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Clinical Use of OCT in the Management of Epiretinal Membranes

Nur Acar

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Abstract

Epiretinal membranes (ERM) are frequently seen in an aging eye, especially after posterior vitreous detachment, and can cause decreased vision, and/or metamorphopsia. Not all of the ERMs detected in routine ophthalmological examination are indicated to be removed with surgery. Optical coherence tomography (OCT) examination reveals the microanatomy of all the retinal layers and enables the vitreoretinal surgeon to make decision to follow-up or to perform a vitrectomy to peel the ERM. OCT imaging clearly shows all the tractions on the retina and the intraretinal layers; and can have a prognostic value for the surgery. OCT imaging is also very valuable in the differential diagnosis of pseudoholes with macular and lameller holes; much better than the clinical examination. It is a routine part of the detailed retinal examination of an eye with an ERM. This chapter covers OCT findings in ERMs, and examples of cases with ERMs indicated for surgery of follow-up will be shown, explaining the clinical results of the cases.

Keywords: central macular thickness, external limiting membrane idiopathicepiretinal membrane, internal limiting membrane, lamellar macular hole, optical coherence tomography, OCT, pars plana vitrectomy, photoreceptor, posterior vitreous detachment, pseudohole, secondary epiretinal membrane

1. Introduction

Optical coherence tomography (OCT) is a noninvasive imaging technique that has very important advantages in the diagnosis, treatment, and management of a variety of macular disorders [1]. Since its first use in the clinics, there has been continuous advancements in OCT technology, and current spectral-domain (SD) OCT, and swept-source (SS) OCTs demonstrate macular structures on a microscopic level further clarifying the pathophysiology of many

diseases and enabling novel therapeutic options. OCT evaluation has become the routine imaging method for any vitreomacular disease in retinal evaluation of the patients in the clinics as well as the essential component in any study design regarding the treatment of retinal diseases. Recently, OCT has also been integrated into our operating rooms by supporting our decision-making during vitrectomy known as intraoperative OCT (iOCT).

Epiretinal membrane (ERM), which has also been named as epimacular membrane, cellophane maculopathy, preretinal macular fibrosis, and surface-wrinkling retinopathy, is a disorder of the vitreomacular interface. It is a fibrocellular membrane lying on the inner surface of the retina, which can cause decreased vision and/or metamorphopsia. Epiretinal membranes are frequently seen in an aging eye, especially after posterior vitreous detachment (PVD), and its prevalence increases with increased age [2]. The mean age of ERM diagnosis is 65 years old, affecting both sexes equally [3]. The prevalence of ERM varies from 2.2 to 28.9% depending on the population being studied [4, 5]. The incidence of developing an ERM in the primary eye is 1.1% per year, whereas its incidence in the fellow eye is 2.7% per year. Bilaterality changes between 19 and 31% of the eyes, and mostly with asymmetric involvement.

2. ERM classification

Epiretinal membranes are classified as idiopathic, and secondary regarding their etiology. Idiopathic ERM is the most common form. Secondary ERMs are associated with posterior uveitis, retinal vascular occlusions, diabetic retinopathy, trauma, retinal tear or detachment, and their repair, argon laser photocoagulation, cataract surgery [6]. Other risk factors include age, PVD, and history of ERM in the fellow eye. Secondary ERMs tend to occur in younger patients [7]. Clinically, ERMs are classified as cellophane macular reflex or preretinal macular fibrosis according to their severity [8]. Cellophane macular reflex is an early form, including a thin transparent membrane overlying the macula usually clinically asymptomatic, whereas preretinal macular fibrosis is the later form with thickened and contracted membrane causing visual impairment in most eyes.

3. ERM-pathogenesis

The diagnosis of PVD, which is defined as separation between the posterior vitreous cortex and the internal limiting membrane (ILM) of the retina, has been described in up to 95% of cases of idiopathic ERM [9]. Residual cortical vitreous secondary to a PVD or anomalous PVD leading to vitreoschisis with only partial separation of the posterior hyaloid remain to be factors allowing proliferation of glial cells. Inflammation is a central component of disorders leading to secondary ERMs, with increased inflammatory mediators promoting fibrocellular growth. Retinal glial cells, hyalocytes, fibroblasts, myofibroblasts are the predominant cell types found in the ERMs. Retinal pigment epithelial cells, macrophages, T-, and, B-cells are identified in secondary ERMs [6]. Extracellular matrix production and remodeling are

predominant. The extracellular matrix components that have been described in ERMs include collagen types I, II, III, IV, and VI, fibronectin, and laminin [10–12]. Extracellular fibrils are thin in cellophane macular reflex and are much thicker in preretinal macular fibrosis [10].

4. ERM clinical findings

Epiretinal membrane is relatively common especially after 60 years of age, and both sexes are equally affected. A careful history should be obtained to evaluate for secondary causes of ERMs. The patient more often presents without any symptoms diagnosed on a routine ophthalmological examination especially with very early and thin membranes. He can also present with the symptoms of metamorphopsia, blurred vision, monocular diplopia, and micropsia [13]. Contrast sensitivity is frequently decreased.

In the ophtalmological examination, best corrected visual acuity (BCVA) is noted. Amsler grid test is also performed. On slit lamp examination lens status with any form of cataract is noted. Dilated fundus examination is performed. Careful examination of the macular area for any subtle membrane is important as it can easily be missed on routine examination. The presence of PVD is noted. Detailed examination of the peripheral retina for any missed retinal tear should be performed. The examination of the vitreous for any cells, and of retinal vessels for secondary causes should also be performed. The same examination should also be done for the fellow eye.

