

Advances in Diagnosis and Treatment of Pathologic Myopia

OCT imaging and novel therapies have improved outcomes in eyes with myopic CNV and myopic macular retinoschisis.

BY KYOKO OHNO-MATSUI, MD

Pathologic myopia is a leading cause of visual impairment, estimated to be the fourth to ninth most frequent cause of blindness worldwide.¹⁻⁵ In Asian countries, pathologic myopia is the most frequent cause of visual impairment. The Tajimi Study in Japan showed that myopic macular degeneration is the leading cause of unilateral or bilateral blindness, whereas in China it is the second most common cause of low vision and blindness in people older than 40 years, according to the World Health Organization (WHO).⁶

There have been many advances in our understanding of the pathology of pathologic myopia and in its treatment. With the development of optical coherence tomography (OCT), the novel pathology called myopic macular retinoschisis (MRS) has been described, and pars plana vitrectomy has been shown to be useful in treating this condition. Also, the clinical application of anti-vascular endothelial growth factor (anti-VEGF) therapy has improved outcomes in myopic choroidal neovascularization (CNV). This article describes the pathology and treatment of pathologic myopia, with a focus on MRS and myopic CNV.

PATHOLOGY

The integral characteristic of myopia is an elongation of the eye's axial length.⁷ The development and progression of myopia are due to an increase of vitreous chamber depth. Although the definition of pathologic myopia has not been standardized, the commonly used criteria for pathologic myopia include myopic refractive error (spherical equivalent [SE]) greater than 6.00 D or 8.00 D or an axial length greater than 26.5 mm.

Early studies in human cadaver eyes suggested that eyes with pathologic myopia were not simply elongated but were also deformed and did not retain a spherical shape. Using 3-D

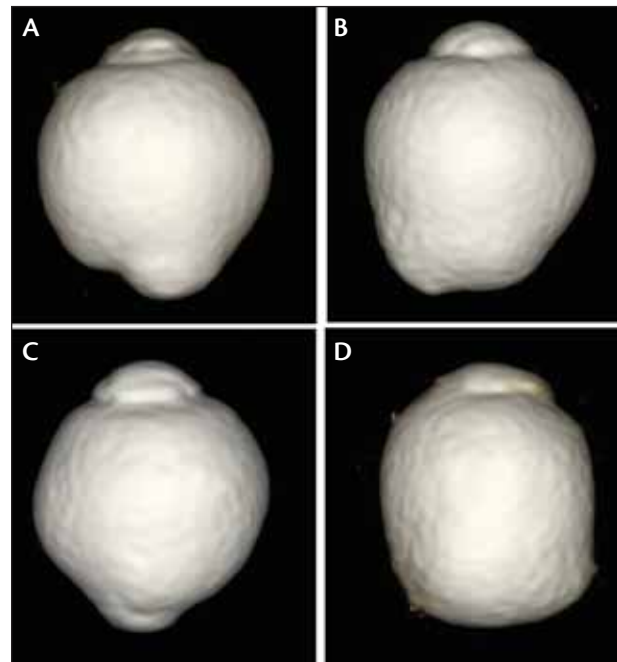


Figure 1. Classification of ocular shape based on 3-D MRI viewed from the inferior. In the nasally distorted type (A), the nasal half and temporal half of the posterior segment are asymmetrical, and the nasal half is more protruded posteriorly than the temporal half. In the temporally distorted type (B), the nasal half and temporal half of the posterior segment are asymmetrical, and the temporal half is more protruded than the nasal half. In the cylindrical type (C), the nasal half and temporal half of the posterior segment are symmetrical, and the radius of curvatures of the nasal half and temporal half are equally steeper than a circle. In the barrel type (D), the nasal half and temporal half of the posterior segment are symmetrical, and the radius of curvatures of the nasal half and temporal half are equally flatter than a circle.

