Lamellar Macular Hole

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ABSTRACT

The lamellar macular hole (LMH) was first described as "partial-thickness injury in neurosensory retina". However, LMH cases are not considered as an uniform clinical and pathological entity now by advancing retinal imaging techniques and since its first description, its treatment has been evolved to use different surgical approaches following observation of 2 distinct clinical types of tractional and degenerative LMH with variations in clinical course and prognosis, responses to surgical treatment and identification of different surgical protocols. In this review, definitions, classification and up-to-date treatments in LMH will be discussed.

Keywords: Epiretinal membrane, Internal limiting membrane, Lamellar macular hole.

1. INTRODUCTION

The lamellar macular hole (LMH) has been expressed using different terminologies and definitions since it was first described by Gass in 1976. In 1976, it was defined as oval-reddish lesion in patients with pseudophakic cystoid macular edema and interpreted as a sign of foveal tissue loss. It was accepted that LMH cases develop as a complication of chronic cystoid macular edema through disruption of development of full-thickness macular hole (FTMH) and perifoveal contraction of epiretinal membrane (ERM) and internal limiting membrane (ILM) complex.[1-4]

The optical coherence tomography (OCT) has been accepted as gold standard in delineation of vitreoretinal interface pathologies and LMH cases since its introduction into ophthalmology practice. The OCT facilitates diagnosis of LMH cases and can detect cases previously undetected as well. In studies by Haouchine and Witkin, fundus examination could made LMH diagnosis in only 28% and 37% of LMH cases diagnosed by OCT.[2-4] Advent of spectral-domain (SD) OCT technology has improved our understanding by detailed analysis of LMH morphology using high-resolution imaging abilities and establishing more specific and prominent diagnostic features in LMH cases.

The current imaging modalities have demonstrated ERM in almost all LMD cases and allowed detecting ellipsoid zone damage and intraretinal cyst that determines functional pathologies and identifying and monitoring measurable and reproducible signs of pathological changes that are closely correlated with prognosis. Today, OCT findings that can be detected for diagnosis, follow-up and decision-making process for surgical treatment include:[4-8]

- Irregular foveal contour
- Thinning of retinal tissue in foveal base
- Intraretinal lamellar dehiscence
- Lack of FTMH
- Disruption of inner segment (IS)/outer segment (OS) integrity (ellipsoid zone damage)
- Detection of preretinal proliferation (ERM) and membrane characteristics

Based on these findings, the diagnosis and follow-up of LMH cases can be performed; in addition, macular pseudo-hole, foveal pseudo-cyst and FTMH cases which resemble LMH in clinical manner could be distinguished as well. The En face SD-OCT imaging allows visualization of contraction foci in addition to extent of ERM on macular surface, and definition of effects of tractional forces in LMH development. In cases with classical ERM, tangential forces can be observed more prominently on en

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face imaging when compared to B-scan images [9-11]. The LMH prevalence ranges from 1.1% to 3.6% in the study by Maastrich and Beaver who investigated the prevalence of vitreoretinal interface disorders. No significant correlation was detected with age and gender. Bilateral involvement rate ranges from 3% and 13%.[7]

