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Review Article

Application of Optical Coherence Tomography in the Diagnosis and Treatment of Idiopathic Macular Epiretinal Membrane

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Abstract

The pathogenesis of idiopathic macular epiretinal membrane (iERM) is still unclear. Its formation is related to the posterior vitreous detachment, renin-angiotensin system activation, estrogen reduction and so on. Optical coherence tomography (OCT) examination is the gold standard for diagnosing iERM, which is helpful for the early detection of macular epithelium, and the staging method based on OCT images can describe the degree of its retinopathy. The retinopathy shown in the images help to choose the timing of surgery, such as the thickness of the fovea, the integrity of the ellipsoid zone, and the central cone bouquet. The optical coherence tomography angiography image of the iERM eye is different from the normal eye and can assess the prognosis of the patient to a certain extent. For example, the area of the foveal avascular area and the postoperative best corrected visual acuity are negatively correlated.

Keywords: Idiopathic Macular Epiretinal Epithelium; Optical Coherence Tomography; Optical Coherence Tomography Angiography

Introduction

Epiretinal membrane (ERM) is a non-vascular fibrous membrane formed by varies cell components proliferating on the inner surface of macular retina. According to the cause of disease, there are two types: idiopathic macular epiretinal membrane (iERM) and secondary macular epiretinal membrane. Secondary macular epithelium is mostly secondary to ocular vascular disease, inflammation, ocular trauma, intraocular surgery or retinal cryosurgery, photocoagulation, etc. IERM accounts for 80% of ERM. The prevalence of people over 50 years old is about 5.1% to 7.8% [1]. Increasing age, diabetes, and hypercholesteremia were found to be risk factors for the epiretinal membrane. At present, the incidence of iERM is increasing and the affected population is gradually getting younger, so the research on iERM is particularly important. Optical coherence tomography (OCT) is the gold standard for diagnosing iERM, and it also plays an important role in preoperative evaluation and postoperative follow-up. At the same time, optical coherence tomography angiography (OCTA) technology has developed rapidly, and the research of iERM has reached the level of retinal capillary structure. This article summarizes the research progress of the application of OCT in the diagnosis and treatment of iERM in recent years.

Pathogenesis

IERM is a non-vascular fibrous membrane located on the surface of macular retina and its nearby region. The extracellular matrix structure such as fibronectin, retinal gliocytes (astrocytes and Müller cells) and retina pigment epithelial cells are main components of the metallic membrane [2,3]. There are many research on the pathogenesis of iERM, and it has not yet been clear. Its formation is related to posterior vitreous detachment (PVD), renin-angiotensin system (RAS) activation, and estrogen reduction. PVD is the most important reason for iERM and exists in about 90% iERM eyes. Internal limiting membrane (ILM), vitreous base and vitreous

post form a vitreous retinal interface. When the PVD occurs, the traction force generated by the posterior pole makes the surface of the ILM broken, and the germline cells from the retinal underlayer are obtained by the cell transition to reach the iERM [3]. RAS activation is another important reason for ERM. RAS can adjust system blood pressure and moisture balance, but also adjust the vascular inflammation (tissue RAS) including various organs including retina. The tissue RAS is activated by renin and renin receptors, which also initiates independent RAS signaling pathway in cells carrying (pro) renin receptors. This double activation is called receptor-associated prorenin system. Transforming growth factor-β1 (TGF-β1), fibroblast growth factor 2 (FGF2), nerve growth factor (NGF), glial cell-derived neurotrophic factor (GDNF) and so on may participate in the formation of the front membrane. When independent RAS systems in the retina are activated, cytokines (FGF2, GDNF, NGF, TGF-β1, etc.) are stimulated and supported in the survival of gelamin cells and converse to fibroblasts, thereby playing in the formation of iERM [4,5]. The appearance of the iERM may be related to gender. Nishikawa Y et al. [6] proves that estrogen can inhibit the pulling effect of retinal colloidal cells, which helps to maintain the retinal shape and structure. Since postmenopausal women's estrogen levels decrease, which can accelerate the liquefaction of the vitreous steric acid, the stability of the vitreous retinal interface is degraded. And the retina is easier to be damaged, resulting in the formation of iERM.

Clinical manifestations and classic diagnostic technology of iERM

iERM has been reported to be mostly slowly progressive, with only a small proportion causing significant effects on vision, including reduced visual acuity, metamorphopsia, and, occasionally, monocular diplopia [7]. Fang IM et al. [7] found that best corrected visual acuity (BCVA) deteriorated when macular edema or IS/OS layer disorder occurred through an average follow-up time of 20.78 months. The classic diagnosis of iERM is achieved by the fundus inspection, while the eye primary disease is required through comprehensive eye examination. iERM in fundus photography showed cellophane reflections, full-thickness folds of the inner limiting membrane or retina, twisted small blood vessels, occasionally bleeding spots and gray-white oozing spots in the early macular area. The late anterior iERM is irregular, opaque, gray-white membranous changes or radial strips of fixed folds, and it rarely extend to the optic disc, except some severe cases. Fraser Bell S et al. [8] observed whether the cumulative area of ERM as shown in the fundus photos increased or decreased by more than 25%. After 5 years of follow-up, it was found that 28.6%, 25.7% and 38.8% of the eyes with ERM progressed, degenerated, or remain stable respectively. However, the diagnosis of iERM through the fundus photography depends on the personal experience level of the diagnosis physician. There is a large subjectiveness, and the condition cannot be quantified. At the same time, the author believes that the latency of the early course is a vital factor of clinical omission and misdiagnosis.

