

Diagnosis and Treatment of Myopic Maculopathy

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Patients with myopia are likely to develop a number of macular pathologies that, if untreated, will likely lead to blindness.

Pathologic myopia is generally defined as globe elongation and a refractive error of at least -6 diopters (D) and/or axial length of greater than 26.5 mm associated with degenerative changes in the retina.¹⁻³ The prevalence of pathologic myopia varies considerably in different geographic regions and has the highest prevalence in Asian populations.^{1,2} Pathologic myopia has a high disease burden, as it has been found to be the first, second, or third most frequent cause of blindness in several population-based studies.² Excessive axial elongation of the eye in pathologic myopia results in mechanical stretching and thinning of the choroid and retinal pigment epithelium (RPE) layers, causing various degenerative changes in the retina.⁴ It is well known that individuals with high myopia have increased risks of macular pathologies such as posterior staphyloma, chorioretinal atrophy, RPE atrophy, lacquer cracks, macular hemorrhage, choroidal neovascularization (CNV), myopic foveoschisis, and myopic macular hole.⁴⁻⁶ In a cross-sectional, community-based epidemiologic study conducted in Hong Kong, 11.3% of subjects with high myopia of less than or equal to -6 D were found to have 1 or more posterior pole pathologies.⁷ In addition, higher magnitude of refractive error and older age were significantly associated with the presence of posterior pole lesions. Because these macular pathologies in pathologic myopia can result in severe, irreversible visual loss, it is important for ophthalmologists to understand how to manage conditions associated with pathologic myopia. This review aims to provide an overview on the diagnosis and treatment of various macular complications associated with pathologic myopia, including myopic foveoschisis, myopic macular hole, and myopic CNV.

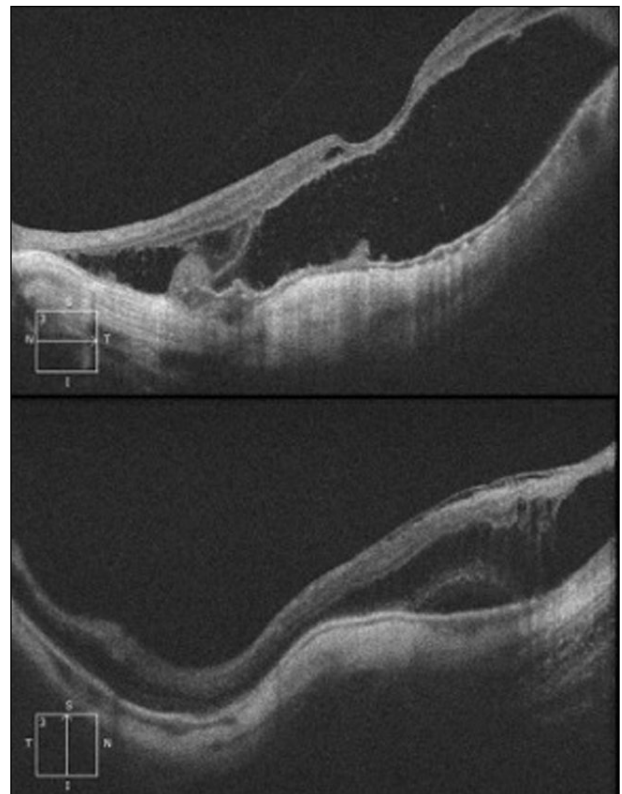


Figure 1. Spectral-domain optical coherence tomography horizontal (top) and vertical (bottom) scans of an eye with myopic foveoschisis showing splitting of the inner retina with intraretinal bridges and foveal detachment. A thin epiretinal membrane causing traction to the macula can also be seen in the vertical scan.

MYOPIC FOVEOSCHISIS

Due to excessive axial elongation of the globe, patients with high myopia can develop posterior bulging or ectasia of the globe, causing posterior staphyloma. The abnormal contour of the posterior staphyloma results

in anatomic changes in the vitreomacular interface, so patients may develop macular pathologies such as myopic foveoschisis and macular hole (MH).