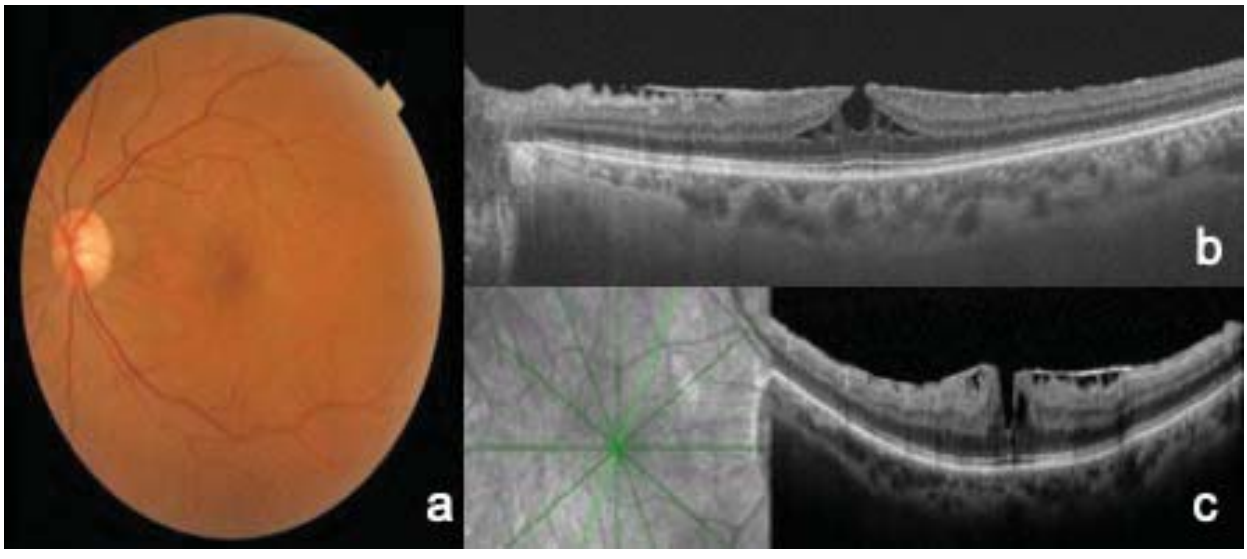
2. PRERETINAL PROLIFERATIONS IN LAMELLAR MACULAR HOLE

The epiretinal (preretinal) proliferation and presence of membrane formation are shown as SD-OCT findings in almost all LMH cases. Classically, the ERM develops through migration and, in turn, proliferation of cells including myofibroblast, fibrocyte, glial cells, hyalocyte and RPE across retinal micro-breaks in the ILM that develop as a result of posterior vitreous detachment and recruitment of vitreous-derived collagen fibers. These membranes contain alpha-SMA (smooth muscle actin filament) that adds contractile features to cells and tissue; thus, they are involved in LMH etiology by causing tangential tractions and pucker in retina through their contractile features.[4-7, 12-16]

On SD-OCT imaging, classical ERM appears as thin, hyper-reflective band involving a large area over epiretinal surface. The tractional effect of ERM leads retinal folding and wrinkles, occasional adhesions with retina and hypo-reflective cleavage. The retinal thickening and cystoid intraretinal spaces develops. The ellipsoid layer damage isn't seen until advanced stages in cases with classical ERM (Picture 1).

In recent years, membranes with distinct morphological characteristics were detected in the clinical course and OCT imaging studies and it was found that retinal morphological alterations were also differentiated accordingly. These membranes, previously considered as a thicker group of classical ERM, was first defined as "thick membranes" distinct from classical ERM by Witkin et al., whereas "dense non-tractional ERM" by Parolini et al. and "atypical epiretinal tissue" by Schumann et al. In subsequent studies, it was reported that this type of ERM was detected in 20-44% of LMH cases. However, it was recognized that the ERM described has distinct clinical characteristics and effects in addition to being thicker and it was defined as "association of thick epiretinal material with LMH cases" and termed as "Lamellar Hole-Associated Epiretinal Proliferation (LHEP)" by Pang et al. Thereafter, in their retrospective study, Pang et al. found LHEP incidence as 30.5% in cases with LMH and observed that no LHEP was detected in ERM cases not associated with LMH. In minority of cases with LHEP, association with FTMH was shown rather than LMH. In another study, various LHEP incidences have been reported (13.1%) with approximately 30% of incidence in association with ERM.[4, 15-23]

On SD-OCT imaging, LHEP appears as homogenous and thick layer on medium reflective images such as inner retinal layers at retinal surface. Although it is fully adhered to retinal surface, it does not cause traction and retinal wrinkling. The proliferation is localized at epiretinal surface and foveal margin corresponding to inner retinal defects. Its thickness shows local variations. Unlike classical ERM, it has lower alpha-SMA content which regulates contractile feature. This explains why LHEP isn't contractile.[7, 15-17]



Picture 1: *Classical ERM and associated LMH case; a) retinal wrinkle in color fundus image; b) dehiscence in outer plexiform and outer nuclear layers and ERM on B-scan OCT; c) another section captured by red-deficient image. It can be seen that outer segment structures are intact in both sections while macular wrinkle can be seen in red-deficient image.*

In electron microscopy and immunohistochemical studies, it was shown that Muller glial cells are key actors in the development of these membranes and fibroblast, hyalocyte and RPE cells are other proliferative cell types involved in membrane. The membrane skeletal structure is formed by cortical vitreous-derived type I and III collagen fibers as well as more thicker collagen bundles with irregular distribution resulting from degradation of normal collagen fibers.[7, 13, 17, 19-21,24-27]

