subretinal neovascularization in 5.2%. Tokoro[17] examined 1106 highly myopic eyes of 653 patients. Diffuse chorioretinal atrophy was observed in 696 eyes (62.8%), patchy chorioretinal atrophy in 144 eyes (13.1%), and choroidal neovascularization in 128 eyes (11.6%). Steidl et al.[6] examined 116 eyes of 58 patients with myopic refractions of -3 D or more. Ages ranged from 12 to 90 years (mean; 42.5 years). Posterior staphyloma formation was observed in 75.9%, and evidence of choroidal neovascular membranes in 22.4%. Grossniklaus[16] and Gozum[14] reported that the prevalence of chorioretinal atrophy was 11.4% and 6.1%, respectively (Table 1). However, the study by Grossniklaus[16] was histopathological study using cadaver eyes, and Gozum[14] used different classification for myopic fundus changes from ours; lacquer cracks were not included in chorioretinal atrophy in their study. Using the same classification as in the present study, we calculated that in the report by Steidl et al.[6] grade 1 chorioretinal atrophy was observed in 37.1%, grade 2 in 12.9%, grade 3 in 18.1%, and grade 4 in 1.7% in their patients.

In our study, posterior staphyloma was detected in only one eye (1.3%), which was markedly lower than that reported in a previous study including patients from all ages. Chorioretinal atrophy was observed in 16.3% of our patients. All of these eyes had grade 1 atrophy only, and no patients demonstrated more severe

atrophy than grade 2, in contrast to the previous study.[6] Also, choroidal neovascularization was never detected in our patients. These findings suggest that posterior staphyloma or severe chorioretinal atrophy is less common in children with high myopia.

It is difficult to simply compare the data in the present study with those from previous reports. Even among the previous studies, ages and myopic degree of the subjects differed considerably, and the prevalence data obtained from these patients are also inconsistent. Despite the inconsistency of the data from the previous studies, however, our results indicate that myopic fundus changes, especially posterior staphyloma, are uncommon among children.

Why the prevalence of posterior staphyloma is low and the severity of chorioretinal atrophy is mild in children? One reason might be that in children, axial length is not as long as in adult highly myopic patients. The difference of axial length might also explain the low prevalence of myopic fundus changes in children. Even when we limit the patients to those with an axial length longer than 25.5 mm, however the prevalence of posterior staphyloma or severe chorioretinal atrophy is rather low. Another explanation might be that, rather than acute stretching of the eyeball, a longer period is necessary for the development of myopic fundus changes.

Data collected during the long-term development of myopia in experimental animals suggests that although the sclera thins rapidly and alters its material properties during the early stages, shifts in collagen fibril diameter are not apparent until later in myopia development.[18] Also, in experimental myopic eyes induced in chicks 2 weeks after visual deprivation, staphyloma formation or the development of chorioretinal atrophy does not occur, whereas acute rupture of Bruch's membrane sometimes occurs.[19] These findings suggest that not only simple mechanical stretching but also long-term, continual mechanical stretching or aging might be necessary for the development of myopic fundus changes. It would be useful to examine the time course of the development of myopic fundus changes in the same child patient during a long-term follow-up.

In contrast, the prevalence of peripapillary crescent formation was 33.8% in our patients, which is similar to previous reports (Table 1), although the size of the crescent was relatively small (mean; 0.46 DA). This might suggest that peripapillary crescent itself can develop due to simple mechanical stretching around the optic disc, however a longer period or an aging effect might facilitate the later enlargement of the peripapillary crescent.

In summary, we describe the characteristics and prevalence of myopic fundus

changes in children with high myopia. The results demonstrated that myopic fundus changes are uncommon or less severe in children, which indicates that the aging effect might be important for the development of myopic fundus changes rather than just simple stretching of the eyeball.

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A. Figure legends

Figure 1. The age distribution among the patients.

Figure 2. The distribution of the refractive errors among patients.

Figure 3. The distribution of the axial length measurements among patients.

Figure 4. Fundus photographs of a 6-year-old girl with chorioretinal atrophy. A. There was yellowish chorioretinal atrophy around the optic disc in the right fundus. Best-corrected visual acuity was 0.4, the refractive error was -5.75 D, and axial length was 24.4 mm. B. There was similar chorioretinal atrophy around the optic disc in the left fundus. Best-corrected visual acuity was 0.2, the refractive error was -7.75 D, and axial length was 25.2 mm.

Figure 5. Fundus photographs of a 7-year-old girl with posterior staphyloma. A. There was posterior staphyloma formation nasal to the optic disc in the right fundus. Best-corrected visual acuity was 0.1, the refractive error was -16.5 D, and axial length was 25.5 mm. B. The left fundus had a normal appearance. Best-corrected visual acuity was 1.5, the refractive error was 0.5 D, and axial length was 22.3 mm.