Clinically, an ERM can be seen as a loss in the normal convex contour of the fovea, an abnormal reflectivity of the macular area, or as wrinkling on the macular area in fundoscopy. As cellophane macular reflex is a thin membrane without causing any distortions in the retina, it usually does not cause visual impairment, and usually observed as an incidental finding in routine fundus examination. More advanced ERMs classified as preretinal macular fibrosis can be easily seen as they are often opaque and whitish in color, obscuring the underlying retina (**Figure 1**). There may be traction, or tortuosity in the vessels in thick membranes
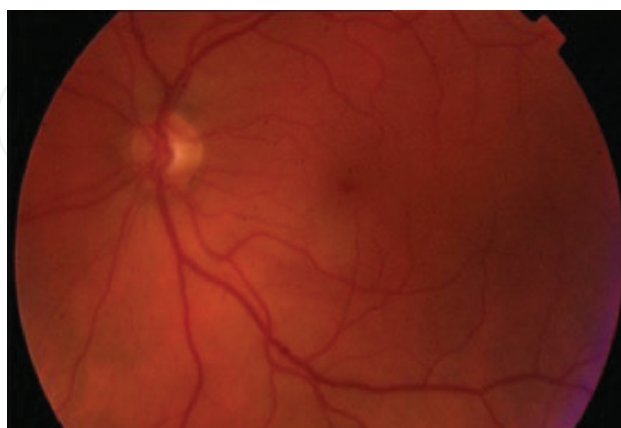

Figure 1. Epiretinal membrane. Color fundus image of the left eye showing grayish tissue over the macula obscuring the details of the underlying retina and causing tortuosity in the retinal vessels. The patient complains of blurred vision and metamorphopsia.

sometimes with intraretinal hemorrhages, or exudates in severe cases. Macular edema can be observed. Preretinal macular fibrosis usually distorts the retina causing visual impairment in nearly 80% of cases [14]. ERMs can give an impression of a macular hole, when there is proliferation on both sides of the fovea, but a gap in the center which looks like a macular hole gives the name as a "pseudohole". The best method to examine it is with a contact macular or a goniolens, though it may be difficult in a busy daily practice. ERMs can also be associated with lamellar macular holes or less commonly with macular holes. The usual course is slow progression over the years with VA decreasing to 0.1.

5. ERM diagnostic tests

5.1. Optical coherence tomography

Despite the fact that ERM can be diagnosed clinically, OCT imaging has become a routine part of the vitreomacular surface examination. OCT has proven to be more sensitive than clinical examination for the diagnosis of numerous disorders of the vitreomacular interface, including ERM [15]. OCT imaging shows the macular area in cross section, and three dimensionally in high resolution, and is extremely helpful in detecting subtle, very thin membranes, associated findings as macular edema, traction on the macula, lamellar macular hole, changes in the contour and the thickness of the macula, or any other macular pathology. 3D OCT imaging can help to evaluate the degree of traction, identify points of attachment and of detachment of the ERM to the retina [16]. OCT not only shows clearly if a lamellar hole is present, but also helps the differential diagnosis of ERMs, macular holes, lamellar macular holes, pseudoholes, and macular edema. OCT evaluation of eyes with ERM has also a prognostic value. It is ideal to follow the patient with the same OCT device and through the same baseline point.

5.1.1. OCT findings

ERMs are observed as highly reflective layer on the retinal surface. ERMs in early stage are seen as thin hyperreflective line with normal foveal contour and retinal architecture (**Figure 2a, b**). Idiopathic ERMs mostly are globally adherent to the retina seen as hyper-reflective band, but in some cases (20–25%), they are clearly separated from the retina with focal points of attachment (**Figure 3a, b**) [17]. Secondary ERMs are more frequently (50%) seen with focal attachments. ERM causes increase in central macular thickness. Usually there is diffuse retinal thickening without any cystic changes in cases with ERM. Especially, the retinal layers above the outer plexiform layers increase in thickness. Increased central macular thickness alone is not usually correlated with VA of the patient. Normal foveal contour is lost. The characteristic foveal depression is not seen (**Figure 4a–c**). Hyperreflectivity between ILM and inner plexiform layers is increased especially in longstanding ERMs, which is a typical finding (**Figure 3b**). This type of fibrosis generally produces traction in retinal layers, causing visual impairment. They may be associated with underlying corrugation of the retinal surface. The surface of the retina where the ERM is more pronounced has a distinctive saw-toothed appearance corresponding to retinal striae from ERM traction [18]. ERMs can also cause irregularities in retinal layers (**Figure 4a**). This feature is seen more frequently
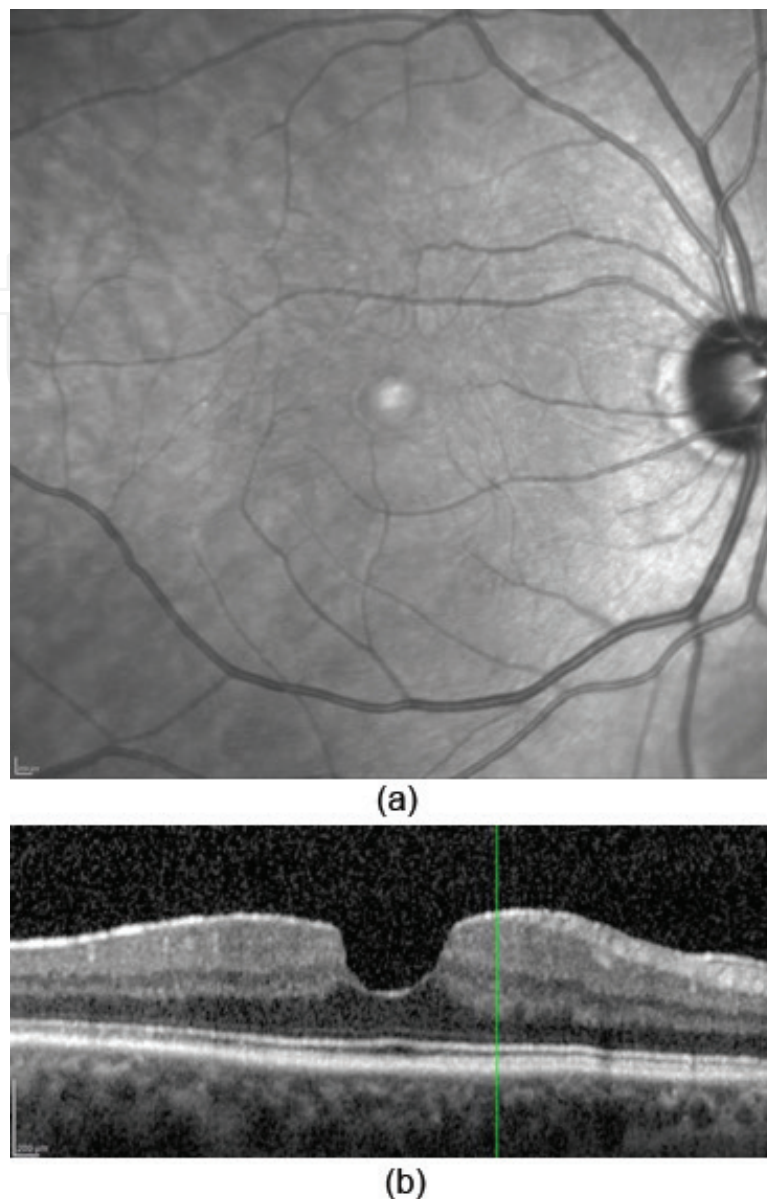
Figure 2. (a) Infrared (IR) photography of an asymptomatic patient with visual acuity of 20/20, and a thin ERM observed in routine fundoscopy. IR imaging shows a pseudo hole image at the fovea with slight wrinkling of the retina. The retinal vasculature looks normal. (b) SD-OCT image of the same eye. A thin hyperreflective line is seen on the retina which is globally adherent. There is no increase in foveal thickness, with the foveal pit contour being steeper, and wider than usual indicating an early form of a pseudohole. The retinal layers are normal. The retinal tissue at the base of the fovea is intact unlike a lamellar hole.