Obana et al. demonstrated presence of macular pigments (lutein, xantophyll) in tissue samples of LHEP, proposing that these pigments are secreted by Muller cells. The outer plexiform layer has the most concentrated lutein and zeaxanthin content in the retina. Given the linkage of LHEP with outer plexiform and other mid-retinal layers, it is thought that these macular pigments are involved in proliferative tissue. The presence of the pigments brings yellowish appearance and elastic structure relatively to LHEP tissue. Based on above-mentioned features, it was recognized that these membranes exhibit distinct characteristics and requires different surgical manipulations.[7, 27-29]

Pang et al. found links between LHEP and outer plexiform and nuclear layers, proposing that LHEP arises from these layers. These proliferations are termed as "degenerative ERM" based on assumption that severe morphological damage of outer retinal layers leads Muller cell proliferation and LHEP formation, and association with degenerative process in outer retinal layers. It has been detected that ellipsoid zone injury develops in majority of cases (Picture 2).[16, 17]

3. CLASSIFICATION OF LAMELLAR MACULAR HOLE

Following demonstration of presence of 2 distinct epiretinal proliferations on SD-OCT which are characterized by different morphopathological processes in almost all cases with LMH, two subtypes of ERM was defined to ensure common terminology in the diagnosis, follow-up and treatment indications.

These two subtypes with different features detected on SD-OCT, which accompanies to LMH, are:

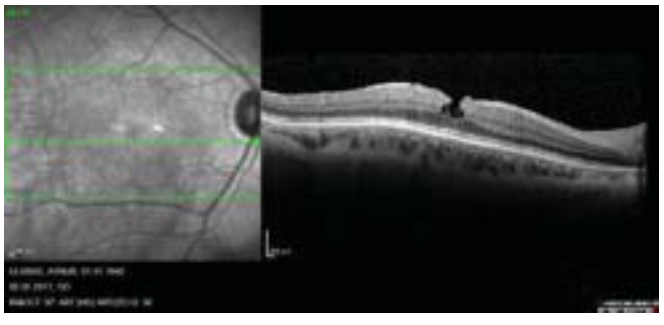
- Classical ERM
- Atypical ERM (LHEP, degenerative ERM)

In addition to confirmed distinction by SD-OCT findings, Govette et al. defined two different clinical presentation based on presence of these membranes and resultant morphological features, which also differ regarding visual prognosis and benefit from surgical treatment.[18]

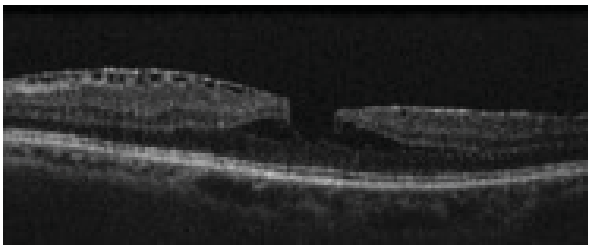
1. Tractional LMH
2. Degenerative LMH
3. Mix type LMH

3.1 Tractional LMH

This defines morphological and functional clinical manifestation which develops as a result of cellular proliferation with contractile features that causes retinal traction and/or vitreomacular traction. In this type, ellipsoid zone damage in smaller number of cases and less foveal retinal thinning are observed as a characteristic of classical ERM cases. Intraretinal lamellar dehiscence (between outer plexiform and outer nuclear layers in neurosensory retina) is in form of schisis. The vertical hyper-reflective bands are observed at the area of hypo-reflective lamellar dehiscence. Due to contractile feature of membrane, these bands correspond to foci of retinal wrinkle and retinal wrinkles. Foveal margins are elevated due to ERM traction. Intraretinal cystic areas are localized at inner plexiform layer (Picture 3).[7, 18, 19]



Picture 2: *Epiretinal proliferation showing iso-reflection with inner retinal surface and mid-retinal layers and dehiscence of inner retinal layers caused by degenerative process (cavitation) foveal thinning and disrupted photoreceptor inner and outer segment line.*



