Parapapillary Diffuse Choroidal Atrophy in Children Is Associated With Extreme Thinning of Parapapillary Choroid

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PURPOSE. To analyze morphologic features of segmental parapapillary diffuse choroidal atrophy (PDCA) in children.

METHODS. The study group included children (age <15 years) with high myopia who attended the Tokyo High Myopia Clinic. Control groups comprised participants of the population-based Gobi Desert Children Eye Study (GobiDCES). Fundus photographs were examined for presence of PDCA and choroidal thickness (CT) was measured by optical coherence tomography.

RESULTS. The study group included 41 eyes of 21 children with PDCA (mean age: 9.4 ± 3.7 years; mean refractive error: -11.5 ± 3.1 diopters) and the GobiDCES included 1463 children (age: 11.8 ± 3.5 years). In the study group, all eyes showed an extreme and abrupt thinning of the temporal parapapillary choroid. At 2500 μm nasal to the foveola, CT was <60 μm in 31 (76%) eyes of the study group but in none (0/1463) of the GobiDCES (P < 0.001), except for one child with PDCA.

CONCLUSIONS. Parapapillary diffuse choroidal atrophy in children is associated with abrupt segmental thinning of the choroid in the temporal parapapillary region, in addition to the thinning of the subfoveal choroid after adjusting for refractive error and age.

Keywords: parapapillary diffuse choroidal atrophy, optical coherence tomography, choroidal thickness, pathologic myopia

Pathologic myopia has become one of the most common causes of loss of best-corrected visual acuity (BCVA), particularly in East Asian countries.1–6 “Pathologic myopia” has been characterized by specific myopia-related complications occurring in the posterior fundus, such as myopic maculopathy or posterior staphyloma.7–10 In East Asian populations, the prevalence of high myopia, parallel to the increase in the prevalence of myopia in general, has markedly increased in the last 50 years.11–14 To cite an example, Morgan and colleagues15 in their recent review article noted the trend that a higher frequency of myopia increases the prevalence of high myopia. It has remained unclear so far whether an increased prevalence of “high myopia” will eventually cause an increased prevalence of “pathologic myopia (which is defined by the presence of its specific complications in the posterior fundus).”9,15

In a recent longitudinal study on 35 eyes of adult patients with signs of myopic maculopathy, who were aged 37.0 ± 5.1 years (range, 33–42 years), 29 of the 35 eyes (83%) showed a parapapillary diffuse choroidal atrophy (PDCA) at the initial visit (age 10.5 ± 2.6 years; range, 5–15 years), with a mean axial length of 27.8 ± 1.2 mm (range, 25.5–29.7 mm).16 Results indicated that PDCA was confined to the area temporal to the optic nerve head outside of the parapapillary alpha, beta, gamma, or delta zones.16 The study suggested that the presence of PDCA in children with high axial myopia might be a biomarker for eventually developing pathologic myopia in adulthood.

Since that previous retrospective longitudinal study started more than 25 years ago when optical coherence tomography (OCT) was not yet available—and since it is of interest to know more about the anatomy of PDCA in children that up to now has only been defined upon ophthalmoscopy—we conducted the present study. Using OCT, we examined the morphologic features of PDCA detected in children attending third-referral high myopia clinics. We additionally compared the OCT findings between the hospital-based study group of children with PDCA and control groups formed on the basis of a population-based recruitment of study participants.

METHODS

Medical records of children with high axial myopia, aged ≤15 years, and who visited the high myopia clinic at Tokyo Medical and Dental University between April 2014 and March 2016

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were retrospectively analyzed. Approval for the study was obtained from the ethics committee of the Tokyo Medical and Dental University. The procedures applied during the examinations conformed to the tenets of the Declaration of Helsinki. Applying the criteria formulated by the Ministry of Health and Welfare in Japan, high myopia was defined as a myopic refractive error of ≥4.0 diopters (D) for children aged ≤5 years, a myopic refractive error of ≥6.0 D for children aged between 6 and 8 years, and a myopic refractive error of ≥8.0 D for children aged ≥9 years. Exclusion criteria were systemic and ocular diseases that caused or were associated with high myopia; (e.g., congenital stationary night blindness, congenital glaucoma, a history of prematurity and chromosomal abnormalities, and presence of intrachoroidal cavitation). Patients with presence of intrachoroidal cavitation were excluded because it was associated with secondary widening of the peripapillary suprachoroidal space. 17–20

