Research Article

Epiretinal membrane; clinical presentation and management

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Abstract
Purpose: to review the causes, pathogenesis, clinical presentation, and modifications in surgical management of epiretinal membranes. **Summary:** Epiretinal membrane (ERM) is caused by proliferation of different cells on the inner retinal surface; it may be idiopathic or secondary to different ocular causes. It can be diagnosed by indirect ophthalmoscopy and optical coherence tomography (OCT) which is useful tool for follow up patients before and after surgery. It may be asymptomatic or causing visual disturbances which indicate its surgical removal.
Key words: Epiretinal membrane, Optical coherence tomography, internal limiting membrane, Pars plana vitrectomy

Introduction
Epiretinal membrane (ERM) is a term used to describe cellular proliferation on the inner retinal surface, it has variable names such as premacular fibroplasia, macular pucker, cellophane maculopathy, and premacular gliosis which reflect the wide spectrum of presentations and clinical findings as ERMs may range from a benign asymptomatic disorder to a condition associated with debilitating metamorphopsia and central visual loss.

Classification of ERM
ERM can be classified into idiopathic ERM without any associated ocular abnormality, secondary ERM which is caused by preexisting or coexisting ocular pathology.[1]

Various conditions associated with 2ry ERM were described such as retinal detachment (RD), RD surgical repair, laser photocoagulation, retinal cryopexy, proliferative vitreoretinopathy (PVR), retinal vascular diseases, intraocular inflammation and ocular trauma.[2,3]

Prevalence:
Evidence regarding the epidemiology of ERM comes from two large population studies, the Beaver Dam Eye Study and the Blue Mountains Eye Study.[4,5]

The overall prevalence of ERM in these populations was 7–11.8%, idiopathic ERMs were bilateral in 19.5–31%, the increased odds of ERM for persons over the age of 70 compared with those younger than 60 was 7:4, 39% in Chinese participants versus 27.5% in Caucasians, whereas lower rates in the Japanese (4%).[6]

The prevalence of ERM was significantly increased following cataract surgery (16.8%) and retinal vein occlusion (12.5%).[4]

Grading of ERM
A clinical grading system was proposed by Gass to describe the different stages of the disease.[7]

- **Grade 0 (cellophane maculopathy):** translucent membrane with no underlying retinal distortion, asymptomatic.
- **Grade 1:** ERM associated with irregular wrinkling of the inner retina. When fovea is involved, patients often complain of distorted or blurred vision. Other symptoms include central

photopsia, macropsia and rarely monocular diplopia.[7]

- **Grade 2:** an opaque membrane causing obscuration of underlying vessels and marked full thickness retinal distortion, 80% of those patients may complain of blurred vision or metamorphopsia.[8]Cystoid macular edema (CME) may be present in 20–40% of those patients [9,10]

Pathogenesis:

ERM represents a reactive gliosis in response to retinal injury or disease, ERMs have two main components: an extracellular matrix which consist of (collagen, laminin, tenascin, fibronectin, vitronectin, etc.) and cells of retinal and extra retinal origin such as(glial cells, neurites, retinal pigment epithelium [RPE], immune cells, and fibrocytes).[11] Distribution of these components differs according to the underlying pathogenesis of ERM, as more RPE cells are more evident with PVR, glial cells more abundant in idiopathic ERM and vascular components more frequent in ERM due to retinal neovascularization.[12] Also, Growth factors play an important role in the formation, progression, and transformation of these membranes.[13,14]

In idiopathic ERMs, PVD may exert traction on the retina and induces müller cell gliosis, which migrate through small defects in the internal limiting membrane (ILM) and proliferate on the inner retinal surface,[15] while in RD, activated Müller cells and RPE cells penetrate the ILM and pass through retinal breaks and continue to proliferate even after repair of RD.[16]

Clinical presentation:

The disease is usually asymptomatic especially in mild form; symptomatic patients may have blurred vision, metamorphopsia, micropsia and monocular diplopia. Visual affection which occurs with ERM is due to retinal distortion, macular edema, vitreomacular traction and this degree differs according to its thickness, transparency and its relation to fovea. [7]

Avulsion of the ERM may cause reduction in or resolution of symptoms. ERMs may also be associated with macular pseudo holes, lamellar holes and full-thickness macular holes, as a result of tangential traction. It is possible that lamellar holes form when retinal cysts associated with the ERM rupture forming inner neural defects.[17]

There are some conditions that may closely resemble an ERM and should be considered when making the diagnosis, such as Vitreomacular traction (VMT) and CME.

- **VMT**, ERMs may coexist with VMT in 26–83% of cases, VMT differs from ERM by the degree of vitreous separation in the midperiphery as it is detached in VMT with ERM, while it is attached in ERM without PVD. [18,19]
- **CME** may also have similar appearance. It differs that there is no distortion of the microvasculature, it is always centered on the fovea, and may be seen on fluorescein angiography as a star pattern in late pictures.[7]

Diagnostic investigations:

- **Optical Coherence Tomography (OCT)**

The introduction of spectral domain OCT (SD-OCT), which offers higher axial resolution, has allowed more detailed visualization of the effect of ERM on the underlying retinal layers.[20, 21]

