coherence tomography; RRD = rhegmatogenous retinal detachment; SD = spectral domain; SS = swept source.

^aA macular hole developed at the next visit of the foveal crack sign appearance.

them, 464 eyes (90%) were postoperatively followed for 12 months or more. ILM peeling was performed in 160 of 211 eyes (76%) that had macula-off RRD and in 139

of 307 eyes (45%) that had macula-on RRD. No eyes that underwent PPV for RRD with ILM peeling developed postoperative ERM and FCS. Postoperative ERM was

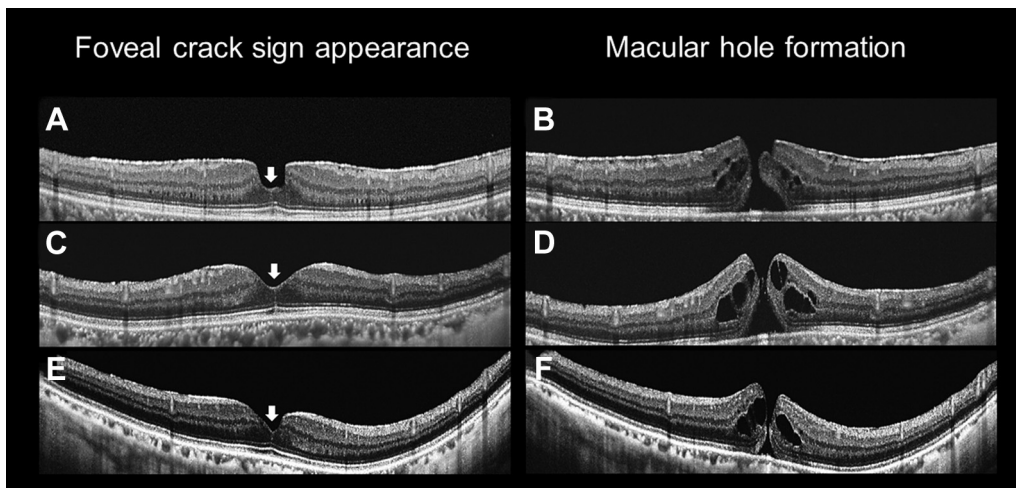


FIGURE 2. A characteristic optical coherence tomography sign preceding formation of a macular hole after a vitrectomy for rhegmatogenous retinal detachment. (A, B) Optical coherence tomography images of Case 3. (A) Twelve months after rhegmatogenous retinal detachment repair, a foveal crack sign (white arrow) was observed. This sign was accompanied by parafoveal epiretinal membrane. Visual acuity was 20/13. (B) Seventeen months after rhegmatogenous retinal detachment repair, a macular hole developed. Visual acuity deteriorated to 20/25. (C, D) Optical coherence tomography images of Case 7. (C) Six months after rhegmatogenous retinal detachment repair, a foveal crack sign (white arrow) appeared along with parafoveal epiretinal membrane. Visual acuity was 20/16. (D) Twelve months after rhegmatogenous retinal detachment repair, a macular hole developed. Visual acuity deteriorated to 20/40. (E, F) Optical coherence tomography images of Case 10. (E) Twenty-six months after rhegmatogenous retinal detachment repair, a foveal crack sign (white arrow) appeared along with parafoveal epiretinal membrane. Visual acuity was 20/16. (F) Thirty-seven months after rhegmatogenous retinal detachment repair, a macular hole developed. Visual acuity deteriorated to 20/32.

TABLE 2. Characteristics of Patients With MH Formation After a Vitrectomy for RRD

Case	Age/Sex	Axial Length (mm)	Macular Status	BCVA at RRD Diagnosis (Decimal Units)	PPV for RRD			BCVA After RRD Repair (Decimal Units)
					ILM Peeling	Gas Tamponade	Recurrent RRD	
1	56/M	26.4	On	0.3	No	SF6	No	1.0
2	64/M	24.7	On	0.7	No	SF6	No	1.0
3	54/M	25.2	On	1.0	No	Air	No	1.5
4	43/F	26.8	On	1.2	No	SF6	No	1.5
5	62/M	27.3	On	0.02	No	Air	No	1.2
6	73/F	23.4	On	1.2	No	SF6	No	1.5
7	62/M	26.2	On	0.9	No	Air	No	1.2
8	64/F	24.9	On	1.0	No	Air	No	1.2
9	43/M	25.6	On	0.7	No	Air	No	1.2
10	58/M	27.5	On	0.9	No	Air	No	1.2

BCVA = best-corrected visual acuity; F = female; ILM = internal limiting membrane; M = male; PPV = pars plana vitrectomy; RRD = rhegmatogenous retinal detachment; SF6 = sulfur hexafluoride.

observed in 58 of 518 eyes (11%) (11 eyes had macula-off RRD, 47 eyes had macula-on RRD). Parafoveal ERM was observed in 2 of 11 eyes with previous macula-off RRD and in 24 of 47 eyes with previous macula-on RRD. Although FCS was found in 13 of 518 eyes (2.5%), of which 10 eyes (Cases 1 to 10) developed MH after PPV for RRD, 3 eyes (Table 3, Cases 11 to 13) developed FCS without proceeding to MH formation (Figure 3). Table 3 shows the characteristics of the 3 eyes (Cases

11-13). All 3 eyes underwent PPV for RRD without ILM peeling and achieved retinal reattachment with primary surgery. Postoperative parafoveal ERM developed in each case, and FCS was found 363 ± 4 days after PPV for RRD. Cases 11 and 13 (Table 3) were followed after FCS appearance, and their MFT decreased during their follow-up period. Although Case 11 (Table 3) was still being followed as of the writing of this paper, all eyes have not developed an MH in their follow-up period.