Dilated choroidal artery in the macula causes secondary RPE atrophy after a long-term in a highly myopic patient.

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Running title: RPE atrophy along choroidal artery in high myopia

Abstract

A highly myopic patient was examined by ICG angiography, and a markedly bented and tortuous choroidal artery was delineated in the macula of his left fundus. His corrected visual acuity was 20/20 in both eyes, and he had no visual symptoms. At 10 years after the initial examination, RPE atrophy develops above this dilated choroidal artery. Optical coherence tomography demonstrated that RPE was stretched above the marked dilation of choroidal artery beneath the RPE. As a mechanism of RPE atrophy development, mechanical stretch of RPE by abnormally dilated choroidal artery might be considered. It should also be noted that abnormality of choroidal artery may become a cause of RPE atrophy in the macula.

Keywords

High myopia, choroidal artery, retinal pigment epithelium, SLO microperimetry, indocyanine green angiography

Introduction

Previous studies[1-5] using corrosion cast technique as well as fluorescein fundus angiography have demonstrated that in the choroid, short posterior ciliary arteries divide up into a great number of small branches and perforate the sclera in the macular region. They usually run radially from the posterior pole out to the periphery in order to supply the choroid. Choroidal blood then drains out through six or eight vortex veins located in the equator, then penetrates the sclera and exits the eyeball. The recent advancement of ICG angiography has enabled us dynamic observations of choroidal vascular structure in human eyes in a real time. Using ICG angiography, variations of structural pattern of choroidal venous systems have been demonstrated in various retinochoroidal disorders,[6,7] in highly myopic eyes,[8] and in normal aging.[9] However, regarding choroidal artery in the posterior pole, no apparent abnormalities than cilio-retinal artery have been detected even by using ICG angiography so far.

Here we report a case with a marked tortuosisty of choroidal artery in the macula identified by ICG angiography in highly myopic fundus. RPE atrophy secondarily developed above this choroidal artery in a long-term in this patient.

Case report

A 55-year-old man was referred to us on May 14, 1993 for evaluation of myopic

fundus change. His corrected visual acuity was 20/20 in both eyes. His refractive errors were OD -12.0 D sphere and OS -11.0 D sphere, and axial length measurements were OD 29.4 mm and OS 28.8 mm. He had no visual symptoms, and he had no general diseases which might affect ocular circulation like hypertension or diabetes mellitus.

Fundus examination at the initial examination showed tessellated fundus in both eyes (Fig. 1A & 1B), however, there were no apparent abnormalities in the macula ophthalmoscopically (Fig. 1C) and by using fluorescein fundus angiography (Fig. 1D). Indocyanine green (ICG) angiography was performed on the same day. In the early phase of ICG angiography, just after short posterior ciliary artery penetrates into the choroid just beneath the macula, choroid artery markedly bends and dilated and becomes tortuous like an inverse "U" character (Fig. 2A, arrow). After bending, sludging-like blood flow is observed in this choroidal artery (Fig. 2). This dilated choroidal artery showed consistent bright fluorescence by ICG angiography during the entire angiographic phase (Fig. 2B). The retina above this dilated choroidal artery seemed a little elevated by stereoscopic observations using +90 D lens and slit lamp.

He was followed-up once a year after initial examination. Until 9 years after the initial visit, no remarkable change was detected in the macular area of his right fundus ophthalmoscopically (Fig. 3A, 3B). However, at 10 years after the initial visit, retinal pigment

epithelium (RPE) atrophy accompanying slight pigmentation appeared above the tortuous choroidal artery in the macula (Fig. 4A). Fluorescein fundus angiography revealed the granular hyperfluorescence caused by window defect as well as blocked fluorescence due to pigmentation (Fig. 4B). Choroidal filling defect was not apparent in the early angiographic phase. ICG angiography delineated dilated, bented, and tortuous choroidal artery in the macula like that seen at the initial visit, and blocked fluorescence caused by pigmentation appeared above this choroidal artery (Fig. 4C & 4D). Optical coherence tomography (OCT) performed on that day revealed that RPE was pushed, elevated and stretched because of marked dilation of choroidal artery beneath RPE (Fig. 5). Scanning laser ophthalmoscopy (SLO) microperimetry demonstrated relative scotoma (30 dB) at the site of RPE atrophy (Fig. 6). His visual acuity in the left eye was unchanged (20/20) throughout the observation period, and he complained no visual symptoms related RPE atrophy.