Myopic foveoschisis is the splitting of the retinal layers in the macula, causing accumulation of intraretinal and subretinal fluid at the macula in the absence of a full-thickness macular hole (FTMH).⁸ Abnormal traction caused by posterior hyaloid surface in eyes with posterior staphyloma is the current pathogenesis of myopic foveoschisis. Patients with myopic foveoschisis might be asymptomatic in the early stage and in the later stage can develop progressive increases in metamorphopsia and visual loss as the foveoschisis progresses. Fundus examination might detect mild amount of subretinal fluid in the macula. However, the small amount of subretinal fluid associated with early stage myopic foveoschisis might be very difficult to detect on fundus examination, and therefore spectral-domain optical coherence tomography (SD-OCT) is extremely useful in the assessment of myopic foveoschisis. Scans from SD-OCT can show splitting of the neurosensory retina and epiretinal membrane associated with vitreomacular traction (VMT; Figure 1).

The natural history of myopic foveoschisis is generally poor. Gaucher et al performed a retrospective review of 29 eyes with myopic foveoschisis.⁹ After a mean follow-up of 31.2 months, visual acuity worsened in 20 (69%) eyes and was stable in 9 (31%) eyes. In 9 of the 29 eyes, myopic MH developed during the follow-up period; 6 of the 9 eyes that developed myopic MH had foveal detachment prior to MH formation. Therefore, patients with myopic foveoschisis should be monitored regularly for foveal detachment, and surgical treatment should be considered when foveal detachment develops.

Pars plana vitrectomy (PPV) with internal limiting membrane (ILM) peeling (with or without gas tamponade) is the main treatment for myopic foveoschisis.¹⁰⁻¹³ Surgery is indicated in patients with symptomatic metamorphopsia and progressive visual loss. The main goal of surgery is to relieve any abnormal VMT that causes the foveoschisis. Kumagai et al¹² reported the outcomes of PPV with ILM peeling in 39 eyes with myopic foveoschisis. Following surgery, OCT showed complete resolution of myopic foveoschisis in all eyes. Regarding visual outcome, it was found that significant best corrected visual acuity (BCVA) improvement was observed only in eyes with foveal detachment, not in eyes without foveal detachment. Similar findings were seen in a study by Ikuno et al,¹³ in which 44 eyes with myopic foveoschisis underwent PPV with ILM peeling and gas tamponade. Eyes with foveal detachment had the most visual improvement, while retinoschisis eyes without foveal

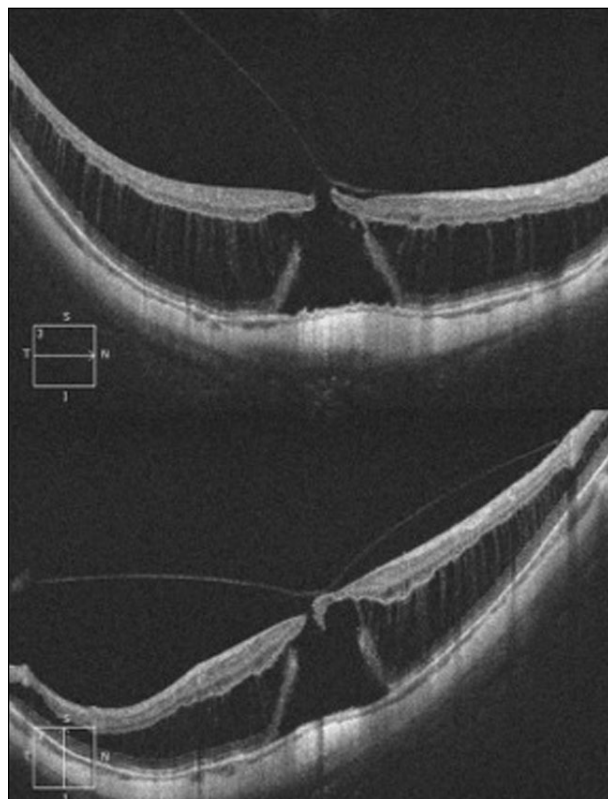


Figure 2. Spectral-domain optical coherence tomography horizontal (top) and vertical (bottom) scans of an eye with myopic macular hole. Posterior hyaloid surface with traction to the parafoveal area is visible in both horizontal and vertical scans. Complete separation of the neurosensory retina from the retinal pigment epithelium can also be seen beneath the macular hole.

detachment had only borderline visual improvement. Therefore, it appears that the optimal timing for surgery in patients with myopic foveoschisis might be when foveal detachment develops, as this helps improve the patients' vision and prevent formation of myopic MH.

