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Late-onset Hypotony Maculopathy After Trabeculectomy in a Highly Myopic Patient With Juvenile Open-angle Glaucoma

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Abstract: Hypotony maculopathy is a sight-threatening complication after trabeculectomy. We report on a 34-year-old man with juvenile open-angle glaucoma and high myopia, who developed hypotony maculopathy 14 years after trabeculectomy without bleb leak. This represents the longest known period from trabeculectomy to the development of hypotony maculopathy without bleb leak. The possible mechanisms for the development of late-onset hypotony maculopathy in the highly myopic patient are progressive scleral thinning, reduced scleral rigidity, and scleral morphologic change with aging. These changes might weaken the biomechanical properties of sclera and then contribute to the collapse of the scleral wall during hypotony. This case serves as a reminder that hypotony maculopathy can happen up to 14 years after tabeculectomy even without bleb leak and hypotony should be avoided after trabeculectomy in highly myopic patients with juvenile open-angle glaucoma.

Key Word: hypotony maculopathy, trabeculectomy, high myopia, sclera

(*J Glaucoma* 2017;26:e137–e141)

Ocular hypotony can be categorized into 2 types: statistical and clinical hypotony.[1] Statistical hypotony is defined as having intraocular pressure (IOP) < 6.5 mm Hg or 3 SDs below the mean, whereas clinical hypotony is defined as having IOP too low to maintain the shape of the eyeball, resulting in the structural and functional changes named hypotony maculopathy.[1,2]

Hypotony maculopathy is a sight-threatening complication after glaucoma-filtering surgery with a reported incidence rate between 1.3% and 18%.[3,4] Gass[5] discussed hypotony maculopathy, which is caused by the sclera falling inward during hypotony, accompanied by secondary redundant folds of the retina and choroid over the posterior pole. Retinal foldings radiating from the fovea are created by shrinkage and thickening of the sclera, which lead to compromised visual acuity. The level of IOP alone does not determine who will develop hypotony maculopathy. Other factors such as biomechanical properties of the sclera, which are related to scleral thickness, scleral rigidity, and structural variations in the sclera are also important in the pathogenesis of hypotony maculopathy.[6] The compromised biomechanical properties of the sclera may be primarily responsible for causing the eyeball to collapse inward during hypotony and subsequent hypotony maculopathy.[7]

The worldwide usage of antifibrotic agents during trabeculectomy is leading to increased risk of overfiltration, which may increase the incidence of hypotony maculopathy.[8] Besides the application of antifibrotic agent, male sex, high myopia, young age, and patients receiving primary filtering surgery have also been associated with an increased risk of hypotony maculopathy.[9,10] After trabeculectomy, hypotony maculopathy can develop postoperatively or several years later, with the longest interval from trabeculectomy to the development of hypotony maculopathy ever reported being 80 months.[11] Bleb leak is an important risk factor associated with late-onset hypotony maculopathy.[12] We report on a patient with juvenile open-angle glaucoma and high myopia, who had almost all mentioned risk factors for hypotony maculopathy except bleb leak, developed hypotony maculopathy 14 years after trabeculectomy. The possible mechanisms of late-onset hypotony maculopathy are discussed.

CASE REPORT

A 34-year-old man had a history of juvenile open-angle glaucoma on both eyes since age 19. Poor IOP control as high as 25 mm Hg in the right eye (RE) and 29 mm Hg in the left eye (LE) was noted on maximal antiglaucoma medications. He underwent trabeculectomies with mitomycin C (0.2 mg/mL applied for 2 min)

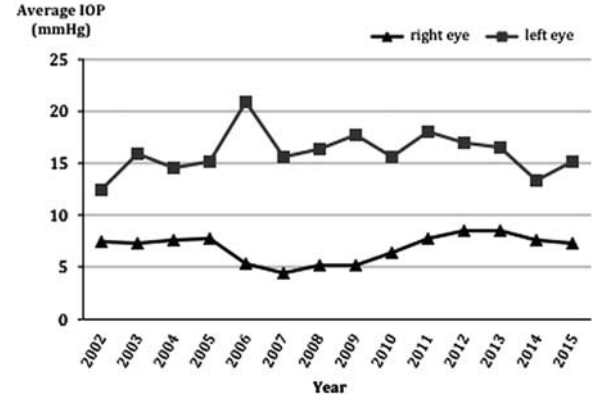

FIGURE 1. Annual average intraocular pressure (IOP) after trabeculectomy.