Discussion

To our knowledge, this is the first report describing the abnormally dilated, bented choroidal artery in the macula. This patient had no general diseases which might affect ocular circulation like hypertension or diabetes. Also, no other abnormalities of choroidal vascular system were observed in other areas of his left fundus and in his entire right fundus. The angiographic findings of this choroidal artery did not change throughout the

follow-up period of 10 years. It is unknown whether this abnormal choroidal artery is congenital or secondary phenomenon, also, it is unclear whether this abonormality of choroidal artery is related to high myopia in this patient (axial length; OS 28.8 mm). It has been reported that abnormalities of choroidal veins are often detected in highly myopic eyes. Ohno-Matsui et al. reported that about 1/4 of highly myopic eyes had choroidal blood flow through posterior routes (like macular vortex vein).[6] However, no abnormalities of choroidal artery related with high myopia development have never been reported. Although we have performed ICG angiography on more than 600 highly myopic patients in our high myopia clinic, we did not detect this kind of abnormality of choroidal artery in any other myopic subjects.

In this patient, RPE just above this choroidal artery has become atrophic in a long-term. As a mechanism of RPE atrophy development in this case, we consider two possibilities. One is that RPE atrophy develops secondary to choroidal circulatory defect. ICG angiography demonstrated that sludging-like phenomenon of blood flow observed in this choroidal artery after marked bending in the macula, also bright fluorescence remained in this dilated choroidal artery in the late angiographic phase. These ICG angiographic findings suggest the existence of stagnated and disturbed blood flow within this choroidal artery. Choriocapillaris filling defect was not apparent around the area of this choroidal artery,

however, in eyes with high myopia it is sometimes difficult to detect a mild change of choriocapillaris because of simultaneous thinning of RPE and choroid. Choriocapillaris in the posterior pole has lobular pattern and there are rich collaterals between lobules.[1] Therefore, it seems difficult to explain the RPE atrophy compatible with the course of dilated choroidal artery seen in this patient only by choroidal circulatory disturbance.

The other possibility of RPE atrophy development in this patient is mechanical stretch of RPE. Elevation of the retina above this choroidal artery was seen by stereoscopic observation using slit lamp, and OCT examination revealed that RPE was elevated and stretched above the dilated choroidal artery (Fig. 5). Some in vitro studies have reported that mechanical stress induced apoptosis in variety kinds of cells.[7,10,11] It is also known that RPE above the choroidal mass (like choroidal nevus) becomes atrophic ophthalmoscopically.[12] From these facts, we consider that RPE atrophy developed in this patient might have been caused by mechanical stretch and pressure by dilated choroidal artery beneath the RPE. Because RPE is somewhat damaged in highly myopic eyes,[13,14] the fact that this patient was highly myopic may have facilitated the development and progression of RPE atrophy.

Although the patient has not complained any visual symptoms related RPE atrophy and visual acuity has been well maintained, SLO microperimetry demonstrated relative scotoma corresponding to the area of RPE atrophy. A careful follow-up regarding

progression of retinal sensitivity and visual decrease might be necessary.

In summary, we report a rare case who RPE atrophy developed in a long-term above the bented and dilated choroidal artery in the macula of highly myopic eye. It should be noted that abnormality of choroidal artery may become a cause of RPE atrophy in the macula.

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Figure legends

Figure 1. Fundus photographs at the initial examination. A: Right fundus, B: Left fundus, C: Magnified photograph of the left fundus. No abnormal findings are observed in the macular area. D: Fluorescein fundus angiogram at the initial examination. No abnormal findings are seen in the macular area.

Figure 2. Indocyanine green (ICG) angiogram at the initial examination. A: 13 seconds after dye injection, a bented and tortuous choroidal artery is detected in the macula (arrow). Sludging like phenomenon is observed in this choroidal artery after marked bending. B: 14 minutes after dye injection, tortuous choroidal artery in the macula still shows bright fluorescence.

Figure 3. Time-course of macular findings in this patient. A: 4 years after the initial visit, B: 9 years after the initial visit. No abnormal findings are observed in the macula.

Figure 4. 10 years after the initial visit. A: Left fundus. Slight pigmentation is observed along tortuous choroidal artery in the macula. B: Fluorescein fundus angiogram of the left fundus. Granular hyperfluorescence due to window defect and hypofluorescence due to pigmentation are detected along tortuous choroidal artery. C: ICG angiogram 15 seconds after dye injection. A bented and tortuous choroidal artery is observed in the macula as seen at the initial visit. D: ICG angiogram 15 minutes of dye injection. Hypofluorescence due to

pigmentation is detected along a tortuous choroidal artery.

Figure 5. Optical coherence tomography (OCT) finding of the macula. RPE is thinned and elevated above the dilated choroidal artery.

Figure 6. Microperimetry using scanning laser ophthalmoscopy (SLO). Relative scotoma is observed at the site of RPE atrophy.