MYOPIC MACULAR HOLE

As myopic foveoschisis progresses to a more advanced stage, further VMT can result in the formation of myopic MH (Figure 2). Patients with myopic MH generally develop severe visual loss, and without treatment the condition may progress to complete retinal detachment. Surgical options for myopic MH with or without retinal detachment include PPV with gas or silicone oil tamponade, macular buckling, and scleral-shortening surgeries.¹⁴⁻¹⁸ Previous studies have shown that procedures that use heavy silicone oil have a reattachment rate of approximately 87%, compared with a reattachment rate of 53% for procedures using standard silicone oil.^{16,17}

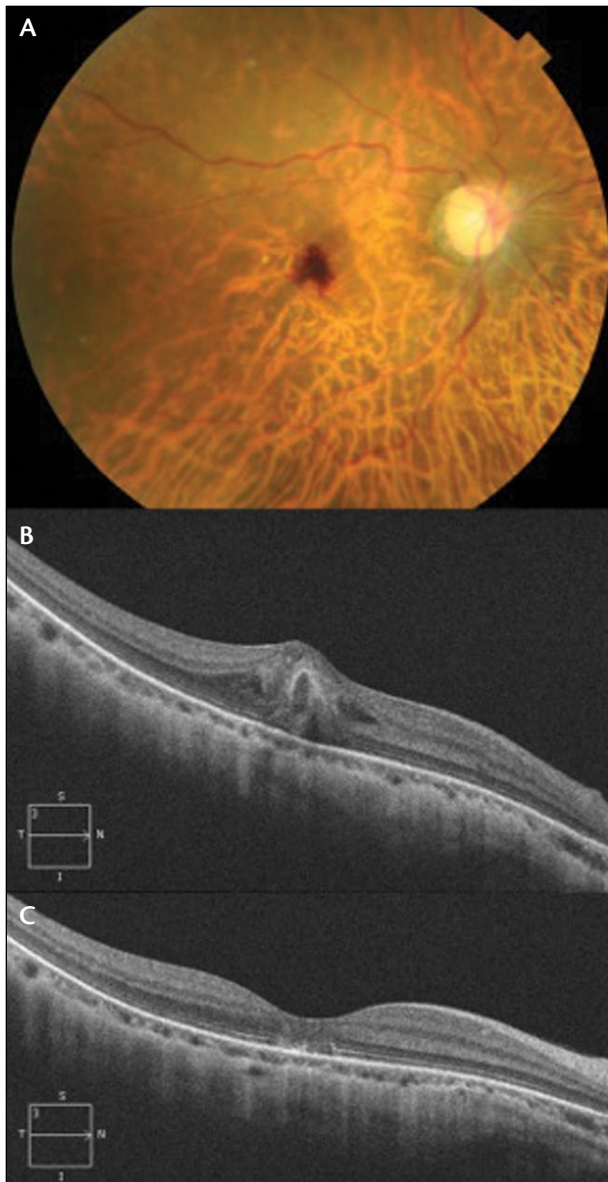


Figure 3. Fundus photo of right eye with high myopia of -13.5 D and myopic choroidal neovascularization (CNV) causing macular hemorrhage. The baseline visual acuity was 20/100 (A). Spectral-domain optical coherence tomography (SD-OCT) showing macular thickening and subretinal fluid due to myopic CNV (B). After 2 intravitreal ranibizumab injections, SD-OCT showed complete regression of the CNV with absence of macular thickening, and the patient's visual acuity improved to 20/30 (C).

However, despite the higher success rate with heavy silicone oil, there was no significant difference in final vision. Moreover, even with these surgical interventions, reopening of the MH and retinal redetachment are not uncommon postoperatively because of the loss of cho-

rioretinal tissue, RPE atrophy, and abnormal shape of the globe associated with posterior staphyloma. Therefore, some patients will require multiple surgeries to achieve closure of the MH and reattachment of the retina.