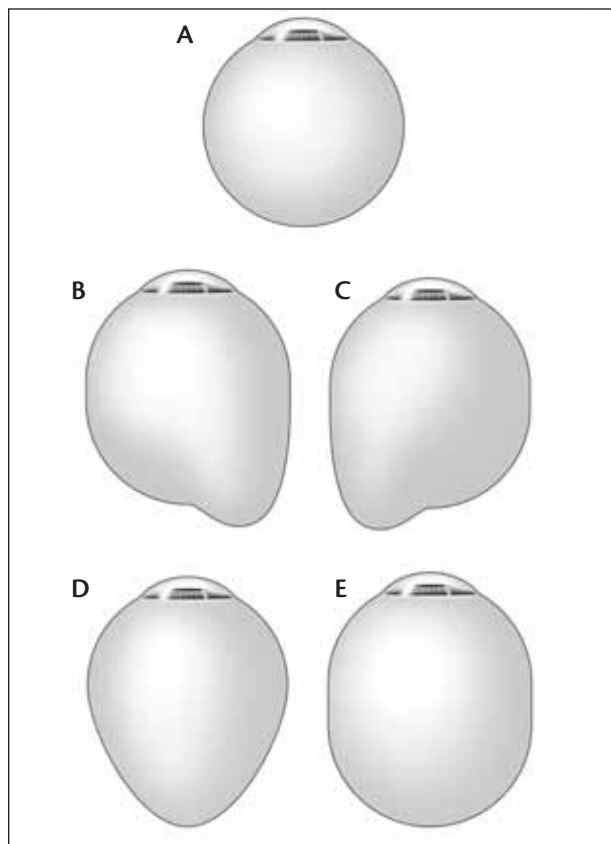


Figure 2. Cartoon showing spherical shape of emmetropic eyes (A) and four distinct ocular shapes (nasally distorted [B], temporally distorted [C], cylinder [D], barrel [E]) observed from inferior in a right eye with pathologic myopia.

magnetic resonance imaging (MRI) analysis, Moriyama et al⁸ recently reported that the globes of highly myopic patients clearly demonstrated distinctly different types of shapes in pathologic myopia (Figures 1 and 2); eyes with pathologic myopia are more prolate in shape than normal eyes, with posterior protrusions. Among the four different types of eye shape seen, visual field defects that were not explained by fundus lesions were significantly more frequently observed in eyes with a temporally dislocated shape (Figure 3).⁸

Posterior staphylomas are not common in children with pathologic myopia,⁹ and the incidence of staphyloma is significantly higher in older patients (96.7% in patients 50 years or older) than in younger patients (80.7% in patients younger than 50 years).¹⁰ Thus, staphyloma is considered to be a phenomenon of aging. Posterior staphyloma has been classified into 10 types according to the area of protrusion.¹¹ With increasing age, the incidence and height of staphyloma increase and the morphologic features worsen.¹⁰ This change is considered to accelerate the stretching and thinning of the posterior fundus and could cause the development of various macular lesions specific to pathologic myopia. Myopic maculopathies include diffuse chorioretinal atrophy, patchy chorioretinal atrophy, lacquer cracks, and myopic CNV (Figure 4).¹² In addition to these ophthalmoscopically detected lesions, Takano and Kishi¹³ identified the novel pathology MRS using OCT.

MYOPIC CNV

Pathologic myopia is the most common cause of macular CNV in patients younger than 50 years.¹⁴ Myopic CNV

