Alterations of the Lamina Cribrosa Are Associated with Peripapillary Retinoschisis in Glaucoma and Pachychoroid Spectrum Disease

Jae Hyung Lee, MD, PhD,* Hae-Young Lopilly Park, MD, PhD,* Jiwon Baek, MD, Won Ki Lee, MD, PhD

Purpose: To describe the findings of enhanced depth imaging (EDI) optical coherence tomography (OCT) of the lamina cribrosa (LC) in glaucoma and pachychoroid spectrum diseases associated with peripapillary retinoschisis.

Design: Retrospective, observational case series.

Participants: A total of 16 patients from 1 institution.

Methods: Detailed medical case histories, optic disc and retinal imaging with EDI using the Spectralis OCT (Heidelberg Engineering, Heidelberg, Germany), and clinical course were reviewed for patients with peripapillary retinoschisis without a known predisposing condition.

Main Outcome Measures: Clinical features and findings of the EDI OCT.

Results: Among the 16 eyes with peripapillary retinoschisis that had abnormal findings on EDI of the LC, 8 had glaucoma and 8 had pachychoroid spectrum diseases, including chronic central serous chorioretinopathy (CSC) (6 eyes), small pigment epithelium detachment (1 eye), and polypoidal choroidal vasculopathy (PCV) (1 eye). The abnormal LC findings were central or peripheral focal LC defects in eyes with glaucoma and LC disinsertions or peripheral focal LC defects in eyes with pachychoroid spectrum diseases. Central LC defects were related to inner layer retinoschisis, whereas LC disinsertions and peripheral LC defects were related to outer layer retinoschisis. The peripapillary retinoschisis did not show a topographic association with the underlying chronic CSC- or PCV-associated lesions. In 6 treated eyes with pachychoroid, peripapillary retinoschisis resolved along with subretinal fluid after anti–vascular endothelial growth factor injection in 4 eyes, whereas retinoschisis persisted after the resolution of subretinal fluid in 2 eyes.


Retinoschisis is a splitting of the neurosensory retina and has been described in various ocular conditions, including X-linked retinoschisis, congenital optic disc abnormalities such as optic disc pit and optic disc coloboma, and myopia.1,2 Recently, retinoschisis has been found in eyes with glaucoma. Glaucomatous eyes often have focal structural abnormalities of the optic nerve head (ONH), referred to as “acquired pits of the optic nerve” (APONs).3 Previous case reports have suggested that APONs are correlated with the presence of macular retinoschisis or macular detachment.4,5 With the advent of spectral-domain (SD) optical coherence tomography (OCT) with enhanced depth imaging (EDI), evaluation of the detailed and deep architecture of the ONH has been accessible, and approximately 77% of the APONs in glaucoma showed alterations in the lamina cribrosa (LC).6 Choi et al6 reported that, among glaucomatous eyes with APON, only eyes with associated LC alterations had episodes of retinoschisis (incidence of 13%) compared with eyes without LC alterations (incidence of 0%). That study suggested that the LC defect in the peripheral region of the ONH may serve as an entrance of fluid from the subarachnoid space and contribute to retinoschisis. A study by Yoshitake et al7 observed the presence of late fluorescein staining at the optic disc corresponding to the location of focal LC alterations in glaucomatous eyes with macular retinoschisis, also suggesting that changes in the LC may provide a conduit that allows fluid into the intraretinal space.7 Although the exact pathogenic mechanism and the source of intraretinal fluid of retinoschisis require further evaluation, we can assume from these studies that the LC alterations may play a role in the development of retinoschisis.