All patients underwent a detailed ophthalmologic examination including refractometry; ocular biometry with measurement of axial length (IOLMaster; Carl Zeiss, Oberkochen, Germany); slit-lamp based examination of the anterior segment and posterior segment under medical mydriasis; color fundus photography (fundus camera: Topcon TRC 50DX; Topcon, Tokyo, Japan, or Kowa Pro 1 or VX-10; Kowa, Tokyo, Japan); and optical coherence tomography (DRI-OCT-1; Topcon, Tokyo, Japan). The presence of PDCA was identified by two retinal specialists (TY, KOM). Lastly, the children with PDCA were enrolled in the study group.

The study group was compared with a control group formed by the Gobi Desert Children Eye Study (GobiD-CES) 21,22; a cross-sectional, school-based study performed in the city oasis of Ejina in the Gobi desert. The ethics board of the Inner Mongolia Medical University Affiliated Hospital, Hohhot and the local administration of the School Board of Education of Ejina approved the study and informed written consent was obtained from the parents or guardians of all children. The study included all three schools in Ejina with an overall 1911 eligible children, out of whom 1565 (81.9%) children with a mean age of 11.9 ± 3.5 years (range, 6–21 years) participated. Refractometry was performed under cycloplegic conditions, and fundus photography was carried out. Spectral domain OCT (Spectrasl, wavelength: 870 nm; Heidelberg Engineering Co., Heidelberg, Germany) with enhanced depth imaging (EDI) modality was performed after pupil dilation. The horizontal section running through the center of the fovea was selected for measurement of choroidal thickness (CT). Choroidal thickness was defined as the distance from the outer surface of the hyperreflective line referred to Bruch’s membrane to the hyperreflective line of the inner sclera border. Presence of PDCA was assessed on the color fundus photographs and PDCA was identified as ill-defined yellowish atrophy with decreased pigmentation and bright fundus reflex (Figs. 1, 2). 16

Statistical analysis was carried out using a commercially available statistical software package (SPSS for Windows, version 22.0; SPSS, Inc., Chicago, IL, USA). We calculated the mean and the standard deviations of the thickness of the choroid at the various measurement locations. In univariate analysis, we assessed the associations between choroidal thickness and other ocular and general parameters. A multivariate analysis included choroidal thickness as a dependent variable and all variables as independent parameters that were significantly correlated with choroidal thickness in the univariate analysis. We then dropped all those parameters that either showed a high collinearity or were no longer significantly associated with choroidal thickness, in a stepwise fashion. We calculated the standardized regression coefficient β and the nonstandardized regression coefficient β and its 95% confidence interval (CI).

RESULTS

Between April 2014 and March 2016, 34 children visiting the Tokyo High Myopia Clinic met the criteria of a highly myopic refractive error as defined by the Japanese Ministry of Health and Welfare. One patient was excluded because he was diagnosed with congenital stationary night blindness due to characteristic findings in the electroretinogram. Four patients had unilateral high myopia, and their nonhighly myopic eyes were not included in the study. Another patient was excluded due to parapapillary suprachoroidal cavitation. Out of the remaining 60 eyes of 32 children (mean age: 7.7 ± 4.1 years, mean refractive error: −9.3 ± 3.0 D, mean axial length: 26.5 ± 1.7 mm), 41 eyes of 21 patients showed PDCA and were included in the study group of our investigation. The mean age was 9.4 ± 3.7 years (range, 5–15 years); mean refractive error (spherical equivalent) was −11.5 ± 3.1 D (range, −18.5 to −6.75 D); and mean axial length was 27.5 ± 1.4 mm (range, 24.2–30.5 mm; Table 1).