Received for publication February 16, 2016; accepted June 8, 2016.
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Disclosure: The authors declare no conflict of interest.
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DOI: 10.1097/IJG.0000000000000485

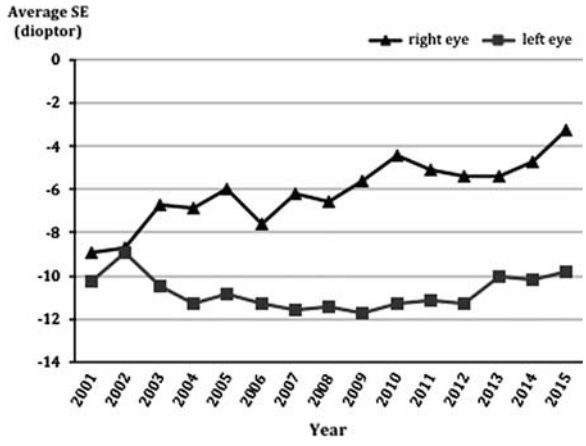

FIGURE 2. Annual average spherical equivalent (SE) before and after trebeculectomy. The right eye showed a trend of hyperopic shift, while the SE of the left eye is steady.

in January 2001 and August 2001 on the LE and RE, respectively. The preoperative spherical equivalent (SE) refraction was −9.375 D with best-corrected visual acuity (BCVA) of 20/25 on the RE and SE was −9.875 D with BCVA of 20/50 on the LE. During the 14 years after trabeculectomy, the IOPs of the RE ranged from 3 to 10 mm Hg without any antiglaucoma medication and the IOPs of the LE ranged from 11 to 21 mm Hg under antiglaucoma medication (Fig. 1). A trend of hyperopic shift of + 5.7 D of SE on the RE was noted during the 14 years and the SE on the LE was steady (Fig. 2). The results of visual field examinations indicated no progression of either eye during the follow-up period.

The patient experienced a decrease in BCVA of RE, from 20/25 to 20/200 in March 2015. History of trauma was denied. The IOP of RE was 7 mm Hg in March 2015 and the IOPs of RE in 2014 were 8, 8, and 7 mm Hg. Under slit-lamp examination, anterior chamber was found to be deep and without reaction, and no corneal striae were noted. The thin avascular cystic bleb on the RE did not reveal bleb leak with negative Seidel test. On funduscopic examination, irregular foldings of the retina on the RE were noted, radiating outward from the fovea in a stellate pattern at the macular area, associated with optic disc swelling surrounded by tortuous retinal vessels and engorged retinal veins (Fig. 3). Spectral-domain optical coherence tomography (Cirrus HD-OCT; Carl Zeiss Meditec, Dublin, CA) demonstrated the chorioretinal foldings in the macula (Fig. 4) and the thickening of the retina at the macular area in the RE (Fig. 5). The peripapillary retinal nerve fiber layer of the RE thickened consistently with the thickening of the neuroretinal rim (Fig. 6). All clinical features were consistent with hypotony maculopathy of the RE. After treating the RE with topical steroids, which consisted of betamethasone eyedrop 0.1% 4 times a day and Tobradex ointment(tobramycin 0.3% and dethamethasone 0.1%) before bedtime, IOPs ranged from 6 to 8 mm Hg and the improvement of BCVA from 20/200 to 20/50 on the RE were noted in the following 4 months. The persistence of retinal foldings at the macular area on RE was confirmed by optical coherence tomography in July 2015.

DISCUSSION

The level of IOP and the biomechanical properties of the sclera primarily determine the development of hypotony maculopathy. The biomechanical properties of the sclera are mainly regulated by the specialized dense irregular extracellular matrix (ECM) composed of collagen fibrils embedded in a matrix of proteoglycans. In human eyes, scleral tissue contains approximately 90% collagen by dry weight.[13] The collagen plays structural roles and contributes to mechanical properties, organization, and shape of tissues. Collagen fibrillogenesis, fibril orientation, size, and arrangement are mainly influenced by proteoglycans. The proteoglycans are composed of core proteins with at least one end attached to a glycosaminoglycan (GAG) side chain and this side chain supplies negative charge to mediate interaction with collagen.[14] The core proteins of the proteoglycans are classified into the large core protein with resilience, aggrecan, and the small core protein, including biglycan and decorin.[15]