with partially attached ERMs. Also, slight elevation of photoreceptor layer above RPE layer has been described as "outer retinal defect", which may be related with traction of retina (**Figure 5a**). Cystoid changes in the retina observed as hyporeflective round spaces are usually accompanying longstanding ERMs as a result of intraretinal traction in idiopathic ERMs. If cystoid retinal thickening is more dominant, vascular reasons of a secondary ERM should be kept in mind. Pseudohole formation is usually accompanied by globally attached membranes (**Figure 6**). There is abnormally steep and wide foveal pit contour. The retinal tissue at the base of the fovea is preserved differentiating it from a lamellar (**Figure 7a**) or a full-thickness macular hole, and ERM is seen as hyperreflective band on the macular surface.
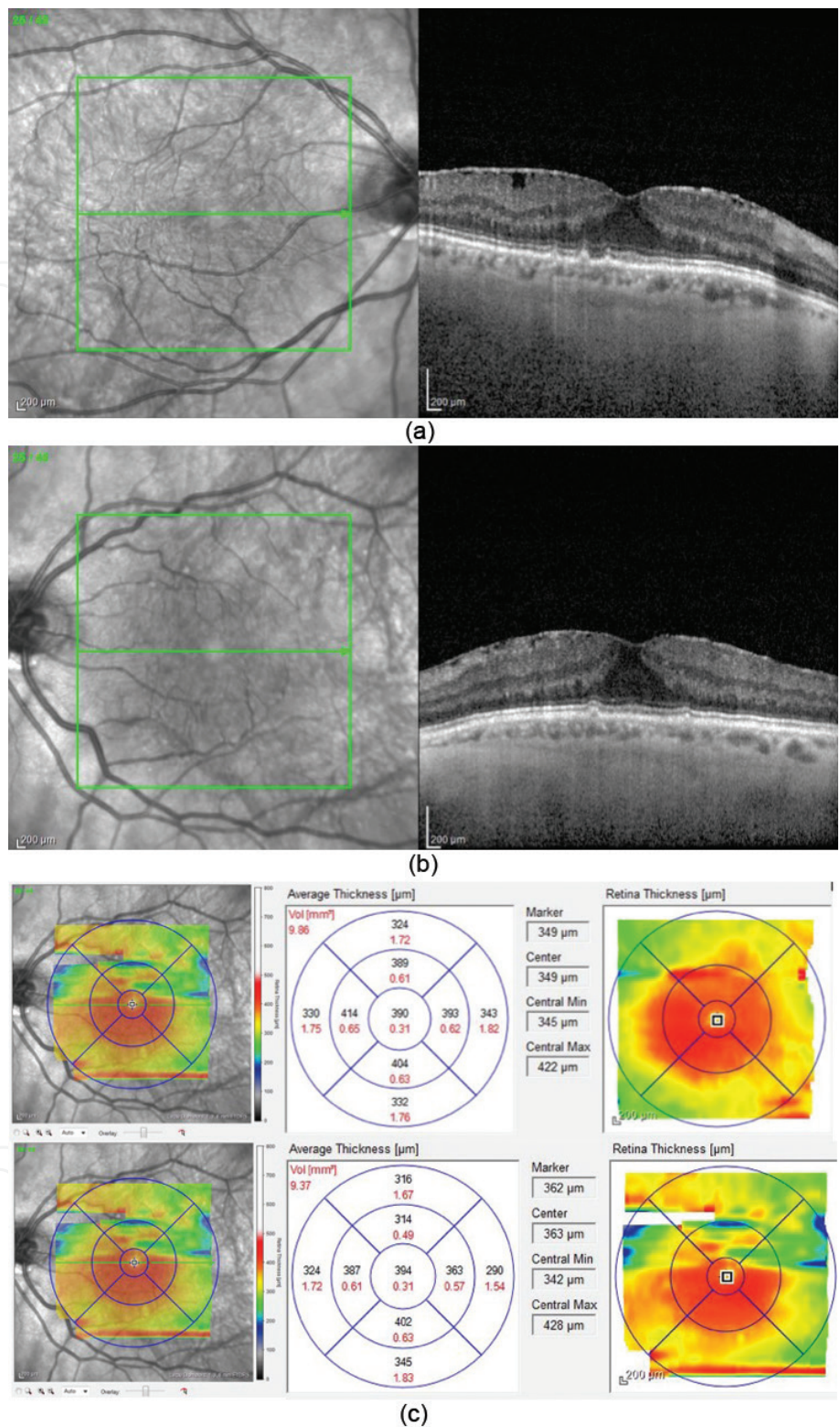
Figure 3. The SD-OCT imaging of both eyes of a patient with a complaint of slight blurring in vision, but no metamorphopsia. The VA in both eyes are 20/32 with early nuclear sclerosis in both eyes. The patient has also drusen bilaterally. (a) RE; ERM is seen as a hyperreflective layer on the macula, and we can clearly see the separated areas of ERM from the retina. There is also associated corrugation of the underlying retinal surface prominent on the temporal side. Slight intraretinal traction can be seen, and the normal foveal depression is decreased. (b) LE; The similar appearance is seen. Hyperreflectivity between ILM and inner plexiform layers is also increased at the nasal side as a typical finding. (c) The central macular thickness map shows that the central foveal thickness is increased to 390 μ in RE, and to 394 μ in LE.