FIGURE 1. Extreme and sudden thinning of the peripapillary choroid in a child with PDCA. (A) Left fundus of an 11-year-old child with refractive error of −9.0 D (spherical equivalent) and with axial length of 27.1 mm shows yellowish diffuse atrophy temporal to the gamma zone. (B) A horizontal section of OCT shows extreme thinning of choroid temporal to the optic nerve. Almost the entire thickness of the choroid has disappeared in the area of PDCA nasal to the central fovea, although the choroid seems to maintain its thickness temporal to the fovea. The transition from relatively normal choroid around the fovea to almost absent choroid in the area of PDCA is sudden.
Out of 1911 primarily eligible children in the GobiDCES, 1565 (81.9%) children participated in the study, among which 1463 (93.5%) children had EDI-OCT images available for measuring choroidal thickness. Their mean age was 11.8 ± 3.5 years and their mean refractive error was −1.20 ± 2.03 D (Table 1).

In all 41 eyes of the study group with PDCA, OCT images showed an extreme and abrupt thinning of the temporal parapapillary choroid (Figs. 1, 2). At 2500 μm nasal to the foveola, CT was <60 μm in 31 of the 41 eyes (76%); ≤50 μm in 25 of the 41 eyes (61%); and ≤25 μm in 11 eyes (27%). In contrast, none of the participants of the GobiDCES, except for the child with PDCA, had a CT as measured at 2500 μm nasally to the foveola of <60 μm (Fig. 3). Choroidal thickness in the macular region was also thinner (P < 0.001) in the study group than in the GobiDCES after adjusting for age, refractive error, and corneal refractive power (Table 2). Thicker CT at 2500 μm nasal to the fovea was significantly associated (r² = 0.30) with the control group versus study group (P < 0.001) after adjusting for younger age (P = 0.002); higher hyperopic refractive error (P < 0.001); and higher corneal refractive power (P < 0.001; Table 3; Fig. 3). Thicker CT at 2500 μm temporal to the fovea was significantly associated (r² = 0.16) with the control group versus study group (P < 0.001) after adjusting for younger age (P = 0.002); higher hyperopic refractive error (P < 0.001); and higher corneal refractive power (P < 0.001).

### Table 1. General and Eye Characteristics of the Children With PDCA and Children From the GobiDCES

<table>
<thead>
<tr>
<th></th>
<th>Study Group (Children PCDA, n = 41)</th>
<th>Control Group (GobiDCES, n = 1463)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y (range)</td>
<td>9.4 ± 3.7 (3–15)</td>
<td>11.8 ± 3.5 (6.0–20.7)</td>
<td>0.54</td>
</tr>
<tr>
<td>Boys/Girls</td>
<td>23/18</td>
<td>747/716</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Refractive error, D (range)</td>
<td>−11.5 ± 3.6 (−18.5 to −6.75)</td>
<td>−1.31 ± 1.92 (−12.75 to +5.75)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Corneal refractive power, D</td>
<td>43.1 ± 1.6</td>
<td>43.1 ± 1.6</td>
<td>0.77</td>
</tr>
<tr>
<td>CT, μm</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Subfoveal region</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1000 μm nasal to the foveola</td>
<td>282 ± 49 (91–417)</td>
<td>129 ± 59 (40–282)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2500 μm nasal to the foveola</td>
<td>254 ± 49 (87–407)</td>
<td>95 ± 50 (8–207)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1000 μm temporal to the foveola</td>
<td>197 ± 50 (60–388)</td>
<td>43 ± 22 (7–88)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2500 μm temporal to the foveola</td>
<td>286 ± 49 (117–430)</td>
<td>149 ± 61 (57–313)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1000 μm temporal to the foveola/subfoveal</td>
<td>278 ± 49 (111–431)</td>
<td>174 ± 62 (66–335)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2500 μm nasal to the foveola/subfoveal</td>
<td>0.73 ± 0.23 (0.11–1.26)</td>
<td>0.90 ± 0.06 (0.66–1.25)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2500 μm temporal to the foveola/subfoveal</td>
<td>0.39 ± 0.29 (0.08–1.56)</td>
<td>0.70 ± 0.13 (0.28–1.23)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1000 μm temporal to the foveola/subfoveal</td>
<td>1.20 ± 0.25 (0.88–2.22)</td>
<td>1.02 ± 0.06 (0.56–1.37)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2500 μm temporal to the foveola/subfoveal</td>
<td>1.49 ± 0.61 (0.74–3.47)</td>
<td>0.99 ± 0.11 (0.54–1.84)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Figure 2.** Extreme and sudden thinning of the peripapillary choroid in children with PDCA. (A) Right fundus of a 9-year-old child with refractive error of −10.25 D (spherical equivalent) and with an axial length of 26.4 mm shows yellowish diffuse atrophy temporal to the gamma zone. (B) A horizontal section of OCT shows extreme thinning of the choroid in the area of diffuse atrophy. Almost the entire thickness of the choroid has disappeared in the area of PDCA nasal to the central fovea, although the subfoveal choroid seems to maintain its thickness. The transition from relatively normal choroid around the fovea to almost absent choroid in the area of PDCA is relatively sudden.