We present 16 cases with peripapillary retinoschisis to add important evidence demonstrating that LC alteration may contribute to retinoschisis. These patients had abnormal LC findings as revealed by EDI of the ONH. We separated these patients into 2 categories by the underlying causative
focused on the presence of any alteration in the smooth curvilinear U- or W-shaped cross-sectional contour of the LC with an upward slope at the far periphery of the LC toward its insertion. Al -terations of the LC were defined using the guidelines that were specified by Kiiumer et al and classified as focal LC defects or LC disinsertions for this study. A focal LC defect was defined as a hole-like defect with a discontinuous anterior laminar surface, which appeared to be a full-thickness defect. An LC disinsertion was defined as a posteriorly displaced laminar insertion with downward sloping at the far periphery of the LC toward the neural canal wall. Focal LC defects were classified into 2 types—peripheral or central—according to their location from the neural canal wall. A peripheral LC defect was defined as a defect located near the LC insertion but maintaining the contour of the U- or W-shaped LC, with the anterior LC visible on only the central side of the defect. A central LC defect referred to an LC defect with the LC visible on either side of the defect. These LC findings had to be present in 2 neighboring B-scans to avoid false-positives in both the horizontal and vertical scans; therefore, the LC defect was expected in 4 scans to be defined.

**Results**

During the 1-year study period, a total of 23 patients with peripapillary retinoschisis (8 patients from the glaucoma clinic and 15 patients from the retina clinic) received ONH scanning with EDI OCT. In the glaucoma clinic, 8 eyes of 8 patients (normal-tension glaucoma in 6 eyes and primary open-angle glaucoma in 2 eyes) demonstrated LC alterations on EDI of the OHN. In the retina clinic, 8 eyes of 7 patients did not show discernable LC abnormalities: chronic CSC in 6 eyes (5 patients), choroidal hemangioma in 1 eye, and unknown cause in 1 eye. The diagnosis of the 8 included eyes (8 patients) was chronic CSC in 6 eyes, small pigment epithelium detachment in 1 eye, and PCV in 1 eye. The characteristics of imaging examinations and clinical features in these patients are summarized in Tables 1 and 2.

**Lamina Cribrosa Alterations**

The abnormal LC findings were focal LC defects or LC disinsertions, which varied according to the underlying diseases. Among 8 eyes with choriotetinal diseases with pachychoroid, 6 had LC disinsertions and 2 had peripheral focal LC defects near the LC insertions. Among 8 eyes with glaucoma, 2 had central focal LC defects, 5 had peripheral focal LC defects, and 1 had both features. The clock-hour location of LC deformity was mainly at the 7 o’clock position in eyes with glaucoma in right eye format, which was more variable in eyes with pachychoroid spectrum diseases (Fig 1).

**Association between Peripapillary Retinoschisis and Lamina Cribrosa Alterations**

In all eyes, the clock-hour location of the LC abnormalities correlated well with the location of the retinoschisis. The involved retinal layers ranged from the RNFL to the outer nuclear layer (ONL), which varied according to the pattern and location of LC abnormalities. When LC disinsertions were present or focal LC defects were located in the peripheral region near the LC insertion, retinoschisis involved the inner nuclear layer (INL) to the ONL. In 8 pachychoroid cases with LC disinsertions or peripheral focal defects, 6 involved both the INL and the ONL, and 2 involved the ONL. Among 5 glaucoma cases with peripheral LC defects, 1 involved both the INL and the ONL, and 4 had ONL retinoschisis. In contrast, in 2 glaucoma cases with central focal LC defects, only
Table 1. Summary of Patients’ Characteristics with Peripapillary Retinoschisis in Eyes with Pachychoroid-Related Retinal Diseases