With aging, the sclera undergoes a progressive degeneration of collagen fiber, a loss of GAG, and scleral dehydration, which are associated with an increase in scleral density and an increase in scleral rigidity.[16] On the contrary, the scleral rigidity is relatively less in young people. Myopic eyes have been found to be associated with thinner sclera, particularly at the posterior pole of the eye due to physical loss of scleral ECM and altered ECM content. Previous studies have shown that scleral thinning is

FIGURE 3. Fundus photography of the right eye. A, Glaucomatous optic disc change with normal appearance of macula in November 2014 before the development of hypotony maculopathy. B, Irregular retinal folds radiating outward from the fovea and optic disc swelling, surrounded by tortuous retinal vessels in March 2015.

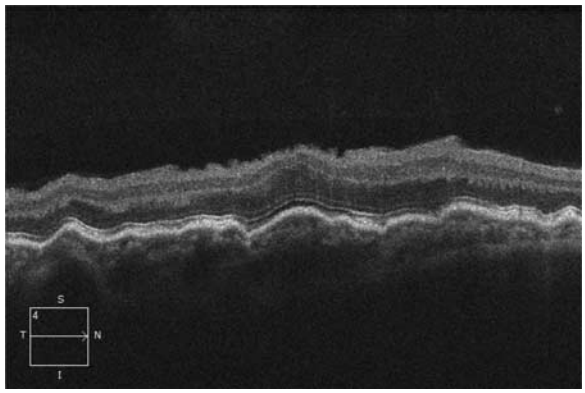

FIGURE 4. Optical coherence tomography using Cirrus HD-OCT showed chorioretinal foldings in the macular area of the right eye in March 2015.

related to a general loss of collagen and proteoglycan (especially aggrecan), a narrowing and dissociation of the collagen fiber bundles, and a reduction in collagen fibril diameter.[17] The reduction of scleral collagen fibril diameter in highly myopic eyes can result in reduced rigidity of the sclera.[18] Therefore, in young myopic eyes, the sclera is thinner with less rigidity at the posterior pole and the changes are associated with weaker biochemical properties, which might make the sclera vulnerable to collapse during hypotony.[19]

Although the axial length (AL) of the eye was found to reach adult length by the age of 13 years, AL might continue to increase after adolescence in highly myopic patients, leading to the stretching and thinning of the posterior ocular tissues and further pathologic changes.[20,21] Besides the continuing elongation of the eyeball with aging, the morphology of posterior staphyloma also changes as the patient ages.[22] Both structural changes might indicate that the sclera in highly myopic eyes is mechanically weakened with aging.[18] Other than the anatomic changes, the scleral ECM remodeling in aging myopic eyes has also been documented, including progressive reduction in scleral collagen and GAG content and reduction of fibril diameter. All these changes in aging myopic eyes contribute to scleral thinning with less rigidity.[15,21] In summary, the progressive thinning of sclera and reduction of scleral rigidity are observed in aging myopic eyes and these changes might result in progressively weakened biomechanical properties of sclera, which make sclera more likely to collapse under the condition of hypotony.[18,19]

Hyphema, flat anterior chamber, and bleb leak are the most frequent early-onset complications within the first 3 months after trabeculectomy.[23,24] Late bleb leak, which is noted >3 months after trabeculectomy, contributes to the most late-onset hypotony maculopathy. Young age and application of antifibrotic agent are risk factors for bleb leak and our patient had both these risk factors.[12,25] However, there was no bleb leak or IOP change in our patient during the period of hypotony maculopathy, which implies that other factors other than the level of IOP contribute to the development of late-onset hypotony maculopathy. Furthermore, early hypotony of RE was noted after trabeculectomy, but hypontony maculopathy did not develop until 14 years later. The postulated mechanism is that the sclera of RE was biomechanically strong enough not to collapse during hypotony in the early period after trabeculectomy. After 14 years, the biomechanical