ERM is seen as a hyper reflective layer on the retinal surface which may be associated with underlying retinal corrugations, disruption of the foveal pit, retinal edema, and intraretinal cysts. Idiopathic ERMs are more likely to be associated with diffuse retinal adhesion, while secondary membranes may be characterized by focal retinal adhesion.[22]

OCT allowed investigators to monitor the clinical course of ERMs pre, post-operatively and also intraoperative OCT has been used at the time of surgery with some success.[23]

Successful surgical removal of ERM is associated with reduction in macular thickness and improvement of foveal contour while little or no improvement in visual function.[17]

- **Fluorescein Angiography**

Despite the advantages of OCT, fluorescein angiography (FA) still remains a useful tool, particularly in cases with an underlying vascular event or choroidal neovascular membrane. FA can highlight the extent of retinal wrinkling, degree of retinal vascular tortuosity, and presence of macular edema.[7]

Surgical Management of ERM

The principal indications for ERM surgery are patient-reported symptoms of reduced VA with or without metamorphopsia.

Introduction of small sutureless micro-incision vitrectomy systems offered shorter operating times, less corneal astigmatism, diminished conjunctival scarring, improved patient comfort and in some cases, earlier visual recovery.[24]

Core vitrectomy is performed, followed by posterior vitreous detachment (PVD) either actively with the vitreous cutter, or passively with a flute needle, starting by elevating the posterior hyaloid membrane at the level of the optic disc, subsequently, complete vitreous shaving is performed.

After performing complete vitrectomy vital dyes are essentially used for adequate visualization of ERM such as:

- **Indocyanine green (ICG)** which has a greater affinity for ILM than ERM and may be more useful when viewed as a negative stain, many studies found that RPE toxicity may occur with a solution that has an osmolarity <270 mOsm, a concentration above 0.5%, incubation time >30 seconds, and other additional factors such as application technique and duration of light exposure.[25]
- **Brilliant blue G** (0.25 mg/mL) stains ILM but ERM is also stained to some degree, It is preferred when dual staining is necessary, for simultaneous removal of ERM and ILM [26]. It is also injected under air and washed away after a few minutes. It does not appear to have the concerns regarding toxicity of ICG and thus may be a good alternative.[25]
- **Trypan blue (TB)** (0.15%) highlights and stains ERMs due to its strong affinity for glial cells, allowing good visualization of the extent of the membrane and thus aiding peeling but it doesn't stain ILM .It is an excellent, non-toxic, heavy TB can be used which does not need an air-fluid exchange , left for one- to three-minutes and is then washed away.[27, 28]

The edge of ERM is elevated using Tano diamond dusted membrane scraper (DDMS), a pick, microvitreoretinal (MVR) blade or forceps, then it is grasped with the forceps to create circumscribed flap, then gentle dissection is started from the periphery to the center of the membrane (outside-in technique). Alternatively, the membrane is grasped centrally and peeled away from the center, always in a circumferential pattern (inside-out technique), the latter is preferred by many surgeons because the central retina is thicker and stronger, making it easier for the surgeon to find a tissue plane to begin with.[29]

Pinch peeling is an alternative method for minimizing tissue damage, in which the forceps is used to pinch the membrane without creating an edge and grasp it with the two blades on the surface of the membrane thus avoiding retinal contact and minimizing the risk of retinal injury.[30]

Although patches of ILM are often removed at the time of ERM surgery, there is debate as to the potential benefit of completing ILM peeling following the removal of ERM. It has been proposed that removal of

ILM at the time of surgery removes the scaffold for myofibroblast proliferation and any residual microscopic ERM, thus reducing the risk of recurrence as well as improving visual outcomes.[31,32] Conversely, there are concerns that loss of retinal tissue and damage to müller cell footplates may adversely affect visual function and that rates of recurrence are not affected.[33]

Surgical outcomes:

Visual improvement of two or more lines may occur in 60–85% of cases 6–12 months after surgery; visual prognosis depends on preoperative vision, the duration of symptoms and the preoperative anatomical status of the fovea and retinal layers. [34, 35]

Both idiopathic and secondary ERMs appear to benefit to an equal extent from surgery; however, in some cases a preexisting macular pathology may limit the visual recovery.[36]

Other parameters of visual function such as contrast sensitivity have been shown to improve significantly following surgery, even without improvement of vision.[37] Contrast sensitivity appears more closely correlated with improvements in quality of life measures than visual acuity and may therefore be a better indicator of the benefits of surgery.[38] Stereopsis has also been shown to be significantly worse in patients presenting with ERM as compared with controls. Successful surgery may result in a significant improvement but does not return to normal levels within 6 months.[39, 40]

Regarding anatomical outcomes, postoperative reduction of the central macular thickness (CMT) has been a consistent finding in most studies, however, visual acuity is not always correlated with the decrease of retinal thickness.[41]

Secondary epiretinal membranes have worse prognosis than idiopathic membranes with limited visual recovery, higher recurrence rates.[42]

Conclusion

Accidental finding of ERM on OCT is not an indication for surgical interference; we should depend on patient complaint and debilitating symptoms in our decision for surgery.

Pars plana vitrectomy, ERM removal and ILM peeling is currently the preferred surgical treatment option to decrease recurrence rate of ERM. OCT is an essential tool for follow up the patients before surgery in decision making, intraoperative to ensure complete removal and after surgery to e detect any recurrence.

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Conflicts of Interest

None of the authors have any proprietary interest in this work.

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