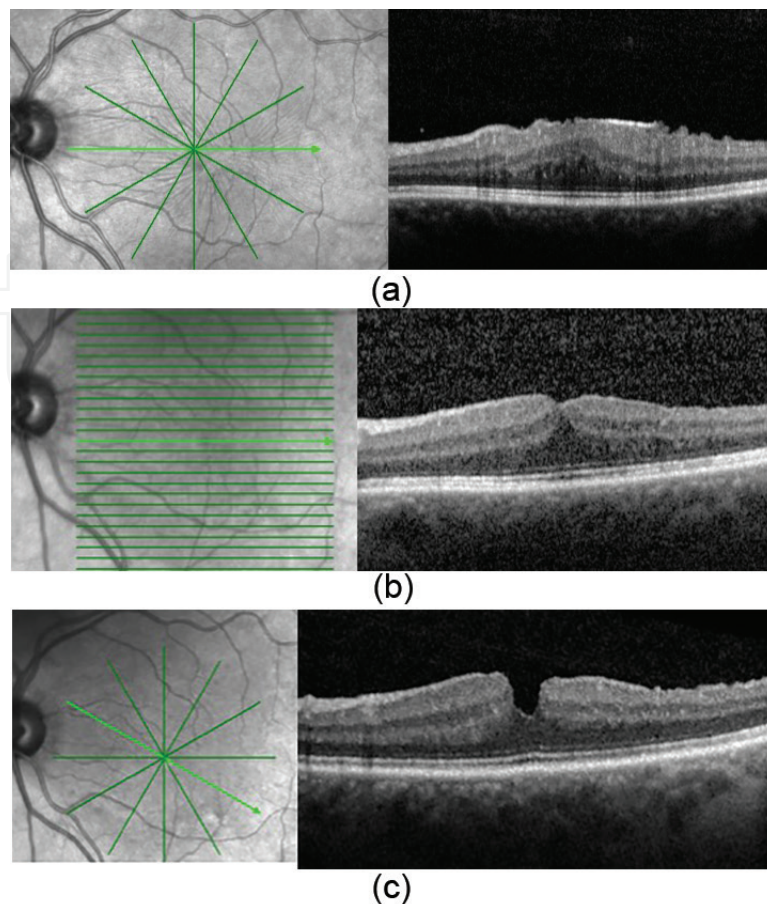
Figure 4. (a) SD-OCT imaging of a symptomatic eye with decreased VA of 0.3, and metamorphopsia shows increased central macular thickness with loss of foveal depression. Especially the inner retinal layers are increased in thickness with associated traction of the retina. The inner segment ellipsoid band and ELM can be seen undisrupted associated with better postoperative VA. The retinal surface is irregular due to ERM, and there is traction on the retinal vasculature at the temporal side of the fovea seen in IR photograph on the left. The 62-year-old male underwent 23 g pars plana vitrectomy with ERM and ILM peeling. (b) SD-OCT image at postoperative month 1 shows decreased central macular thickness with no traction of the retina. The retinal surface is smooth. The VA increased to 0.5. However, during follow-up, the VA decreased to 0.2 at postoperative month 10 due to nuclear cataract formation. Following phacoemulsification and IOL implantation, VA increased to 1.0. (c) SD-OCT image 3 months following lens surgery shows the intraretinal architecture is almost normal with normal retinal thickness and foveal depression is formed. The focal small depressions on the retinal surface of temporal side of the fovea are seen probably associated with ILM peeling. The VA is 1.0 with no symptoms.