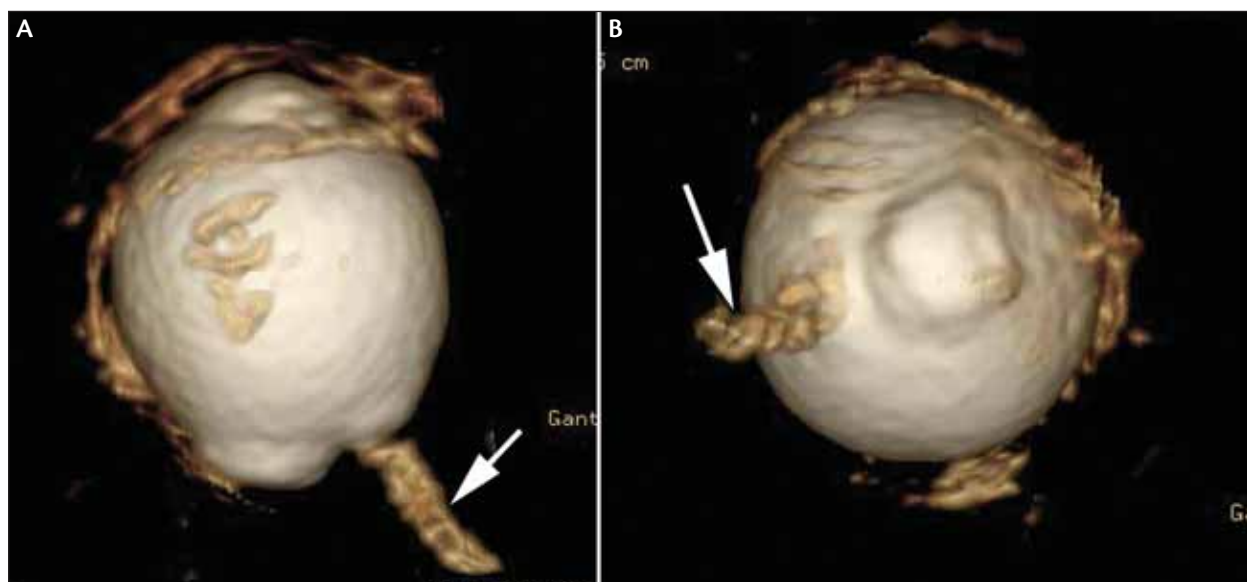


Figure 3. Representative images of 3-D MRI showing the site of attachment of the optic nerve to the eye (arrows). Optic nerve is attached nasal to the edge of posterior protrusion. Inferior (A) and posterior (B) view of 3-D MRI image of right eye.



Figure 4. Representative fundus photographs of different types of myopic retinopathies according to Tokoro.⁸ Tessellated fundus (A). Diffuse chorioretinal atrophy (B); the posterior fundus appears yellowish white. Patchy chorioretinal atrophy (C); a grayish-white, well-defined lesion (arrow) can be seen. Macular hemorrhage (D); a fibrovascular membrane (arrow) is observed within the area of hemorrhage. Lacquer cracks (E); many yellowish lacquer cracks are observed.

is one of the most frequent complications that reduces central vision in patients with pathologic myopia. Myopic CNV develops in 10% of highly myopic patients,¹⁵ and 30% of the patients who have CNV in one eye eventually develop CNV in the other eye. Patchy chorioretinal atrophy and lacquer cracks near the central fovea are considered predisposing findings for CNV development.¹⁵

Myopic CNV is almost always classic CNV, and CNV lesions tend to be smaller than those seen in age-related macular degeneration (AMD). The activity of myopic CNV is usually less than in AMD-related CNV and regresses spontaneously without treatment. However, the main problem in myopic CNV is that distinct chorioretinal atrophy gradually develops and enlarges around the scarred CNV, disturbing vision progressively over the long term.¹⁶ The prognosis of myopic CNV is poor; 89% of patients have a best corrected visual acuity (BCVA) of 0.1 or less at 5 years after the onset of CNV.¹⁶

The principal advance in the treatment of myopic CNV has been the use of anti-VEGF drugs.¹⁷ Intravitreal injection of bevacizumab (Avastin, Genentech)¹⁸⁻²² or ranibizumab (Lucentis, Genentech)²³⁻²⁶ has been shown to improve or maintain baseline visual acuity. Juxtafoveal CNV tends to disappear after successful anti-VEGF therapy and does not develop chorioretinal atrophy over the long term (Figure 5).²⁷ Based on these promising results, two multicenter clinical trials investigating the effectiveness of ranibizumab or aflibercept ophthalmic solution (Eylea, formerly VEGF Trap- Eye, Regeneron Pharmaceuticals, Inc./Bayer HealthCare) are currently ongoing in Asia.