MYOPIC CHOROIDAL NEOVASCULARIZATION

Myopic CNV is among the most vision-threatening complications in pathologic myopia.¹⁹ It has been estimated to develop in 5% to 10% of eyes with high myopia and is the most common cause of CNV in individuals 50 years old or younger.^{20,21} The chance of developing myopic CNV in a fellow eye if myopic CNV is present in 1 eye is even higher: It has been reported that more than 30% of patients will develop CNV in the fellow eye within 8 years of developing it in the first eye.²¹ Patients with myopic CNV generally present with metamorphopsia, central or paracentral scotoma, and reduced visual acuity. On ophthalmic examination, myopic CNV appears as a flat, small, greyish subretinal membrane beneath or in close proximity to the fovea with or without macular hemorrhage. Fluorescein angiography and OCT can be used to evaluate the CNV activity and to assess the CNV location for treatment planning.

The natural history of myopic CNV is generally poor, as a large proportion of patients will have visual acuity of 20/200 or worse after 5 years.^{22,23} Poor prognostic factors for patients with myopic CNV include advanced age, large area of CNV, and poor initial visual acuity.^{24,25} Due to the poor natural history of myopic CNV, active interventions should be considered to avoid visual loss. Direct thermal laser photocoagulation of myopic CNV has been used for treating myopic CNV, but this will likely lead to visual loss due to expansion of the laser scar in the long term, so the procedure is no longer performed. Other treatment modalities such as submacular surgery and macular translocation surgery for myopic CNV have also been performed, but these procedures are technically demanding and are potentially associated with a high CNV recurrence rate.^{26,27} Photodynamic therapy (PDT) with verteporfin (Visudyne, Novartis) was the first treatment approved for myopic CNV, and studies have shown that PDT can result in stabilization of vision following treatment.^{28,29} Only around 20% to 30% of patients, however, will have improvement in vision after PDT. At 2 years, the beneficial effects of PDT were completely lost, as the difference in vision compared with placebo was no longer statistically significant.²⁸ The long-term visual outcomes with PDT for myopic CNV were even worse, with significant mean visual loss observed at 3 years after PDT.³⁰ This may be because many highly myopic eyes have preexisting RPE atrophy, and PDT further exacerbates the development of cho-

rioretinal atrophy following treatment.³¹ Photodynamic therapy may also result in possible irreversible damage to the choroidal vasculature and RPE.

The availability of anti-VEGF agents, such as intravitreal bevacizumab (Avastin, Genentech) and ranibizumab (Lucentis, Genentech), has revolutionized the management of various forms of ocular neovascularization, including myopic CNV (Figure 3). A systematic review of more than 30 studies evaluating the use of anti-VEGF therapy in myopic CNV demonstrated beneficial visual outcomes following anti-VEGF therapy for myopic CNV.⁴ Therefore, even without the support of level 1 evidence, many ophthalmologists had been using anti-VEGF therapy as a first-line treatment for myopic CNV.³²

More recently, based on the results of the RADIANCE study,³³ intravitreal ranibizumab has been approved in various countries for the treatment of myopic CNV. The RADIANCE study was a phase 3, multicenter, 12-month, randomized, double-masked, active-control led clinical trial that compared the efficacy and safety of intravitreal ranibizumab guided by visual acuity stabilization criteria or disease activity criteria vs verteporfin PDT. The study showed that, at 3 months, intravitreal ranibizumab guided by either visual acuity stabilization or disease activity resulted in a mean BCVA gain of 10.5 and 10.6 letters, respectively, compared with only 2.2 letters in the verteporfin PDT group. Another large-scale, phase 3, randomized, controlled trial, the MYRROR study, which evaluated the efficacy and safety of the use of intravitreal aflibercept (Eylea, Regeneron) compared with sham injection in patients with myopic CNV, has been completed.³⁴ The 24-weeks results showed that patients receiving intravitreal aflibercept gained a mean of 12.1 letters from baseline, compared with a mean loss of 2.0 letters in patients receiving sham injection.³⁵ Further studies will be useful to evaluate the dosing strategy, the choice of anti-VEGF agent, and long-term safety in the use of anti-VEGF therapy for myopic CNV.³⁶

CONCLUSIONS

Individuals with high myopia are subjected to the development of various macular pathologies such as myopic foveoschisis, myopic MH, and myopic CNV. Recent advances in diagnostic instruments, vitreoretinal surgical techniques, and the use of anti-VEGF agents have led to improved visual outcomes for patients. As more effective surgical and medical treatments become available for the conditions associated with pathologic myopia, clinicians will have the ability to promptly address these macular complications and prevent severe visual loss. ■

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