Application of Oct in iERM Diagnosis

OCT is the gold standard for diagnosing iERM. Govetto et al. [9] proposed a new staging method based on OCT images: Stage 1: Macular fovea exists, and retinal hierarchy is clear; Stage 2: Macular fovea's shape disappears, and retinal levels are clear; Stage 3: Normal shape of macular fovea disappears, the retinal hierarchy is clear, and a continuous ectopic fovea appears; Stage 4: The shape of the fovea disappears, the retinal hierarchy is disordered, and a continuous ectopic fovea appears. The OCT-based staging method can dynamically reflect the pathology and visualize it. It also provides more objective, effective information.

Application of OCT in iERM Treatment

IERM can be treated by surgical treatment. The common type of operation is stripping ERM or ERM combined with ILM, and there is no uniform standard of whether ILM should be peeled off. Ahn SJ and others reports [10] that there were 5% cases among patients without ILM stripped relapsed, and about 2% of recurrence cases need to be treated with secondary surgery. Gandorfer et al. [11] believes that only stripping ERM can hardly remove the fibrous tissue cells in the macular region completely. They recommended stripping ERM combine with ILM, because ILM formed by müller cells can support the proliferation of residual fibrous tissue cells in the pathological conditions, which leads to the recurrance. Chang et al. [12] found that stripping ERM combined with ILM had no advantages in improving postoperative vision and macular fovea thickness, but it can significantly reduce the recurrence rate of ERM. However, Kumagai K et al. [13] observed that stripping ILM changed retinal vessel system in some way, such as the reduction of foval avascular zoon (FAZ). Whether stripping ILM or not in the operation is still the direction of future problems. There are currently no specific indications for the timing of surgery. Whether to operate or not depends on the age of the patient, the condition of the fellow eye, the degree of vision loss in the ill eye, and whether it is accompanied by other ocular diseases. The stable iERM does not require special treatment and can be just followed up regularly. Through a retrospective study of 188 patients, which average follow-up time was 6.64 ± 1.86 years, the author suggests that it supposed to be followed up to exclude progress at least every 2 years. (Not published yet.) Surgery can be performed when the visual acuity does not reach 0.3. And even if the visual acuity is above 0.5, surgery can also be considered if the patient has progressive decline in visual acuity, visual field defects, severe visual distortion, etc. Based on OCT examination, some scholars [14,15] showed that the preoperative central foveal thickness (CFT) has nothing to do with BCVA, but some studies have found that there is a negative correlation between CFT and BVCA [16,17].

That is, the thicker the CFT, the worse the visual acuity, which can be used to evaluate the effect of the ERM on visual acuity, but it cannot be used as the best parameter to predict postoperative visual acuity. Mitamura et al. [18] and Inoue et al. [19] pointed out that the integrity of the ellipsoid zone is closely related to the post-

operative BCVA, which can be used as an index to evaluate the effect of surgery. Intact, this is especially important for judging the timing of surgery for patients with ERM. Ortoli et al. [20] found that surgery can eliminate the changes in the central cone bouquet (CB), and the changes in the central CB have nothing to do with postoperative vision deterioration. Fang IM et al. [21] found that the anterior membrane contraction leads to an increase in the choroidal thickness of patients with iERM. If there is only a slight anterior membrane without contraction, the choroidal thickness does not change. Since vitrectomy can reduce the thickness of the choroid [22], they believe that surgical removal of the ERM can not only reduce the traction of the retina and normalize the thickness of the retina, but also normalize the thickness of the choroid. Dikmetas O et al. [23] found that 86% and 79% of patients had foveal displacement one day and one year after surgery, respectively. They emphasized the necessity to carefully interpret the OCT images of iERM patients after surgery because postoperative fovea was manually determined. The location may be in different vertical or horizontal positions. Through OCTA, Mao JB et al. [24] showed that compared with normal eyes, iERM eyes have smaller foveal avascular zone (FAZ), higher foveal vessel density (FVD) and lower parafoveal vessel density (PRVD). The formation of iERM makes the anteroposterior and tangential force act on the macula; the anterior and posterior force may cause the macula to become thicken, and the tangential force may cause the blood vessel to shift. Liao X et al. [15] also found that the FAZ of the affected eye was smaller than that of the control eye, and it was negatively correlated with the BCVA after the operation. Coppe et al. [25] compared the blood flow density of each part of the ETDRS grid between the iERM eye and the fellow eye. The data showed that the vessel density of each part was significantly reduced, whether superficial capillary plexus or deep capillary plexus. The vessel density of the deep capillary plexus was lower than that of the control eye, which indicates that there are vessel density defects in the macular area and outside the macular area.

Conclusion

In summary, the pathogenesis of iERM is still unclear, and there are no targeted preventive measures. OCT checks the microscopic structure of the retina to facilitate the early discovery of the ERM, and can more accurately describe the range, degree, and stage. The retinal hierarchy shown in the images is helpful for judging the condition and the timing of surgery. It should be treated in time if retinal traction, hole, or detachment emerges. The author suggests that patients should be followed up every 2 years, and it still needs more clinical research.

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