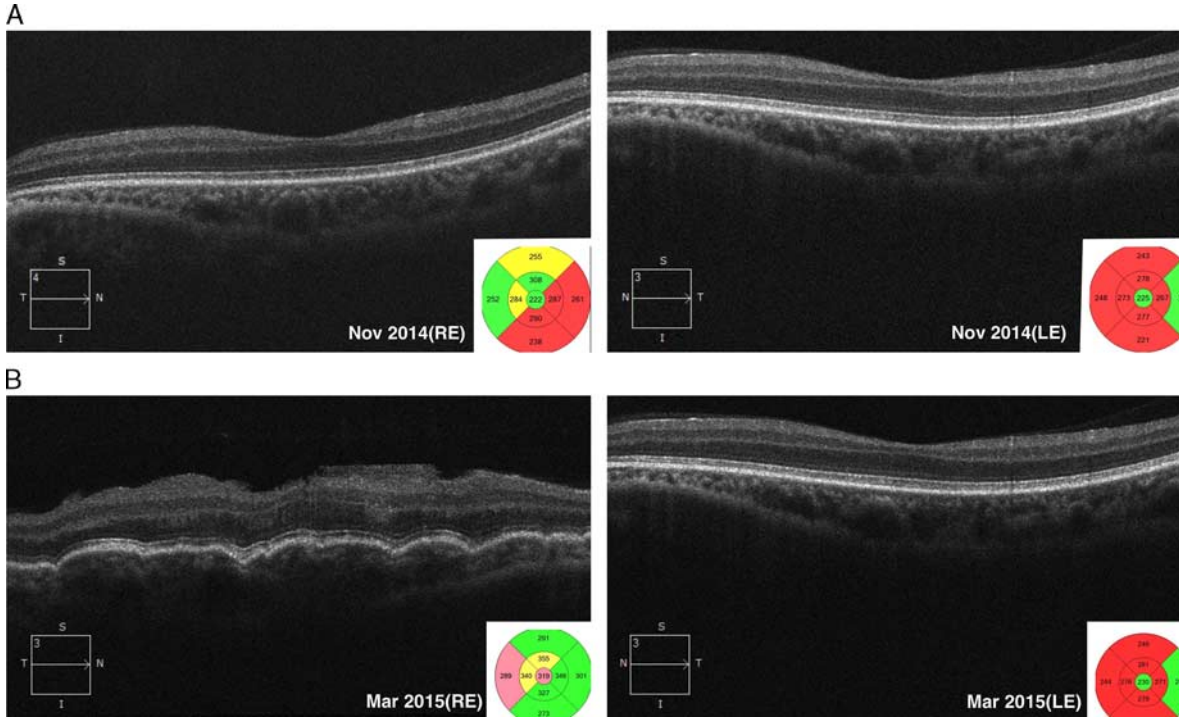

FIGURE 5. Macular scan using Cirrus HD-OCT of both eyes. A, Retinal thickness at the macular area in November 2014 before the development of hypotony maculopathy. B, Thickening of the retina at the macular area was noted on the right eye in March 2015.