Picture 3: *ERM with diffuse hyper-reflective line at inner retinal surface shows some occasional adhesions with retinal surface. Retinal dehiscence at outer plexiform is observed as hypo-reflective while thin hyper-reflective bridges are seen in dehiscence area. It can be seen that outer retinal layers are intact and there is moderate thinning at retina.*

3.2. Degenerative LMH

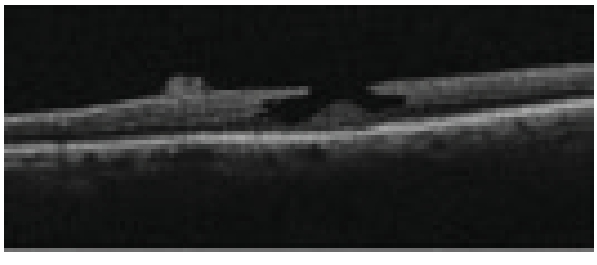
It is the LMH manifestation which develops with presence and effect of atypical, degenerative type epiretinal proliferations termed as LHEP. Clinically, it has more stable, slow and chronic course. Epiretinal proliferation does not cause traction over macular surface. However, associated degenerative process and resultant retinal tissue loss (foveal retinal thinning) and ellipsoid layer damage are negative factors regarding visual prognosis and benefit from surgery. In this type of LMH, retinal dehiscence is in form of intraretinal cavitation and appears as homogeneous, smooth, hypo-reflective area involving all neurosensory layers on OCT. The centripetal traction of LHEP causes enlargement in LMH diameter through traction at intraretinal layers. Migration of Muller glial cells to retinal surface from inner retinal layers also causes enlargement in cavitation area. Maximum horizontal hole diameter indicating extent of cavitation area can be a reliable criterion for progression of degenerative LMH cases (Picture 4).[4, 12, 15-33]

3.3 Mix type LMH

This indicates limited number of cases which harbors characteristics of both types. Its incidence has been reported as 10.78-46.00%) in the literature [>2, 17, 20].

4. NATURAL COURSE/PROGNOSIS ACCORDING TO LMH TPYES

The LMH cases are characterized by stable and slow progression, relative preservation of good visual acuity and resultant mild metamorphopsia. Outer retinal layers are often protected while OCT lesions stay stable at long-term. Thus, common approach is follow-up with clinical findings and OCT imaging studies in cases with moderate morphological changes and good vision. However, progression in morphological finding on OCT, decreased vision and metamorphopsia may develop in some cases, particularly in those with degenerative type LMH characterized by LHEP.[6, 9, 34, 35] Primarily, enlargement of membrane-involved area on macular surface and increased retinal wrinkles and resultant expansion in retinal defect indicate membrane progression while foveal central retinal thickness measurement and thinning are quantitative parameters for LMH progression. Central retinal thinning is a marker for severity of pathological process at outer retinal layers and poor prognosis. These are cases associated with lower expectation of benefit from surgery. Central foveal retinal thickness is lower in cases with degenerative type and LHEP when compared to those with tractional LMH.



Picture 4: *Degenerative LMH; epiretinal proliferative tissue (LHEP) thickened at inner retinal surface, which shows focal variations in thickness: Inner and outer lamellar hole margins are seen. Disrupted IS/OS line showing foveal retinal thickness (decreased) and photoreceptor damage.*

The damage in ellipsoid zone where photoreceptor cells are localized occurs as a result of ERM traction. Prolonged macular traction leads irreversible loss of cells and disruption in hyper-reflective line on OCT. Ellipsoid zone damage is the most effective parameter on visual acuity and metamorphopsia.[37]

In long-term follow-up studies, Theodossiadis et al. found that the cases had either a stable course or progression with decreased vision, irregular photoreceptor layer, decreased foveal thickness and increased diameter of lamellar hole in long-term follow-up while Castro et al. found that these cases can show progression as well as evolution to FTMH.[6, 34, 35]

Although there are studies which found no significant difference between tractional and degenerative type LMH in long-term follow-up, in current studies using SD-OCT, it was found that the extent of foveal thinning is higher in cases with LHEP and that ellipsoid zone damage is more severe and widespread when compared to tractional type LMH cases. Based on these findings, degenerative type LMH cases have poorer visual functions. The difference in pathological process reveals that degenerative type LMH cases have more advanced degenerative clinical pathology when compared to tractional type LMH cases.[9, 13, 17, 18, 21, 22, 28, 30-33]