There is still no internationally approved OCT-based classification system of ERMs. In one study, classification of idiopathic ERM based on the morphologic characteristics of the fovea has been proposed [19]. In another one, the anatomical structure of the vitreoretinal interface and the macula was studied and divided into two major groups according to the presence of PVD, and subdivided by the presence of contraction, edema, lamellar macular hole, and vitreomacular traction [20]. However, their clinical relevance is unclear.

OCT imaging is also helpful for decision-making in the management of an ERM. If the membrane is thin showing near normal contour in OCT not associated with metamorphopsia or blurred vision clinically the patient is usually followed up with periodically checking for symptoms and with OCT. However, some clinically subtle ERMs are better observed with OCT for accompanying vitreomacular traction. These cases may be offered earlier surgery or
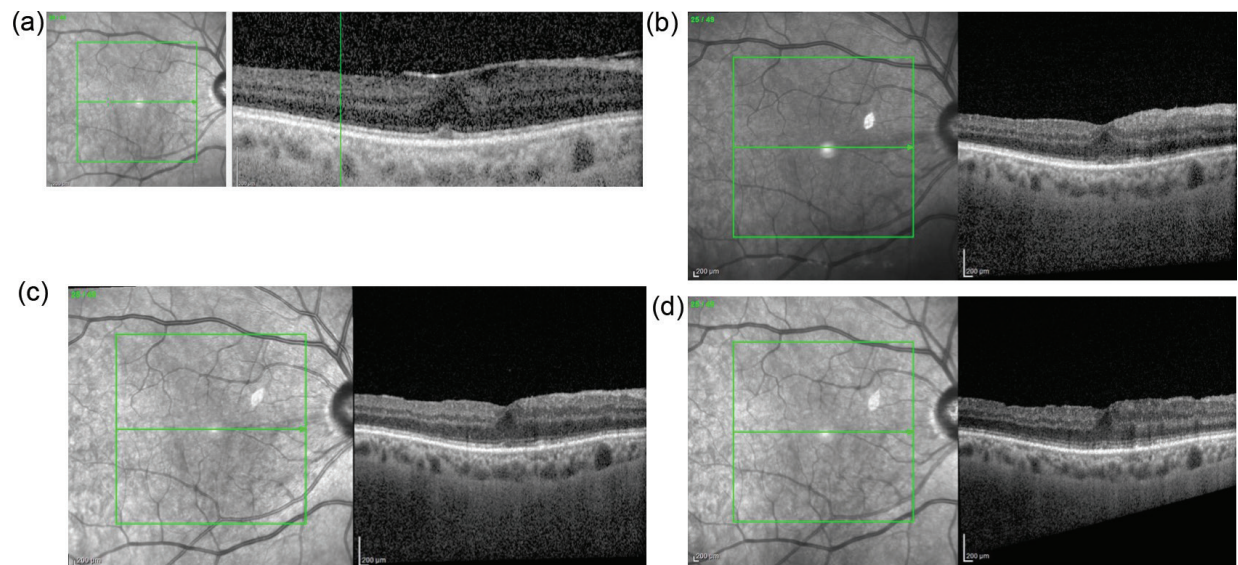
Figure 5. (a) SD-OCT image of a 69-year-old male presenting with decreased vision, and metamorphopsia on the RE. The patient had an ERM with nuclear cataract. ERM is seen as a hyperreflective layer on the macula. The central macular thickness is increased to 398 μ with loss of normal contour of fovea. The ERM is partially attached. Also, there is slight elevation of photoreceptor layer above the RPE layer, which has been described as "outer retinal defect" at the center of the fovea. This feature may be related with traction of retina. The VA was 0.3. (b) The patient underwent combined lens surgery with ERM, and ILM peeling. At postoperative week 2, SD-OCT shows decreased macular thickness, with foveal depression appearing. The photoreceptor layer is still a bit irregular at the fovea. (c) Postoperative month 1, the VA increased to 1.0. Intraretinal architecture is getting better. (d) Postoperative month 3. The photoreceptor and ELM layers look normal and intact.
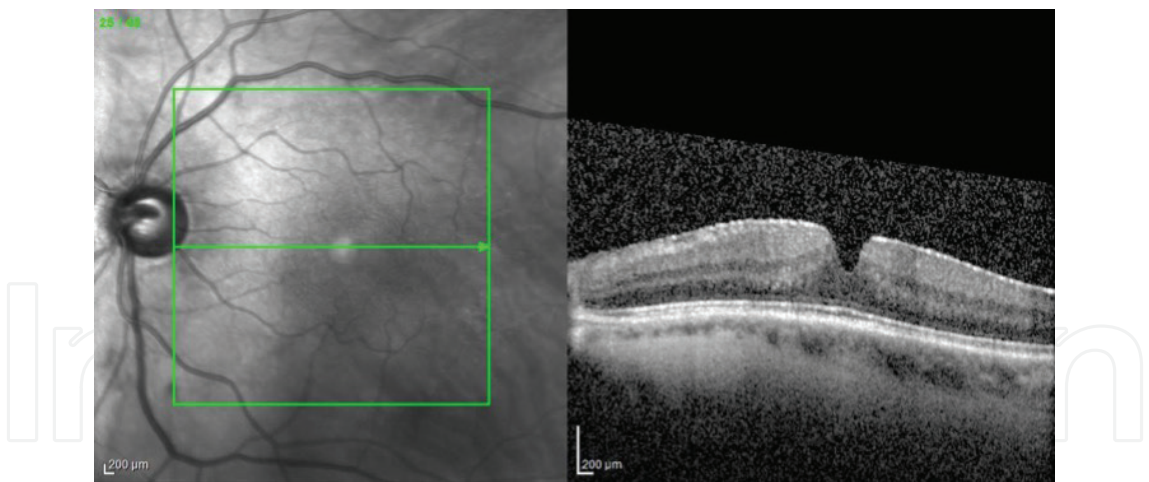

Figure 6. SD-OCT image of a patient shows an ERM as a thin hyperreflective layer on the macula on both sides of the fovea, but there is a gap in the foveal center. Foveal depression is steeper, giving the image of a pseudohole. There is no loss of outer retinal tissue at the base of the fovea.

