기저 망막질환이 없는 눈에서 저반사를 보이는 망막 앞 병변의 유병률과 임상적 특징

Prevalence and Clinical Characteristics of Epiretinal Mass in Eyes without Pre-existing Retinal Conditions

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Purpose: To evaluate the clinical characteristics of epiretinal mass (EM) in eyes without pre-existing retinal conditions.

Methods: The prevalence and the characteristics of eyes showing EM during spectral-domain optical coherence tomography (SD-OCT) examination were reviewed.

Results: Among 2,221 eyes undergoing SD-OCT, 34 (1.5%) were found to have EM, which was detected following onset of posterior vitreous detachment (PVD); 32 of 34 (94.1%) eyes showed PVD, while two eyes (5.9%) showed diffuse vitreomacular adhesion at the time of EM detection. The EM was most commonly located at the superior macula, followed by the nasal macula. Of the 17 eyes with SD-OCT images obtained at the time of EM decrease, EMs from 12 eyes (70.6%) had diminished completely, while EMs from five eyes (29.4%) had resulted in low-grade epiretinal membranes (ERMs). The time interval between EM appearance and disappearance was about 10 to 12 months.

Conclusions: In eyes without pre-existing retinal conditions, EM can develop after PVD and might indicate the existence of a denatured vitreous cortex with a cellular component. These lesions usually resolve spontaneously but can be associated with a low-grade ERM.

Keywords: Epiretinal membrane; Optical coherence tomography; Posterior vitreous detachment

Introduction

Epiretinal proliferation (EP) presents on spectral-domain optical coherence tomography (SD-OCT) as a homogenous material of medium reflectivity at the inner retinal surface.

It was described first by Pang et al. [1] as a thickened epiretinal membrane (ERM) associated with lamellar macular hole (LMH). Similar lesions have been found in 5.1% of eyes with vitreomacular interface (VMI) diseases, such as LMH, full-thickness macular hole (FTMH), ERM, and vit-

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reomacular traction (VMT) [2]. The coexistence of EP and FTMH has been associated with poorer anatomic and visual outcomes after vitrectomy, suggesting chronicity as this lesion was associated with an advanced stage of FTMH [3]. Recently, we detected a homogenous epiretinal mass (EM) of low reflectivity in the vitreoretinal interface (VRI) in eyes without pre-existing retinal conditions. The purpose of this study was to assess the prevalence and long-term prognosis of this kind of EM in eyes without pre-existing retinal conditions.

Materials and Methods

We conducted a retrograde chart review of patients who visited and underwent SD-OCT for cataract surgery at Keye

Figure 1. Representative image of epiretinal mass (arrows).

Eye Center, Seoul, Korea, between February 2018 and June 2020. SD-OCT imaging was performed using the Spectralis ophthalmic imaging platform (Heidelberg Engineering, Heidelberg, Germany). Eyes with retinal diseases, such as those with age-related macular degeneration, diabetic retinopathy, retinal vascular occlusions, retinal detachment, or any kind of retinal break, or those with a previous history of vitreoretinal surgery were excluded from this study. The study was approved by the Institutional Review Board (IRB)/Ethics Committee of Keye Eye Center, and its protocol adhered to the tenets of the Declaration of Helsinki (IRB number: 2020-0724-001).

SD-OCT images were reviewed by two retinal specialists (J. H. P. and S. J.), who agreed on the detection of preretinal weakly reflective mass-like lesions, as shown in Fig. 1. Only eyes with mass-like lesions with a thickness of greater than 20 μ m detected by caliber tool were included. In a previous study, the thickness of clinically significant ERM was about 20 μ m on SD-OCT images [4]. Therefore, we adopted 20 μ m as the minimum thickness for EM diagnosis to avoid imaging error. The maximal thickness and diameter were measured with the caliper tool. The location of the EM was described according to the Early Treatment Diabetic Retinopathy Study map according to the following positions: fovea, superior inner macula, nasal inner macula, inferior inner macula, temporal inner macula, superior outer macula,

Table 1. Baseline characteristics of enrolled subjects

Characteristic	Eyes without EM (n = 2,187)	Eyes with EM (n = 34)	p-value
Age (years)	58.41 $\pm$ 5.67	61.23 $\pm$ 5.82	0.004*
Sex (male)	550 (25.1)	5 (14.7)	0.229 [†]
ERM (yes)	276 (12.6)	18 (52.9)	< 0.001 [†]
PVD (yes)	636 (29.1)	32 (94.1)	< 0.001 [†]
WTW (mm)	11.40 $\pm$ 0.38	11.42 $\pm$ 0.42	0.760*
TCRP 4 mm (diopters)	43.65 $\pm$ 1.51	43.56 $\pm$ 1.92	0.741*
AXL (mm)	23.79 $\pm$ 1.22	23.48 $\pm$ 1.35	0.147*
ACD (mm)	3.17 $\pm$ 0.55	3.06 $\pm$ 0.39	0.214*
LT (mm)	4.43 $\pm$ 0.32	4.54 $\pm$ 0.31	0.046*
UDVA (logMAR)	0.34 $\pm$ 0.30	0.31 $\pm$ 0.25	0.564*
CDVA (logMAR)	0.03 $\pm$ 0.09	0.01 $\pm$ 0.05	0.320*

Values are presented as mean $\pm$ standard deviation or number (%).