**Figure 3.** Boxplots showing the distribution of CT (μm) as measured at 2500 μm nasal to the foveola in the children with PDCA (study group) and in children from the GobiDCES.
adjusting for higher hyperopic refractive error (P < 0.001) and higher corneal refractive power (P < 0.001), while it was not significantly associated with age (P = 0.17; Table 4).

The mean ratio of CT at 2500 μm nasal to the fovea to subfoveal CT was significantly lower (r² = 0.16) in the study group than in the GobiDCES (P < 0.001; β: –0.25; B: –0.22; 95% CI: –0.27, –0.17) after adjusting for higher refractive error (P < 0.001; β: 0.15; B: 0.08; 95% CI: 0.005, 0.012; Fig. 4). Age was not significantly associated in that model (P = 0.30). Mean ratio of CT at 1000 μm nasal to the fovea to subfoveal CT was significantly lower (r² = 0.16) in the study group than in the control group (P < 0.001; β: –0.26; B: –0.12; 95% CI: –0.15, –0.10) after adjusting for higher refractive error (P < 0.001; β: 0.18; B: 0.005; 95% CI: 0.003, 0.007). Age was not significantly associated (P = 0.47).

In contrast, the mean ratio of CT at 2500 μm temporal to the fovea to subfoveal CT was higher (r² = 0.26) in the study group than in the GobiDCES (P < 0.001; β: 0.36; B: 0.37; 95% CI: 0.51, 0.43) after adjusting for lower refractive error (P < 0.001; β: –0.20; B: –0.01; 95% CI: –0.02, –0.01). Also, the mean ratio of CT at 1000 μm temporal to the fovea to subfoveal CT was higher (r² = 0.18) in the study group than in the GobiDCES (P < 0.001; β: 0.28; B: 0.13; 95% CI: 0.10, 0.15) after adjusting for lower refractive error (P < 0.001; β: –0.20; B: –0.006; 95% CI: –0.007, –0.004).

### Discussion

Parapapillary diffuse choroidal atrophy in the children of our study group was characterized by a profound segmental and abrupt thinning of the choroid in the temporal parapapillary region, in addition to a thinning of the subfoveal choroid. The parapapillary segmental thinning of the choroid with an abrupt border in direction to the slightly thicker macular choroid was an OCT feature of PDCA. Using a CT cutoff value of <60 μm at 2500 μm nasal to the foveola, 31 of the 41 eyes with PDCA and none of the eyes in the GobiDCES—except for the child with PDCA—were positive for this sign. The preferential and segmental thinning of the choroid in the parapapillary region in the eyes with PDCA also explained that the choroid in the temporal area of the macula compared with the subfoveal region was relatively thicker in children with PDCA compared with the children of the control group after adjusting for age and refractive error.