at least followed up more closely for worsening of symptoms. On the other hand, with OCT imaging, we can assess the vitreoretinal interface in detail and note how diffuse or how tight is the adherence of the ERM and can decide to approach which site to start peeling of the ERM surgically. 3D OCT imaging can also be helpful in identifying any free edges of the ERM that may help in starting membrane peeling during surgery [16, 21]. A new report using en-face
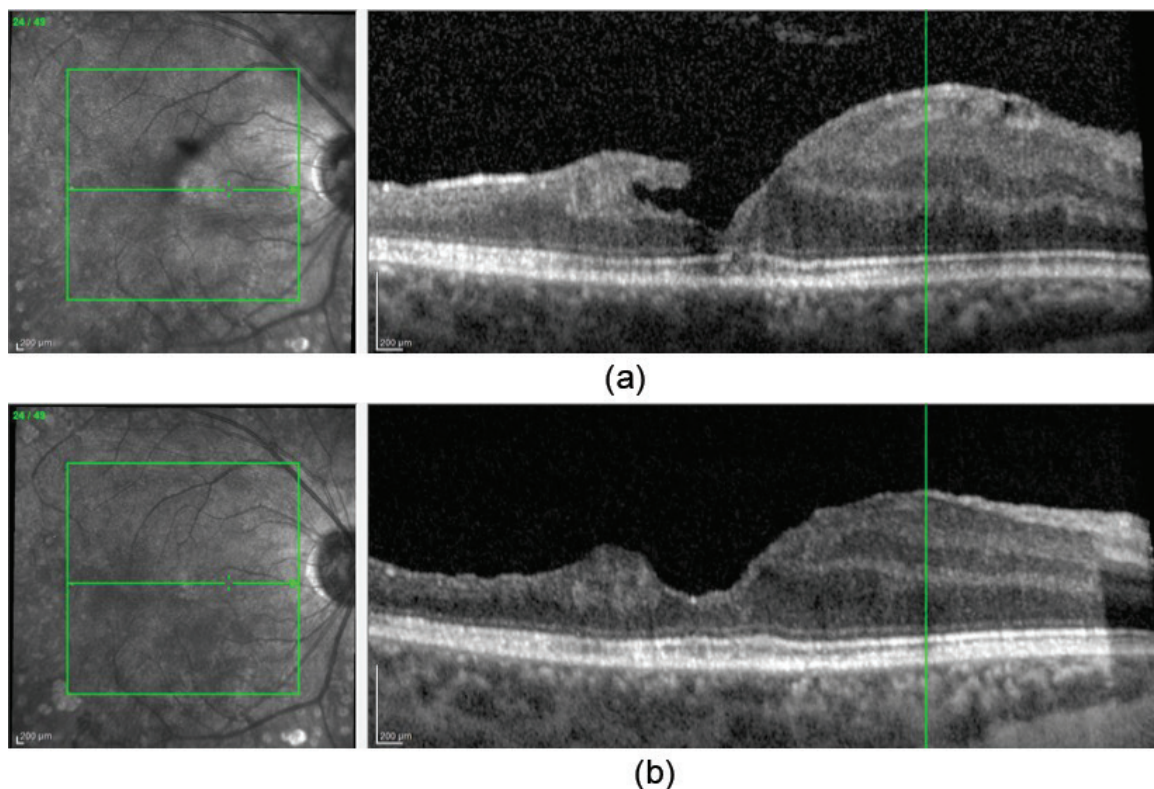
Figure 7. (a) SD-OCT image of a 39-year-old female with an ERM and a lamellar macular hole (LMH) secondary to tractional retinal detachment. There is a hyperreflective layer of ERM on both sides of the fovea, retinal thickness is increased at the nasal side. There is loss of retinal inner layers at the temporal side of the fovea compatible with LMH. The outer layer is also decreased at the center, and disruption of the photoreceptor segment layer is noted. The retinal thickness is decreased due to atrophy at the temporal side of the fovea. The VA decreased to 0.6 during follow-up with symptoms of metamorphopsia. The patient underwent vitrectomy with ERM, and ILM peeling due to TRD, and vitreous hemorrhage from active vessels despite argon laser treatment. (b) At postoperative month 6, SD-OCT image demonstrates that LMH is closed. The retinal layers are better defined at the nasal side. Photoreceptor and ELM layers are continuous with no disruption. The VA increased to 1.0 with totally attached retina.

OCT scans and generating a map, which is called the GapMap, showing the elevated and attached areas between an ERM and the macula stated that this imaging can help surgeons detect elevated areas of ERM preoperatively to avoid excessive retinal contact during surgical manipulation [22]. They commented that in the future, such en-face gliosis reports may be incorporated into computer-assisted surgery systems installed in the operating microscope's oculars, serving as a source of intraoperative guidance for surgeons to facilitate the removal of ERM with reduced trauma [23].

OCT imaging also demonstrates all the layers of the retina, which is also important for the prognosis of the surgical outcome of an ERM removal. These features will be outlined below in "*Surgical Prognosis*" section.

5.1.2. Intraoperative OCT

OCT has become an essential imaging in guiding our clinical decision-making, and it has recently been adapted to use during surgery, known as intraoperative OCT (iOCT). Prospective

studies performed have already shown the safety and feasibility of iOCT imaging [24, 25]. The most common posterior segment procedure was vitrectomy with membrane peeling, in 43% of which iOCT informed surgeon decision-making [24]. The following study, performed to evaluate a microscope-integrated iOCT system with a heads-up display, showed that iOCT data conflicted with the surgeon's impression of membrane peel completeness in 19% of cases [25]. The surgeons reported that use of iOCT provided valuable feedback in 71% posterior-segment surgeries [26]. The author's experience is also compatible with the findings of the studies that, iOCT can show residual membranes if any, unconnected areas between ERM and the retina, and confirm if ERM/ILM peel is completed during ERM surgery. Although iOCT is a nice instrument to supplement surgical assessment, it is not available in most ORs, is costly, and is apt to further advancements of the system in the future.