Although highly stable course is defined in high myopia cases in the presence to LMH, it was shown that there is more outer retinal damage and retinal thinning in the presence of LHEP and they have more severe clinical presentation with progressive nature.[13]

5. CURRENT TREATMENT IN LMH

In general, LMH cases lead a benign clinical process which is characterized by prolonged stability, chronic, slow progression, good visual acuity and mild metamorphopsia and such cases are generally followed by clinical findings. However, there is no consensus on indications and timing

of treatment in patients showing clinical and morphological progression with functional loss. There are studies reporting good surgical outcomes with appropriate indications but some authors argue against surgical treatment because of ineffectiveness of surgical treatment and even risk for complication such as FTMH.

Preliminary surgical outcomes were published by Witkin et al., who proposed that surgery is ineffective. However, the weakness of the study was that cases with high myopia were not excluded and no ILM peeling was performed, all which can be influence negative outcomes in the study.[4, 13, 22, 24]

In almost all long-term, retrospective case-controls studies, it was reported that visual gain was achieved in LMH cases after surgery while there was no change in vision in 20-30% of cases and decreased vision in minority of cases. Currently, surgical treatment with appropriate indication and technique results in functional gain, albeit limited, in almost all cases including degenerative LMH cases with advanced degenerative damage and poor clinical prognosis.[27-34, 38] Although decision-making process in selection of surgical treatment or follow-up is made based on morphological and clinical data in individualized manner, comparative studies are important in this process. In a retrospective study from Turkey, Sanisoğlu et al. found that there was decreased visual acuity and progression in OCT findings in control cases with natural course while vision was preserved or improved in surgery group and OCT findings were recovered in more than one-half of cases, recommending surgical treatment in selected patients with appropriate indications.[39]

Although there is no consensus, presence and enlargement of tractional epimacular proliferation, increased tractions, progression in morphological abnormalities (foveal thinning, retinal dehiscence, ellipsoid zone damage) and/or functional impairment (metamorphopsia and decreased visual acuity) are considered as need for treatment.

The visual acuity below 0.5 attributed to progression of SD-OCT findings of LMH or reduction ≥2 lines and non-tolerable, progressive metamorphopsia are commonly used criteria for surgical treatment decision. In recent years, convenience in surgery and successful outcomes provided by introduction of relatively non-invasive, transconjunctival 23, 25, 27G surgical techniques under local anesthesia and use of advanced imaging systems and dyes improving visualization of membranes during macular surgery have increased rate of surgical treatment decisions in LMH cases.[21-24, 30, 31,37]

Classically, the treatment protocol relies of relieving tractional forces on retina. Etiopathogenetic tractional factors include thickening at posterior hyaloid and incomplete separation of macula adhered (vitreofoveal traction), centripetal traction of ILM and tractions caused by epiretinal proliferations (ERM, LHEP). For this purpose, 23, 25 or 27 G pars plana vitrectomy, releasing posterior hyaloid, peeling of epiretinal proliferation and ILM are employed as standard surgical protocol. There are different arguments about air-gas tamponade and patient positioning. Some studies have proposed that tamponade use is ineffective while some authors advocate that tamponade with patient positioning should be used to achieve effective surgical outcome and there is an increased risk for failure to close lamellar hole and FTMH development despite successful outcome in cases underwent surgery without tamponade. It was reported that tamponade use had no effect on visual gain despite positive effect on thickness by reorganizing central macula.[14, 30-36]

When visual acuity is considered as surgical treatment indication, higher visual acuity level is achieved postoperatively in cases with good visual acuity before surgery. Although visual acuity gain was greater in cases with poor visual acuity before surgery, final visual acuity level was lower. The visual acuity≤0.1 are considered as poor prognosis.[8, 38]

The metamorphopsia is another functional parameter; most common structural abnormality associated to metamorphopsia is photoreceptor cell layer damage. Severe metamorphopsia or progression in metamorphopsia complaints are among surgical treatment indications. The improvement that could positively affect quality of life has been reported despite failure to achieve complete recovery in metamorphopsia following surgery. The improvement in metamorphopsia by surgical treatment is parallel to increased postoperative central retinal thickness, reorganization of ellipsoid zone and recovery of photoreceptor cell layer.[40]

The preoperative LMH diameter, measurement of central foveal retinal thickness and degree of ellipsoid zone damage are important criteria to determine surgical indications and postoperative follow-up and they are effective predictive parameters for surgical outcome.