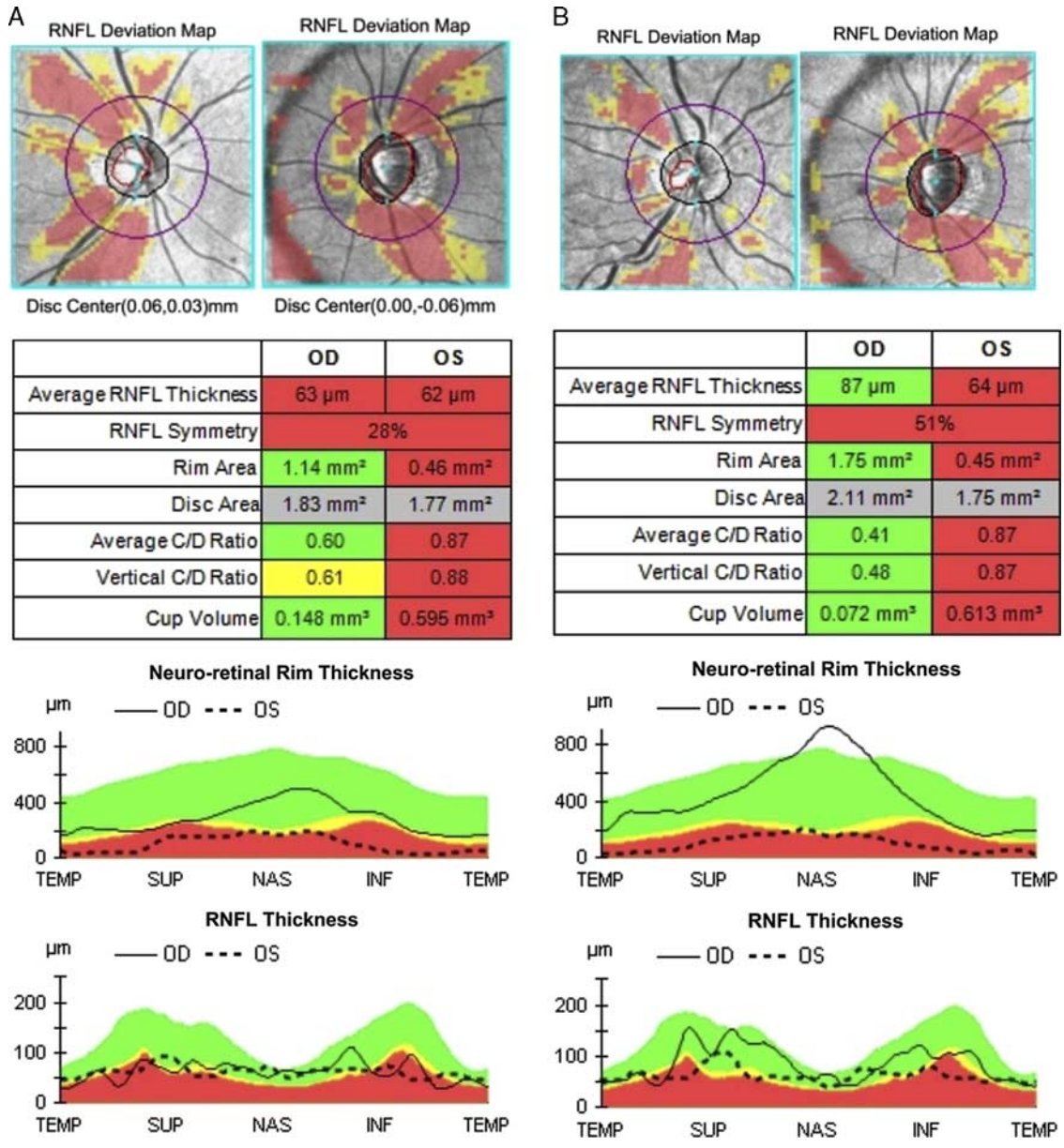

FIGURE 6. Optic nerve head and retinal nerve fiber layer (RNFL) scan using Cirrus HD-OCT of both eyes. A, Peripapillary RNFL and neuroretinal rim thinning of both eyes were confirmed in November 2014 before the development of hypotony maculopathy. B, Peripapillary RNFL and neuroretinal rim thickening of the right eye were noted in March 2015.

properties of the aging myopic sclera had became too weak to maintain the shape of the eyeball during hypotony and therefore subsequently developed hypotony maculopathy.

Matsumoto et al[26] demonstrated that the average AL reduction at 4 weeks after trabeculectomy was 0.38 mm in eyes with hypotony only and 1.59 mm in eyes with hypotony maculopathy. Young age (below 57 y at survey) was associated with larger reduction of AL. The larger AL shortening in eyes with hypotony maculopathy may be due to choroidal thickening and scleral wall shrinkage.[26] As the reported maximal magnitude of choroidal thickening following trabeculectomy is approximately 100 µm, the scleral wall shrinkage might be responsible for most of the AL shortening in the eyes with hypotony maculopathy.[27] Although the AL was not measured in our patient, it can be surmised that the progressive hyperopic shift of 5.7 D in the RE during the 14 years after trabeculectomy indicates a progressive shortening of the AL by 1.9 mm, based on 1 mm change in AL corresponding to a 3D change in refractive power.[28] It might imply that the scleral wall has been progressively shrinking due to the progressively weakening biomechanical properties of the sclera in this young myopic patient. In summary, the possible mechanisms of late-onset hypotony maculopathy without bleb leak in our patient could include progressive scleral thinning, reduced scleral rigidity, and scleral morphology change, which result in the weakening of the biomechanical properties of the sclera in aging myopic eyes. Once the dynamic balance between the sclera and IOP is broken, the

scleral wall could collapse inward during hypotony, leading to hypotony maculopathy.[29]

In conclusion, hypotony maculopathy can happen 14 years after trabeculectomy in a highly myopic patient with juvenile open-angle glaucoma, even without bleb leak. The weakened biomechanical properties of the sclera, which are related to progressive scleral thinning, reduced scleral rigidity, and scleral morphology change, are hypothesized as main factors in the pathogenesis of late-onset hypotony maculopathy in aging highly myopic eyes. In highly myopic patients with juvenile open-angle glaucoma, hypotony should be avoided after trabeculectomy.

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