5.2. Optical coherence tomography angiography

Optical coherence tomography angiography (OCTA) is a new technology for imaging the microvasculature of the retina and choroid, using laser light reflectance of the surface of moving red blood cells to demonstrate vessels noninvasively. The vessels through different segmented areas of the eye can be imaged, and differences can be analyzed between scans. The image is segmented into four zones, namely, the superficial retinal plexus, the deep retinal plexus, the outer retina and the choriocapillaris. OCTA can show the changes in the retinal vasculature caused by macular traction of an ERM. OCTA can help to evaluate the depth and extent of foveal capillary distortion. Reduction in VA is found to be associated with this distortion [27]. Differences in foveal avascular area and decrease in parafoveal vascular density both in superficial and deep capillary plexus are also reported in the eyes following ERM surgery, and these changes were associated with worse postoperative VAs [28]. As more studies will be performed with OCTA imaging, more prognostic findings may be available for surgeons to help decision-making for removal of ERM as well as to determine visual prognosis.

5.3. Fundus fluorescein angiography

Fundus fluorescein angiography (FFA) is usually not necessary in routine evaluation of ERMs, but it is helpful in secondary ERMs following retinal vascular occlusions or inflammations to assess not only the macular area but also the peripheral retinal circulation. It can demonstrate leakage, traction on the vessels, ischemia, or secondary neovascularizations.

6. ERM-management

6.1. Indication for surgery

Most thin ERMs are visually asymptomatic and can be followed up for a long time with periodical visits and with amsler card testing by the patient himself. In reported series regarding the natural evolution of an idiopathic ERM, it is reported that in a mean follow-up of 21 months, there was no significant change in mean VA of CRT or central volume of the macula [29]. The author's experience is also similar, especially for the initial severity, thin membranes without

major tractional components. In asymptomatic cases, the OCT may reveal thickened macula with loss of central depression, and a CRT of higher than 330 microns with a VA of 20/20. So, only thickened macula due to ERM, which is measured with OCT imaging, does not correlate with the complaints of the patients. The retinal distortions induced by ERM contraction are believed to be the primary reason for visual impairment in idiopathic ERM, which can easily be observed with OCT imaging.

When indicated, the management of idiopathic ERMs is surgical. There are still no strict recommendations regarding the exact timing of the surgery. However, the most important indication is deciding the presence of visual complaints of the patients are related with ERMs, but not cataractous or refractive changes. As the mean age of patients with ERM is usually around their 70s, their lenses have frequently cataractous changes, which should be considered as a cause of blurred vision. On the other hand, the complaint of metamorhopsia is often more intolerable for the patient and is an indication for surgical removal of an ERM even though the visual acuity is high. If the tractional distortions in the retinal layers are not prominent, and the patient has cataract without any metamorphopsia, the patient can be offered a lens surgery first, and the ERM can be followed-up, informing the patient has a higher risk of having postoperative macular edema. On the other hand, if the surgical removal is indicated, a combined surgery of a pars plana vitrectomy and a lens surgery is usually preferred as cataractous changes usually increase fastly following PPV, necessitating a lens surgery soon after.

6.2. Surgery

Epiretinal membrane surgery involves a pars plana vitrectomy procedure with ERM peeling. Internal limiting membrane peeling (ILM) is usually performed to prevent secondary membrane formation. It is already reported that ILM peeling decreased secondary membrane formations significantly [30]. A meta-analysis reported that vitrectomy with ILM peeling resulted in better visual improvement in long-term follow-ups and lower ERM recurrence rates [31]. On the other hand, other meta analyses reports found that although additional ILM peeling could result in a significantly lower ERM recurrence rates, it does not significantly influence postoperative best-corrected VA and central macular thickness [32, 33]. The postoperative VA is not found to be different in two groups with or without ILM peeling in idiopathic ERMS in a prospective trial [34]. The author's experience is also similar. In a prospective interventional case series, the efficacy and safety of combined peeling of ERM and ILM membranes with the single injection of mixture of tryphan blue and brilliant blue G dyes in eyes with idiopathic ERM was evaluated (Video). Seven (three pseudophakic and four phakic) eyes underwent vitrectomy and eight eyes had combined phacoemulsification and vitrectomy. Four phakic patients needed lens surgery with a mean of 10 months postoperatively. At postoperative month 6, the mean CMT decreased significantly from 502 ± 35 to 277 ± 43 μ. The mean VA significantly increased from 20/64 to 20/32 in all eyes with no recurrent ERM observed (**Figure 8**) [35].