Although photoreceptor damage in outer retinal layers is more frequent and severe in degenerative type LMH cases, it could also be detected in cases with chronic tractional type and is major cause of functional loss. It is an important cause of failure in achieving functional gain despite closure of successful surgery and stabilization of foveal retinal thinning. In these cases, primary goal of surgical treatment is to stop pathological process and protect vision. It was found that postoperative visual acuity is higher in patients without ellipsoid zone damage. The rate of successful

repair in ellipsoid zone damage and photoreceptor cell layer is low in patients undergoing standard surgical intervention, particularly in those with LHEP positive LMH. Although photoreceptor cell layer is restored in these cases, the restoration is product of gliosis induced by ILM peeling rather than photoreceptor cell regeneration and is not functional. Such reorganization can explain failure to achieve visual improvement despite recovery of ellipsoid zone damage after surgery in some cases. The continuity of photoreceptor layer and lack of cellular damage are markers for good visual acuity in general while there is an impairment in visual functions in cases with photoreceptor damage and it is a poor prognostic marker indicating limited benefit for scheduled surgical treatment. [31, 33, 38,41-43]

Foveolar thinning develops due to foveal traction caused by ERM in cases with tractional LMH and chronic degenerative effect rather than tractional effect in degenerative LMH cases, which is an important cause for functional losses. Previous studies demonstrated that initial visual acuity and postoperative visual gain were lower in cases with foveal retinal thinning.[9, 18, 30, 31,35]

There are studies proposing that extent of intraretinal tissue defect is not a marker for retinal damage and not correlated with visual acuity while there are other studies found width of outer retinal dehiscence as a marker for visual impairment and postoperative visual gain. Reduction and closure of retinal defect by removal of traction is possible in tractional type. However, in degenerative type, it is thought that recovery of cavitation caused by degenerative process requires reorganization of Muller and glial cells and need for neurotrophic factors are important in functional recovery in the pathology.[30, 38]

It was found that the outer retinal tissue damage is lesser and better functional outcomes are achieved while foveal tissue repair is better in tractional LMH cases. The finding that these pathologies are more common in LMH cases with LHEP defines presence of LHEP as a parameter. Given differences in incidences of these morphological abnormalities having prognostic value, type of epiretinal proliferation is an important factor that determines surgical treatment indication and functional outcomes.

Although the contractile characteristic of LHEP tissue is not as prominent as classical ERM, it is thought that peeling of ERM results in improvement in foveal and retinal morphology and functional recovery since it LHEP causes impairment in foveal morphology and cellular damage through traction of retinal layers. Another idea is that it is likely that ILM peeling achieves recovery in distortion resulting from ILM masked by LHEP tissue. Cossin et al. reported that they achieved significant functional gain after surgery in LMH cases at long-term follow-up; however, significant visual gain was achieved in tractional and mix type LMH cases but not in degenerative LMH case when assessed membrane types.[8, 16, 22, 40] Shumpei et al. found significant visual gain in all cases without difference between LMH types. However, it is important that number of cases with preoperative ellipsoid zone damage was small among degenerative LHM cases and that recovery was detected in some cases with ellipsoid damage after surgery in that study. The poorer preoperative visual acuity in degenerative LHM cases and inclusion of chronic cases can explain contradictory results in above-mentioned studies. Visual gain independent from membrane type can be achieved by surgical treatment before onset of severe morphological damage and loss of vision.[18, 42, 43]

In recent years, there is increasing number of studies comparing LMH types regarding morphological characteristics of natural course and surgical outcomes. There are studies reporting no significant difference in natural course and postoperative outcomes between LMH types such as the study by dell' Omo et al.; however, some studies reported that there is limited postoperative visual gain in degenerative LMH cases vs. significant visual gain in tractional type. Coassin and Ko suggested that no significant visual gain was achieved despite anatomic recovery in LHEP positive case because LHEP is associated to irreversible retinal damage and can be considered as a negative factor for treatment response. In standard surgical technique, undesired results such as retinal defect, failure in recovery of ellipsoid zone damage and even FTMH can develop after total ILM peeling in LMH cases with LHEP. [8, 13, 33-34, 27,30, 31,44]