TABLE 3. Characteristics of Patients Who Developed Foveal Crack Sign Without a Succeeding MH After a Vitrectomy for RRD

Case	Age/Sex	Axial Length (mm)	Macular Status	PPV for RRD			Interval from RRD Surgery to FCS Appearance (Days)	Interval from FCS Appearance to the Final Visit (Days)	MFT at FCS Appearance (μm)	MFT at the Final Visit (μm)
				ILM Peeling	Gas	Tamponade				
11	60/F	25.1	On	No	Air	363	729	166	155	
12	59/F	24.6	On	No	Air	359	0 ^a	156	^a	
13	62/M	24.5	On	No	Air	368	364	190	109	

F = female; FCS = foveal crack sign; ILM = internal limiting membrane; M = male; MFT = the minimum foveal thickness; PPV = pars plana vitrectomy; RRD = rhegmatogenous retinal detachment.

^aCase 12 finished follow-up at the time of FCS appearance.

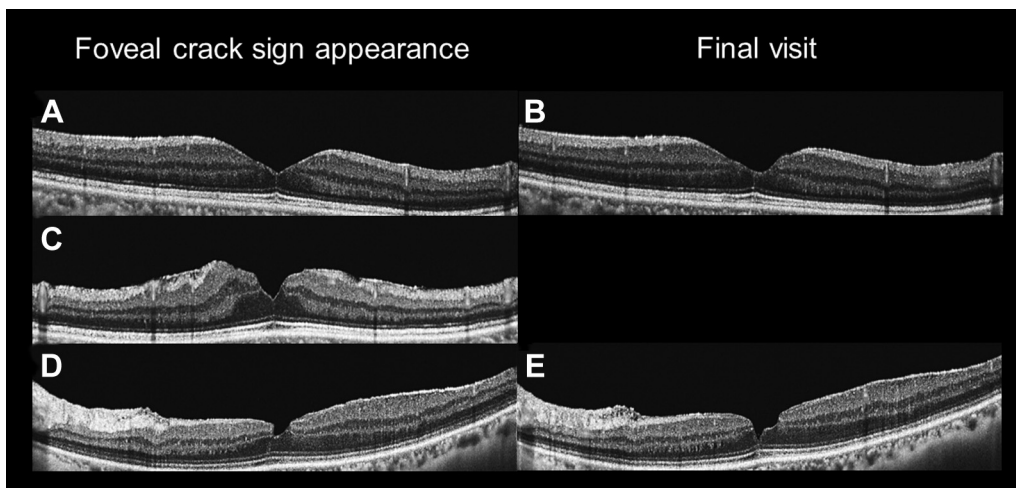


FIGURE 3. Optical coherence tomography images of the cases which developed a foveal crack sign without proceeding to macular hole formation. (A, B) Optical coherence tomography images of Case 11. (A) Twelve months after a vitrectomy for rhegmatogenous retinal detachment, a foveal crack sign appeared, and the minimum foveal thickness was 166 μm . Visual acuity was 20/16. (B) Thirty-six months after rhegmatogenous retinal detachment repair, the sign remained, and the minimum foveal thickness decreased to 155 μm . Visual acuity was 20/13. (C) Optical coherence tomography images of Case 12. Twelve months after a vitrectomy for rhegmatogenous retinal detachment, a foveal crack sign appeared, and the minimum foveal thickness was 156 μm . Visual acuity was 20/16. This visit was the final follow-up at the patient's wishes. (D, E) Optical coherence tomography images of Case 13. (D) Twelve months after a vitrectomy for rhegmatogenous retinal detachment, a foveal crack sign appeared, and the minimum foveal thickness was 190 μm . Visual acuity was 20/20. (E) Twenty-four months after a vitrectomy for rhegmatogenous retinal detachment, the sign with the foveal deformation became clear, and the minimum foveal thickness has decreased to 109 μm . Visual acuity was 20/16.

DISCUSSION

IN THIS RETROSPECTIVE STUDY, FCS WAS FOUND IN ALL cases that had a secondary MH after PPV for RRD. Furthermore, FCS was found in 13 eyes (2.5%) among the eyes that underwent PPV for RRD, of which 10 eyes (77%) developed an MH in the follow-up period of this study. Although the time to appearance of the FCS and the interval from FCS appearance to MH diagnosis varied by case, the FCS appeared after parafoveal ERM development, which implies that the MH occurred in the relatively late stage after PPV for RRD.