<table>
<thead>
<tr>
<th>Age, yrs</th>
<th>Gender</th>
<th>Laterality</th>
<th>Diagnosis</th>
<th>Diagnosis of the Contralateral Eye</th>
<th>Subfoveal Choroidal Thickness (μm)</th>
<th>Features of the Retinoschisis</th>
<th>Features of the LC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Involved Eye</td>
<td>Contralateral Eye</td>
<td>Involved Retinal Layer</td>
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<tr>
<td>Patient 1</td>
<td>58</td>
<td>M</td>
<td>OD</td>
<td>Chronic CSC</td>
<td>506</td>
<td>644</td>
<td>ONL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pachychoroid neovasculopathy</td>
<td></td>
<td></td>
<td>NA</td>
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<tr>
<td>Patient 2</td>
<td>51</td>
<td>M</td>
<td>OD</td>
<td>Chronic CSC</td>
<td>472</td>
<td>513</td>
<td>INL, ONL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Atypical CSC with ERD</td>
<td></td>
<td></td>
<td>ONL</td>
</tr>
<tr>
<td>Patient 3</td>
<td>77</td>
<td>M</td>
<td>OS</td>
<td>Chronic CSC</td>
<td>623</td>
<td>537</td>
<td>INL, ONL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Chronic CSC</td>
<td></td>
<td></td>
<td>ONL</td>
</tr>
<tr>
<td>Patient 4</td>
<td>48</td>
<td>F</td>
<td>OD</td>
<td>Chronic CSC</td>
<td>465</td>
<td>511</td>
<td>INL, ONL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>ONL</td>
</tr>
<tr>
<td>Patient 5</td>
<td>76</td>
<td>M</td>
<td>OD</td>
<td>Chronic CSC</td>
<td>482</td>
<td>NA</td>
<td>INL, ONL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>ONL</td>
</tr>
<tr>
<td>Patient 6</td>
<td>69</td>
<td>M</td>
<td>OD</td>
<td>PED</td>
<td>506</td>
<td>389</td>
<td>INL, ONL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PCV</td>
<td></td>
<td></td>
<td>ONL</td>
</tr>
<tr>
<td>Patient 7</td>
<td>66</td>
<td>M</td>
<td>OS</td>
<td>PCV</td>
<td>402</td>
<td>417</td>
<td>INL, ONL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>ONL</td>
</tr>
<tr>
<td>Patient 8</td>
<td>67</td>
<td>M</td>
<td>OD</td>
<td>Chronic CSC</td>
<td>413</td>
<td>401</td>
<td>INL, ONL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Chronic CSC</td>
<td></td>
<td></td>
<td>ONL</td>
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<table>
<thead>
<tr>
<th>Topographic Association with Underlying Retinal Lesion</th>
<th>Hyperpermeability Next to ONH on ICGA</th>
<th>Late Disc Stain on FA</th>
<th>Initial BCVA</th>
<th>Final BCVA</th>
<th>Follow-up (mos)</th>
<th>Treatment</th>
<th>Treatment Numbers of Each Drug</th>
<th>Response/Recurrence of Retinoschisis after Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>–</td>
<td>–</td>
<td>0.8</td>
<td>1.0</td>
<td>12</td>
<td>Observation</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Patient 2</td>
<td>–</td>
<td>+</td>
<td>1.0</td>
<td>1.0</td>
<td>24</td>
<td>Laser at leaking point</td>
<td>1</td>
<td>No change/NA</td>
</tr>
<tr>
<td>Patient 3</td>
<td>+</td>
<td>–</td>
<td>0.16</td>
<td>0.16</td>
<td>15</td>
<td>Observation</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Patient 4</td>
<td>–</td>
<td>+</td>
<td>0.63</td>
<td>1.0</td>
<td>12</td>
<td>Anti-VEGF (bevacizumab/ aflibercept)</td>
<td>4 (1/3)</td>
<td>Complete regression/+</td>
</tr>
<tr>
<td>Patient 5</td>
<td>+</td>
<td>–</td>
<td>0.5</td>
<td>0.4</td>
<td>40</td>
<td>Anti-VEGF (bevacizumab/ aflibercept)</td>
<td>2 (1/1)</td>
<td>Complete regression/+</td>
</tr>
<tr>
<td>Patient 6</td>
<td>–</td>
<td>+</td>
<td>0.8</td>
<td>0.8</td>
<td>18</td>
<td>Anti-VEGF (ranibizumab)</td>
<td>3</td>
<td>Partial regression/+</td>
</tr>
<tr>
<td>Patient 7</td>
<td>–</td>
<td>–</td>
<td>0.63</td>
<td>0.63</td>
<td>12</td>
<td>Anti-VEGF (aflibercept)</td>
<td>6</td>
<td>Increase/+</td>
</tr>
<tr>
<td>Patient 8</td>
<td>–</td>
<td>–</td>
<td>0.1</td>
<td>0.16</td>
<td>20</td>
<td>Anti-VEGF (bevacizumab/ aflibercept)</td>
<td>2 (1/1)</td>
<td>Complete regression/+</td>
</tr>
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</table>