6. SURGICAL PROCEDURE IN DEGENERATIVE LMH

The LHEP tissue with abundant macular pigment content can be readily distinguished from classical ERM by its appearance and strict adherence to retinal surface, elasticity and yellowish color in addition to its collagen content differing from Muller cell and vitreous cortex collagen. In recent years, it was recognized that, due to elastic membrane structure, it requires numerous grip attempts with difficulty in grasping, peeling and removing ILM and it was seen that LHEP is adhered strictly enough to cause iatrogenic foveal avulsion and concern for retinal tear. Given these characteristics, iatrogenic retinal tractions, photoreceptor damage due to excessive surgical trauma and FTMH development can be observed more frequently if standard surgical approaches are used during membrane peeling.[33] To minimize such complications and achieve convenient application, creating a tip to grasp by

sweeping from periphery to central using scraper with diamond powder is a technique used occasionally in order to remove LHEP tissue from retinal surface.[31] To avoid foveal avulsion during peeling of these membranes, the membranes should be peeled from periphery to centre and one should prefer to complete surgery by leaving stumps without forcing membrane to remove from retina and shave membrane using vitreous cutter at foveal area if needed [20, 28, 29, 31,40]. To attempt peeling membrane completely and peeling of ILM which is basal membrane of Muller cells can lead a process resulting in iatrogenic damage in Muller cells, photoreceptor cell damage via tractions in foveal tissue and eventual FTMH in 3.7-16.7 of cases. The risk for FTMH is higher in cases with LHEP than those with classical ERM and it is a complication more frequently seen in cases with ellipsoid zone damage and foveal thinnin.[27, 29, 31-33] Such experiences warrant different surgical approaches and planning in two types of LHM. In surgical planning process, preoperative OCT findings should be evaluated cautiously and iso-reflective LHPE tissue and inner retinal layers should be assessed particularly in order to provide appropriate surgical materials and assess surgical alternative as an option. Andreas et al. performed a pilot study including 3 cases, in which autologous platelet suspension (platelet-derived growth factor [PDGF]) was added to surgical protocol in order to reduce risk for FTHM after surgery. Authors reported effective surgical outcomes without FTMH development.[45] By inspiration from improved closure success rates in cases with FTMH via addition of ILM peeling to surgery, ILM peeling improved morphological reorganization including closure of retinal defect and success in visual recovery. However, total ILM peeling has low success rate in the repair of ellipsoid zone damage and visual gain in LHEP positive LMH cases when compared to tractional cases. In seek for alternative surgical techniques in cases with degenerative LMH, Shiraga et al. developed fovea-sparing surgical technique which is defined as air tamponade and head position with peeling of ILM but not epimacular tissue containing macular pigment in strictly adhered region around foveal margin. By this technique, significant visual gain and morphological recovery in fovea were reported in 75% of cases.[41]

Muller cells are involved in retinal tissue repair and retinal reorganization while release of neurotrophic factors mediated by Muller cells ensures reorganization of neural fiber layer. Given the assumption that such features can be effective in repair of ellipsoid zone damage and restoration of retinal thinning in the repair process of retinal tissue defect, LHEP embedding technique where LHEP enriched from glial cells is embedded to retinal gap or double inverting technique where both LHEP and ILM are folded over lamellar hole are recommended as alternatives. It is thought that these techniques will prevent FTMH development while ensuring retinal restoration. It was shown that there is also functional recovery in these cases by improved vision and recovery in metamorphopsia.[19, 20, 42] Takashi et al. applied embedding technique where atypical membrane tissue is filled into lamellar hole in degenerative LMH cases as an alternative to standard surgery. The LHEP is peeled from periphery to centre using micro-forceps and left attached to edge of hole. The ILM is peeled and LHEP is filled into hole by massaging. Head positioning over 24 hours is applied by air tamponade. By this technique, a significant improvement was achieved in visual acuity while marked increase in foveal thickness was detected. In majority of cases, recovery was observed in ELM (58%) and ellipsoid zone damage (46.7%) detected preoperatively. No complication such as FTMH or recurrence of LHEP, ERM or LMH was observed.[19]