MYOPIC MACULAR RETINOSCHISIS

Eyes with high myopia have a higher incidence of a macular hole retinal detachment (MHRD) than emmetropic eyes. This condition is commonly seen in Asians, often in women aged 50 to 60 years. MHRD almost always develops in eyes with a posterior staphyloma, particularly in eyes with a deep staphyloma. Various surgical procedures, including vitrectomy and macular scleral buckling, are used to repair MHRD. Although retinal reattachment is achieved in most cases,²⁸ the rate of closure of the macular

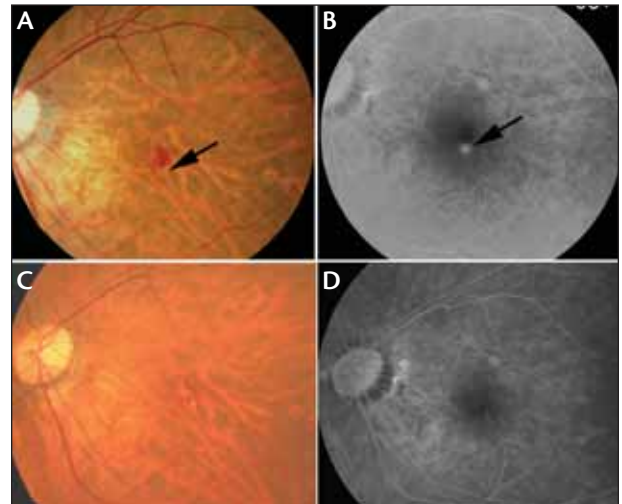


Figure 5. Disappearance of myopic CNV after intravitreal injection of bevacizumab: Left fundus (A) shows grayish fibrovascular membrane suggestive of CNV (arrow). Fluorescein fundus angiogram (B) shows a dye leakage from CNV (arrow). Two years after a single injection, no CNV is observed (C). Fluorescein angiogram shows no abnormalities (D).

hole is not high in highly myopic eyes.

MRS, a relatively new category of disease, is reported to precede the formation of macular hole in eyes with pathologic myopia,^{13,29-31} and myopic MRS progresses to retinal detachment in 21% to 62% of eyes.^{29,30,32} Vitrectomy is recommended to treat MRS; surgery is indicated when visual acuity is reduced or when progression toward MHRD is strongly suspected.

The pathogenesis of myopic MRS has been attributed to a forceful traction on the retina by residual posterior vitreous cortex or the internal limiting membrane (ILM), the basement membrane of the retinal Mueller glial cells, retinal vessels, or a combination of these. The presence of paravascular retinal abnormalities might be important in the analysis of the pathogenesis of macular hole and MRS in eyes with pathological myopia, and OCT has been shown to be a useful method to detect these abnormalities. In multiple OCT scans of the entire posterior fundus, 83% of eyes with MRS