EM = epiretinal mass; ERM = epiretinal membrane; PVD = posterior vitreous detachment; WTW = white to white; TCRP = total corneal refractive power; AXL = axial length; ACD = anterior chamber depth; LT = lens thickness; UDVA = uncorrected distance visual acuity; CDVA = corrected distance visual acuity.

*Student's *t*-test or Mann-Whitney *U* test; [†]chi-square or Fisher's exact test.

nasal outer macula, inferior outer macula, and temporal outer macula. The total duration of the presence of EM on optical coherence tomography (OCT) during follow-up was calculated. The interval between the onset of posterior vitreous detachment (PVD) and the appearance of EM was calculated when possible. The VMI and the presence of ERM on SD-OCT images also were evaluated. VMI was classified as previously defined by the International Vitreomacular Traction study group [5] as follows: 1) no PVD; 2) focal vitreomacular adhesion (VMA) of 1,500 μm or less; 3) broad VMA greater than 1,500 μm ; 4) focal VMT of 1,500 μm or less; 5) broad VMT greater than 1,500 μm ; and 6) PVD. VMA was defined as an elevation of the cortical vitreous above the retinal surface, with the vitreous remaining attached within a 3-mm radius of the fovea. The presence of an ERM was evaluated as previously defined by Delyfer et al. [6].

Ultra-wide-field fundus photography (Optos Optomap Panoramic 200A Imaging System; Optos plc, Dunfermline, Scotland) was used to evaluate the visible retinal findings of EM in the cohort. The following ocular parameters were collected to evaluate the potential correlation of ocular shape and the presence of EM: white-to-white (WTW) diameter and total corneal refractive power (TCRP) of 4 mm, using the Pentacam Scheimpflug System (Oculus Inc., Berlin, Germany), axial length (AXL), anterior chamber depth (ACD),

and lens thickness (LT) by optical biometry with a partial coherence interferometry device (IOL Master; Carl Zeiss Meditec, Jena, Germany), respectively. SD-OCT scans were obtained at one, two, six, and 12 months after first visit.

The Statistical Package for the Social Sciences version 15.0 for Windows (IBM Corp., Armonk, NY, USA) was used for statistical analysis. Descriptive data were recorded as mean $\pm$ standard deviation unless otherwise specified. Visual acuity was recorded as a decimal value and then converted to a logarithm of the minimum angle of resolution (logMAR) scale value for statistical analysis. The Student's *t*-test or the Mann-Whitney *U* test was used for the comparison of continuous variables between groups. The chi-square test was used for comparison of categorical variables between groups. A *p*-value less than 0.05 was considered statistically significant.

Results

Of the 2,221 eyes that underwent ocular screening with SD-OCT during the period mentioned above, 34 (1.5%) had EM. Table 1 presents the characteristics of the enrolled patients. The mean age was 61.23 ± 5.82 years among patients with EM and 58.41 ± 5.67 years among patients without EM

Figure 2. Bar graphs showing the characteristics of epiretinal mass (EM) in the study. (A) Distribution of the number of EMs per eye. (B) The location of EMs according to the early treatment diabetic retinopathy study circle. (C) The distribution of EM height (μm). (D) The distribution of EM diameter (μm). F = fovea; SIM = superior inner macular; SOM = superior outer macular; NIM = nasal inner macular; NOM = nasal outer macular; TIM = temporal inner macular; TOM = temporal outer macular; IIM = inferior inner macular; IOM = inferior outer macular.

($p = 0.004$). Eyes with EM had greater LT values and higher proportions of ERM and PVD ($p = 0.046$, $p < 0.001$, and $p < 0.001$, respectively). However, there was no difference in sex, WTW, TCRP of 4 mm, AXL, ACD, uncorrected distance visual acuity, or corrected distance visual acuity ($p = 0.229$, $p = 0.760$, $p = 0.741$, $p = 0.147$, $p = 0.214$, $p = 0.564$, and $p = 0.320$, respectively).

Thirty eyes (88.2%) had one EM, while there were three eyes (8.8%) with two EMs and one eye (5.9%) with three EMs (Fig. 2A). The EM was most commonly located in the superior part of the macula, followed by in the nasal part of the macula (Fig. 2B). The mean values of the maximal EM height and diameter were $38.03 \pm 15.26 \mu\text{m}$ (range: 21–88 μm) and $1,028.38 \pm 480.77 \mu\text{m}$ (range: 123–2,342 μm), respectively. The distributions of the maximal EM thickness and diameter are illustrated in Fig. 2C and 2D.