Based on the idea that foveolar epiretinal proliferation tissue can be peeled involuntarily or uncontrolled manner and lamellar defect could not be peeled when ILM is peeled completely in embedding technique, Morescalchi et al. developed foveolar non-peeling technique. Faithfully to original procedure, instead of total ILM peeling, retinal defect is filled with epiretinal proliferation tissue and ILM peeling is reduced using vitrector in order to leave a fovea-centered ILM area (1 or 2 disc diameter in size). Meantime, margins of ILM residue at fovea can remain elevated with proliferative tissue over ILM residue, causing an irregular postoperative surface. It was emphasized that surgical outcome is improved by this limited technique and that the technique resulting in improved visual acuity and foveal retinal thickness with increased sensitivity in foveal retina is effective in these cases. Authors suggested that further studies are needed to optimize this technique. In this technique modified to spare foveola by Tzyy-chang et al., epiretinal tissue is elevated and reduced using vitrector, which is then reposed into lamellar hole; differently, ILM is restricted at 400 micron to foveola by marking in the form of can-opener using tip of MVR blade. Thus, ILM at 400 micron to foveola was preserved while peeling. No postoperative retinal defect was detected foveola is protected against traction during ILM peeling. In these cases, all lamellar holes were closed; visual acuity was markedly improved and ellipsoid zone repair was foveal contour formation were better as retinal defect was restored.[41, 44, 46]

Double inverting technique was developed by Frisina et al. through inspiration from inverted flap technique used in large FTMH cases by Michalewska et al. After partial peeling by vitrector and reduction in size by very low vacuum and high cutting velocity, ERM and ILM are

stroked in all quadrants until reposition over LMH by massaging. At this point, authors advocating coverage of LMH using flap alone and those reposing flap into hole vary from each other. Although filling defective area with glial cell-enriched LHEP tissue allows early and strong tissue repair, no morphological or functional difference was detected in defect-covering technique which avoids from additional maneuvers. The reposition of ILM over LHEP which covers retinal defect prevents shift during fluid-gas exchange and eliminates ILM-derived traction; glial proliferation is induced; and it acts as skeleton for glial cell spread and plays role in retinal reorganization. Then, gas tamponade is applied. When compared to standard technique in which ERM and ILM are peeled, visual gain was achieved in all patients operated with double inverted technique without complication while no visual gain was detected in control group underwent surgery using standard technique and FTMH was developed in 3 of 18 patients. The visual gain has been reported in cases with ellipsoid zone damage in this technique. The major advantage is avoiding iatrogenic retinal injury by conservative approach and achieving improvement in ellipsoid zone damage and vision in cases with poor prognosis due to presence of ellipsoid zone damage.[20] There is no established protocol, experience or recommendation in LMD cases in which LHEP is lacking or small to fill lamellar hole with epiretinal proliferative tissue. However, I think that ILM inversion to cover lamellar defect can be effective in these cases.

The other LMH configuration includes cases with mix type LMH where LHEP and ERM are found together. In these cases, LHEP tissue can be reposed into defect if it can be separated in isolated manner. However, ILM and ERM should be peeled and ERM tissue should not be placed into lamellar retinal defect since ERM primarily consists from hyalocyte, myofibroblast and fibroblast, which do not play role in cellular reorganization and cause risk for recurrence of membrane.[19]

After successful and effective surgery, completion of reorganization in macular region and formation of foveal contour takes several months. Foveal contour formation has no direct relationship with visual acuity. Development and process of postoperative foveal OCT configuration do not differ for two types of LMH. Postoperative foveal contour formation can occur in 3 different ways:

1) Flat fovea: no intraretinal pseudo-cyst or residual retinal dehiscence

2) Incomplete recovery: there are pseudo-cysts but not dehiscence

3) Persistent lamellar defect.[23, 29]

7. CONCLUSION

Although LMH comprises a small group among vitreomacular interface disorders, it represents cases associated with ongoing obscurity and need for further investigation regarding clinical manifestation and treatment criteria due to its functional and morphological pathological process.

Today, LMH cases are classified as tractional and degenerative type LMH with distinct clinical manifestations and courses as a result of development of two different epiretinal proliferation, namely classical ERM and LHEP (atypical ERM). These types differ with characteristics of natural course as well surgical intervention technique and treatment response characteristics.

Although more clear criteria for treatment indications have been established in the shed of recent studies, still, there are uncertainties to be elucidated with ongoing studies. The dilemma whether LMH cases are treated or followed with their natural course has evolved to different options and even to specialized surgical treatment using foveola-sparing embedding and ILM inverting techniques in LMH cases.

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