ILM peeling maneuver should be performed cautiously to avoid secondary complications as a retinal hole formation, traumatic defects in the macular area, as well as phototoxicity. The surgery itself has the possible complications of a PPV, such as retinal tear and detachment, endophthalmitis, loss of ganglion cells, and others, which must be discussed with the patient.
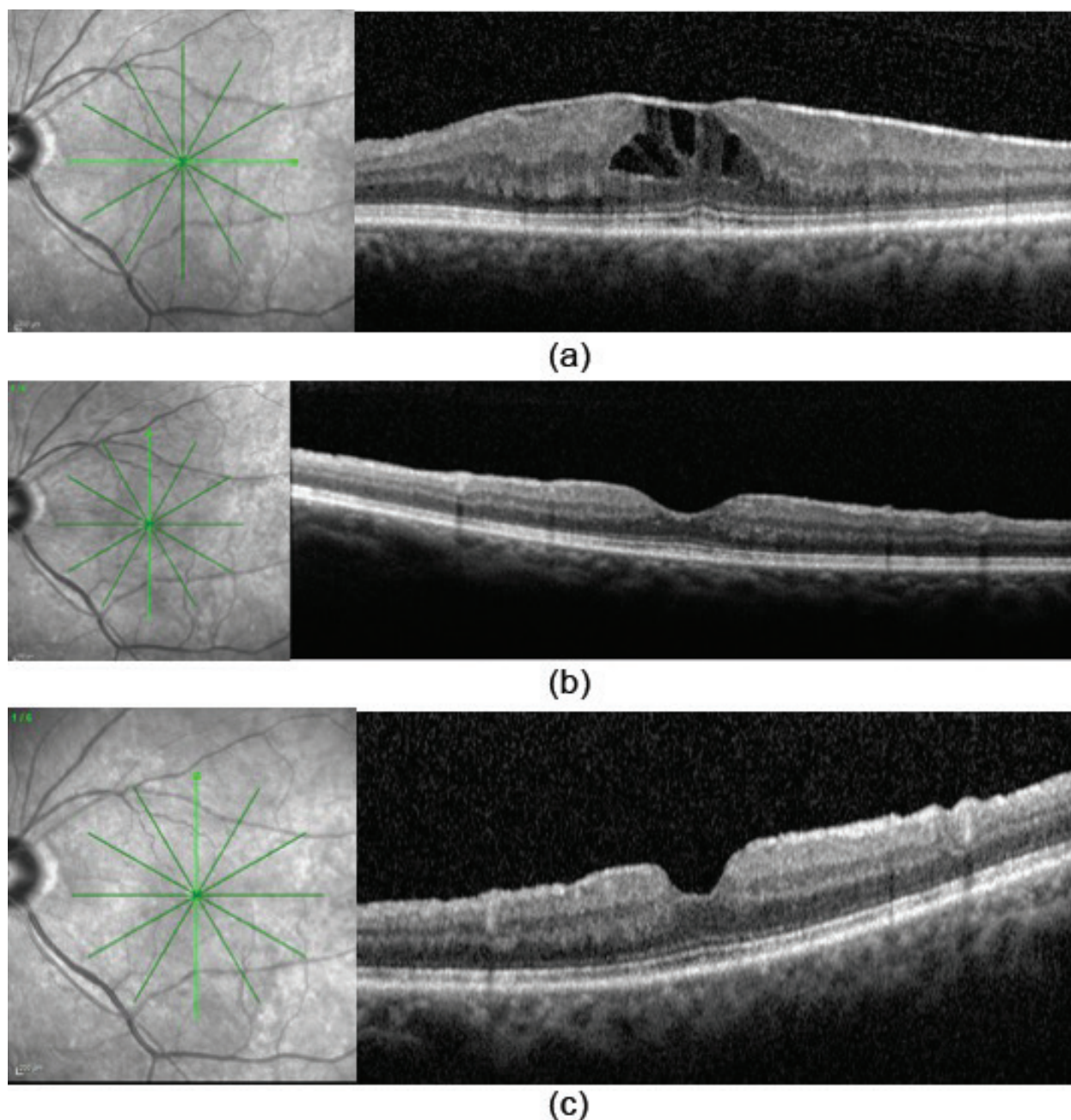
Figure 8. (a) SD-OCT image of a 73-year-old female presented with visual blurring and metamorphopsia with a VA of 0.6 shows a tightly adherent hyperreflective layer of ERM on the macula. The central retinal thickness is increased with traction on the fovea causing intraretinal cystic changes seen as hyporeflective spaces in the inner retina. The outer retinal layers are intact. The symptomatic patient underwent vitrectomy with ERM and ILM peeling. (b) SD-OCT at postoperative month 1 shows normal retinal architecture with normal retinal thickness. There is small depression on the superior side. The patient's metamorphopsia decreased with a VA of 1.0. (c) SD-OCT image at postoperative year 5 is the same with no recurrent ERM observed during 5 years of follow-up.

6.3. Surgical prognosis

Following ERM removal increase in VA of two or more lines in 60–85% of cases 6–12 months postoperatively with around 50% gaining a VA of 20/50 or better [36]. The mean preoperative and postoperative VA has been reported to be 20/110 and 20/55 [37]. This data were a

meta-analysis of three studies reporting surgical results following small incision pars plana vit-rectomy, in which the recurrence of ERM was around 1% [37]. Those with worse VA preopera-tively gain more lines postoperatively. However, the eyes with higher preoperative VA tend to have a higher postoperative VA [38–40]. Poor preoperative VA, and long duration of symptoms are poor prognostic factors [36, 38–39]. Visual acuity improves in 1–6 months postoperatively. However, VA improvement can continue to increase following 1–2 years of surgery. Successful surgical intervention is associated with both decreased central foveal thickness (CFT) and improved VA [30–42]. However, central macular thickness is not necessarily correlated with postoperative VA [4–43]. Although CFT may be useful for evaluating the impact of ERM on baseline VA, it is probably not useful for predicting postoperative VA [6]. The preoperative OCT characteristics are more important. Intact preoperative inner segment ellipsoid (ISe) band is associated with a better postoperative VA than a disrupted preoperative ISe band in both idio-pathic and secondary ERMs [38, 41–49]. The longer photoreceptor outer segment (PROS) length is also reported to be a good prognostic factor for the postoperative VA [39, 42]. It has also been shown that the integrity of outer photoreceptor cell layer as well as of ELM is related with better postoperative VA [50]. Postoperative increase in contrast sensitivity is associated with the thick-ness of outer retinal layer [44]. The preoperative degree of metamorphopsia was also found to be a prognostic factor for the postoperative degree of metamorphopsia, suggesting that surgery for ERM should be performed before development of severe metamorphopsia [39].

7. Conclusion

In conclusion, OCT provides a very detailed information of all the retinal layers, and the vitreomacular interface. Epiretinal membranes are a frequent clinical finding in an aging eye, and sometimes result in decreased vision, and/or metamorphopsia. OCT, as a noninvasive, fast imaging system of the macula being more sensitive than the clinical examination has become the routine evaluation of ERMs. OCT imaging is used to diagnose, differentiate, man-age, and follow ERMs. It also gives valuable information regarding the visual prognosis of the operated eye. Intact and continuous preoperative inner segment ellipsoid band, the longer photoreceptor outer segment, and the integrity of ELM are reported to be good prognostic signs. On the other hand, preoperative three-dimensional OCT evaluation of an ERM can also help the surgeons to identify any free edges of the ERM that may help in starting membrane peeling with reduced trauma. Lastly, OCT has recently been integrated into our operating rooms as intraoperative OCT and may support our decision-making during vitrectomy.

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