FCS along with parafoveal ERM were found in all cases that developed an MH after PPV for RRD. Recent studies have reported that ERM is the most relevant factor for MH formation after RRD repair,^{15–17} which is consistent with the result of the current study. The current authors previously reported that postoperative ERM tended to occur in the early stage after PPV for RRD.¹⁹ The long-term ERM traction could contribute to MH formation after RRD repair considering the current result that MH occurred in the relatively late phase after the appearance of FCS with parafoveal ERM. In addition, all FCS appeared in the foveola, where a characteristic structure composed of

Müller cells exists.^{22,23} Given the result that all FCS appeared with parafoveal ERM but no cases with ERM covering the umbo developed FCS, FCS would imply the dehiscence of the Müller cell cone caused by parafoveal ERM traction to the umbo. The current study also showed that 13 of 58 (22%) eyes with postoperative ERM developed FCS, of which 10 eyes developed a secondary MH in the follow-up period. In addition, the thinning of the MFT in Cases 11 and 13 (Table 3) may suggest their potential for secondary MH formation. Cases with FCS need careful follow-up because FCS could be considered a predictive sign of MH formation after PPV for RRD.

Although the interval from the appearance of FCS to diagnosis of MH varied by case, the MH tended to develop relatively late after FCS appearance (232 ± 171 days; range, 61-623 days). Considering the wide range of the interval from FCS appearance to MH diagnosis, there would remain the possibility of subsequent MH formation in the cases without a secondary MH (Table 3, Cases 11 to 13). Regarding these 3 eyes, each FCS appeared at the 1-year follow-up after PPV for RRD, which was relatively later than in the cases with a secondary MH. Considering some previous studies have reported that an MH could develop more than 4 years after RRD repair,^{8,12,15,17} the current results suggest that long-term follow-up is needed in cases with FCS appearance after PPV for RRD.

Factors reported for the formation of the MH, other than postoperative ERM, such as CME, macula-off RRD, recurrent RRD, and high myopia,^{8,10,11,14-16,24} appeared to have no relationship with MH formation after PPV for RRD in this study. CME has been speculated as another cause of secondary MH formation^{8,14,24}; however, the current study did not detect an association with CME. It should be noted that there is the possibility of CME omission because fluorescein angiography was not performed in all cases. In the present study, no MH cases had either macula-off or recurrent RRD, which is not consistent with previous reports.^{10,11,15,16} These differences may be attributed to the surgeons' tendency to perform ILM peeling for complicated RRD cases. The current study showed that no eyes with ILM peeling developed postoperative ERM, which is consistent with the authors' previous report.¹⁹ FCS and a secondary MH formation would be restrained by ILM peeling because tangential traction by parafoveal ERM was absent in such cases. Additionally, although 11 eyes with macula-off RRD developed postoperative ERM, parafoveal ERM was observed in only 2 eyes among that group. This small number may have affected the current result that no cases with macula-off RRD developed FCS.

This study had several limitations. First, this study was retrospective, hence, prospective studies are needed to evaluate the prognosis of the eyes with FCS. Second, horizontal and vertical B-scan cross-sectional images were used to find FCS and MH in this study; however, high-density radial scanning may be more appropriate to detect microstructural changes in the fovea.²⁵ Moreover, radial scanning would enable evaluation of the relationship between the direction of parafoveal ERM traction to the fovea and the deformation of the fovea. OCT scan pattern should be considered to elucidate the pathogenesis of FCS formation. Third, the sample size was small because MH formation after PPV for RRD is a rare complication. Although a larger study is needed, it is noteworthy that FCS with preceding ERM was detected in each case before MH formation after RRD repair. Finally, most of the cases that underwent PPV for RRD in the current study were followed for only 1 year postoperatively. There is a possibility that some cases with a secondary MH were overlooked; therefore, a longer follow-up period should be performed in a future study.

In conclusion, the current study reports the OCT foveal crack sign preceding MH formation after PPV for RRD. All cases with a secondary MH after PPV for RRD had FCS, and this sign appeared after parafoveal ERM development. Compared with secondary ERM, a secondary MH is a rare and relatively late complication after PPV for RRD, but the cases with FCS should be followed for a long term because the sign may reflect an ERM-induced anatomic stress that leads to MH formation. Prospective studies are needed to evaluate the prognostic accuracy for MH formation in eyes with FCS.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

TOMOYUKI ISHIBASHI: VALIDATION, FORMAL ANALYSIS, Investigation, Data curation, Writing - original draft, Visualization. **Yasuaki Iwama:** Conceptualization, Methodology, Validation, Formal analysis, Investigation, Data curation, Resources, Writing - review & editing, Project administration. **Hiroshi Nakashima:** Conceptualization, Investigation, Resources, Writing - review & editing, Project administration. **Toshihide Ikeda:** Resources, Project administration. **Kazuyuki Emi:** Resources, Writing - review & editing, Supervision, Project administration.

ALL AUTHORS HAVE COMPLETED AND SUBMITTED THE ICMJE FORM FOR DISCLOSURE OF POTENTIAL CONFLICTS OF INTEREST and none were reported.

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