Among those 34 eyes with EM, 32 eyes (94.1%) showed PVD, while two eyes (5.9%) showed diffuse VMA (Fig. 3) at the time of EM appearance. We assessed seven eyes (20.6%) with OCT before PVD occurred; among those seven eyes, the EM developed with PVD onset in three eyes (42.9%; Fig. 4) and at one, two, four, and six months after PVD in one eye each (2.9% for each). Among the two eyes with EM and VMA, EM in one eye diminished after PVD, and the

other eye showed steady VMA and EM.

Of the 34 eyes, 17 eyes had OCT images taken at the time of EM disappearance (Fig. 5); among these, EMs from 12 eyes (70.6%) diminished completely (Fig. 6A–C), while

Figure 4. Representative images from an enrolled patient. (A) The posterior hyaloid membrane (PHM) was partially attached to the retinal surface (arrowheads). (B) The PHM was detached one month later. A small amount of epiretinal mass (arrows) was detected on the inner retinal site where the PHM was attached.

Figure 3. Representative images from an enrolled patient. (A) The fundus image showed no specific findings. The upper (B), foveal (C), and lower (D) spectral-domain optical coherence tomography shows epiretinal mass on the inner retinal surface (arrows) and same density materials on the posterior hyaloid membrane (PHM; arrowheads), suggesting the interaction between PHM and the inner retinal structure.

EMs from five eyes resulted in low-grade ERMs (Fig. 6D-F). There were four eyes with OCT data available from the time of EM appearance to disappearance; among these, the process of EM appearance to disappearance took 10 months in one eye and 12 months in three eyes.

Discussion

In this study, the prevalence of EM in eyes without pre-existing retinal conditions was 1.5% of our study population. Though the subjects with EM were older and had greater LT values, there was no significant difference in the ocular characteristics of eyes with EM compared with those without EM, suggesting that EM is a physiological phenomenon. This result is in agreement with those of many studies that have shown that the LT increases with age [7]. Also, eyes with EM had larger proportions of ERM and PVD. It is well known that ERM occurs typically after PVD, and ERM and PVD generally develop with VRI changes, which progress with aging. Therefore, this study showed that EM is expected to have associations with ERM, PVD, and LT due to VRI change or aging.

The cellular sources of EP [8] and ERM [9-18] have been speculated to be Müller glial cells, vitreous components,

or retinal pigment epithelial cells. We speculate for the following reasons that the EM in this cohort represents mostly denatured collagen from remnant vitreous with less of a cellular component: 1) with SD-OCT imaging, in our cohort, EM appears as homogenous material of low reflectivity compared with the EP with medium reflectivity seen in VRI diseases; 2) the EM in our cohort was detected most abundantly at the superior macular area, followed by the nasal macular area, while the EP seen with VRI diseases is usually detected around the fovea; 3) there was no inner retinal defect around the EM in our cohort; 4) the EM resolved spontaneously in most of our cases except for a few cases that resulted in mild ERM; and 5) since there was no case with retinal detachment or retinal breaks in the present study, we could rule out retinal pigment epithelial cells as the source of the EM in this cohort.

Given the temporal relationship between PVD and development of EM, EM might have been induced by PVD at the posterior pole. It could be that, during PVD onset, portions of the vitreous cortex and posterior hyaloid membrane (PHM) remained on the inner retinal surface (Fig. 4). The tractional force induced during PVD onset might have activated cellular proliferation and extracellular matrix production on both

Figure 5. A bar graph showing the prognosis of epiretinal mass. ERM = epiretinal membrane; FU = follow-up; OCT = optical coherence tomography.

Figure 6. Representative images showing the prognosis of epiretinal mass (EM) from two enrolled patients. (A) The EM (arrows) detected at the superior macular from a 59-year-old male subject, which (B) decreased five months later, and (C) eventually disappeared 12 months later. (D) The EM from a 61-year-old female detected at the superior macular. (E) The EM was decreased at five months later, but a low grade epiretinal membrane (arrowheads) was detected at the nasal side of the EM. (F) Ten months later, the EM was not detected, but a low grade epiretinal membrane was detected.

the inner retinal surface and the PHM (Fig. 3). The actual tractional force from the PVD on the retinal structure can be strongest in the superior macula—and stronger than that on the inferior macula due to gravity—which might explain the higher frequency of EM in the superior macula.

There are several limitations in this study. First, this was a retrospective study of eyes without apparent retinal disease. There is the possibility that subclinical retinal diseases exist in our study population that were not detected by conventional imaging. Second, given that the distance between the OCT line scans is 200 μm , overestimation of the spontaneous resolution of EM might have occurred.

Although the EM spontaneously disappeared in many cases, some cases showed formation of ERM. It is not clear whether the component of EM directly contributed to formation of ERM or whether ERM formation took place at the same time. By reviewing the macular OCT scans of eyes without pre-existing retinal disease, we found that the VMI experienced dynamic changes during PVD. Meticulous observation of the VMI during PVD will yield more insights into VMI diseases, such as ERM.

Conflicts of Interest

The authors declare no conflicts of interest relevant to this article.

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