The observations made in our study are new and cannot directly be compared with results of other investigations. The finding of a general thinning of the choroid at the posterior pole in axially elongated eyes has been reported in several previous studies. A study examining choroidal thickness in children in the fovea and in a circle of 1 mm diameter around the fovea showed that the choroid was thinnest at 500 μm nasal of the fovea (268 μm) and thickest at 500 μm temporal to the foveal zone (290 μm). It indicated that in children in general, the choroid is thinner in the region nasal to the fovea than temporal to the fovea. While most of the previous investigations included adults, Read and colleagues recently reported on the peripapillary choroidal thickness in children. They examined 93 children (37 myopes and 56 nonmyopes) aged between 11 and 16 years and measured the choroidal thickness in five concentric annuli with a distance of 250 μm between each annulus and starting at the edge of parapapillary gamma zone. The mean CT at a distance of 250 μm from the edge of the gamma zone was 77 ± 16 μm. This value was higher than the mean CT at the same location measured in our study population with 46 μm, confirming the finding of an extreme thinning of parapapillary choroid in our study group with PDCA.

Since the ophthalmoscopic assessment of PDCA is subjective and depends on the experience of the examiner, the present study showed the usefulness of OCT to detect a PDCA by measuring choroidal thickness and assessing the pattern of choroidal thickness including the observation of an abrupt change in choroidal thickness in the temporal parapapillary region. A potentially useful cutoff value for the CT at a distance of 2500 μm nasal to the foveola may be the value of <60 μm, since it is significantly differentiated in the group of children with PDCA versus those without PDCA.

A recent longitudinal study suggested that the presence of PDCA in children with high axial myopia might potentially be a biomarker for eventual pathologic myopia in adulthood in some individuals. The reasons for this potential association have remained inconclusive. Recent histologic studies have suggested that myopic axial elongation of the eye is associated with thinning of the sclera and choroid most marked at the posterior pole while the thickness of Bruch’s membrane in all regions of the eye did not decrease significantly with longer axial length. It has remained unclear which of these three layers, sclera, choroid, Bruch’s membrane, or a combination, is involved in the etiology of PDCA as a potential precursor of...
pathologic myopia in some patients. Future studies may address which morphologic signs of the fundus occur first in eyes developing pathologic myopia, and the sequence of changes could further elucidate the mechanism leading to myopic maculopathy.

Potential limitations of our study should be mentioned. First, it was a cross-sectional study, so any conclusions drawn on the longitudinal development of pathologic myopia have to be cautiously interpreted. Second, the children of our study group were highly selected from specialized third-referral clinics. It remains unclear just how representative they are of myopic children in general. Third, based on the marked selection of the children of the hospital-based study group in the present investigation and in particular in the previous study underlying the present investigation, it cannot be concluded that PDCA was a predictor of all or, ultimately, pathologic myopia. It is possible that PDCA represented only one (if at all) out of several biomarkers in children for eventual pathologic myopia. It is possible that PDCA represented only one (if at all) out of several biomarkers in children for eventual pathologic myopia in adulthood. This assumption is supported by results of a recent population-based study in which the prevalence of PDCA in children was considerably lower than the prevalence of pathologic myopia in adults.21 It is also possible that there is no biomarker of later myopic pathology at the young age at all.

Fourth, a recent study showed that high myopia in children and teenage cohorts from East and Southeast Asia showed associations with the level of education, whereas cohorts of adults did not.22 Since the children of our study group were Japanese, the children of the control group were mostly Chinese, thus interethnic differences may have confounded a difference between the populations. However, previous studies have shown that in all ethnic groups examined, the choroid thickness decreased with longer axial length and older age, and that overall the mean choroidal thickness measurements did not markedly differ between Japanese and Chinese patients.

In conclusion, PDCA in children was associated with a profound segmental abrupt choroidal thinning in the temporal parapapillary region, in addition to a generalized thinning of the choroid in the macular region overall. A potentially useful cutoff value of CT at a distance of 2500 μm nasal to the foveola may be the value of <60 μm, which may be helpful for the detection and diagnosis of PDCA in myopic children.

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