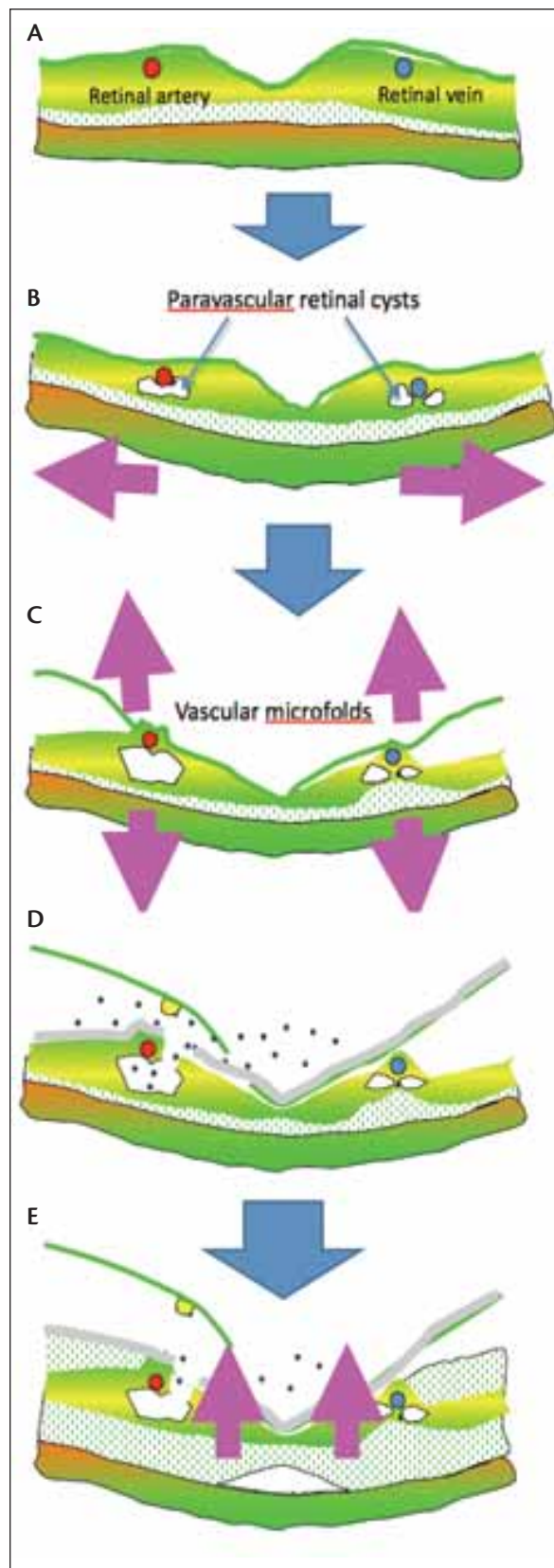


Figure 6. Cartoons showing hypothetical mechanism of developing myopic macular retinoschisis (MRS). Cross-sectional image of normal macula (A). In response to uniform expansion of the globe due to increased axial length, paravascular retinal cysts develop along the retinal vessels because of the difference of expansion between retinal vessels and other parts of the retina (B). Secondary to posterior staphyloma, retinal vascular microfolds develop and paravascular retinal cysts enlarge and fuse with one another (C). With the development of posterior vitreous detachment, the inner wall of paravascular retinal cysts is pulled away, and inner lamellar holes develop (D). Through the paravascular lamellar holes, the glial cells migrate and produce collagen, enhancing the proliferative and contractile property of the inner internal limiting membrane (ILM) (E). Due to increased contractility of ILM, MRS finally develops.

had paravascular lamellar holes.³³ It has been suggested that glial cells such as astrocytes, which exist abundantly around the retinal vessels, might migrate through the paravascular lamellar holes and inner retina onto the surface of the retina. The migrated cells might then produce collagen fibers and facilitate a proliferative and contractile response of the ILM. The rigid ILM would prevent the retina from stretching to adjust to the contour of the posterior staphyloma, and this may play a role in the development of MRS (Figure 6).^{33,34}

CONCLUSION

The developmental mechanisms of many lesions specific to pathologic myopia have been clarified through OCT. Additionally, novel treatments such as anti-VEGF therapy and vitrectomy have improved visual outcomes in patients with pathologic myopia. We may expect that, based on the results of experimental myopia studies and human gene analyses, therapies to prevent vision-threatening complications due to posterior staphyloma formation or axial length increase will be developed in the future.

In addition to macular lesions, optic nerve damage is another problem in eyes with pathologic myopia. Highly myopic patients with optic nerve damage will eventually become totally blind. Due to its features and mechanisms, my colleagues and I propose that this condition be called myopic optic neuropathy. It is anticipated that preventive therapies against axial length increase and posterior staphyloma formation will be developed and diagnostic and treatment strategies for myopic optic neuropathy will be established in the future. ■

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