BCVA = best-corrected visual acuity; CSC = central serous chorioretinopathy; ERD = exudative retinal detachment; FA = fluorescein angiography; ICGA = indocyanine green angiography; INL = inner nuclear layer; LC = lamina cribrosa; NA = not available; OD = right eye; ONH = optic nerve head; ONL = outer nuclear layer; OS = left eye; PCV = polypoidal choroidal vasculopathy; PED = pigment epithelial detachment; VEGF = vascular endothelial growth factor.
Table 2. Summary of Patients' Characteristics with Peripapillary Retinoschisis in Glaucoma

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age, yrs</th>
<th>Gender</th>
<th>Laterality</th>
<th>IOP Initial</th>
<th>BCVA Baseline</th>
<th>Refraction</th>
<th>VF MD</th>
<th>IOP Last</th>
<th>BCVA Refraction</th>
<th>OCT Extent</th>
<th>Location</th>
<th>Type</th>
<th>Involved Retinal Layer</th>
<th>Diagnosis</th>
<th>Extent of Involvement</th>
<th>Other Features on Imaging Examinations and Clinical Course</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>60</td>
<td>F</td>
<td>OD</td>
<td>NTG</td>
<td>1.0</td>
<td>0.8</td>
<td>High myopia</td>
<td>13</td>
<td>1.28 ONL</td>
<td>OCT to near macula</td>
<td>Peripheral</td>
<td>Focal defect</td>
<td>Peripapillary retinoschisis</td>
<td>POAG</td>
<td>50.0%</td>
<td>The subfoveal choroidal thickness of the 8 cases with chorioretinal diseases accompanying pachychoroid spectrum diseases had LC findings of a peripheral focal LC defect (Fig 2) or an LC disinsertion (Figs 3 and 4). These cases showed thickened choroid with dilated choroidal vessels on macular OCT (Figs 2 and 3). A hyporeflective tract connecting the LC disinsertion and the retinoschisis cavity was observed (Fig 3), suggesting an association between the LC disinsertion and the peripapillary retinoschisis. Late fluorescein staining at the temporal ONH border was observed (Fig 4F) where the LC disinsertion site may be located, suggesting the LC disinsertion as a conduit of the leakage. Eyes with peripapillary retinoschisis related to glaucoma had central (Fig 5) or peripheral focal LC defects (Figs 6 and 7). A hyporeflective tract connecting the LC defect and the retinoschisis cavity also was observed in several cases (Figs 6 and 7). In some cases, a retinoschisis-like change in the RNFL or ganglion cell layer was involved. The other glaucoma case that had both central and peripheral LC defects involved the nerve fiber layer, INL, and ONL. The extent of retinoschisis was restricted around the ONH in 4 (25.0%), extended near the macula in 8 (50.0%), and involved the fovea in 4 (25.0%) of 16 eyes, which was closely related to the location of LC deformity (central or peripheral). In eyes with central focal LC defects, the extent was limited around the ONH. In contrast, retinoschisis involved the macula or the foveal region in eyes with peripheral LC defects or LC disinsertions.</td>
</tr>
<tr>
<td>10</td>
<td>42</td>
<td>M</td>
<td>OS</td>
<td>NTG</td>
<td>1.0</td>
<td>1.0</td>
<td>Myopia</td>
<td>18</td>
<td>2.67 NFL</td>
<td>OCT to near macula</td>
<td>Central</td>
<td>Focal defect</td>
<td>Peripapillary retinoschisis</td>
<td>Myopia</td>
<td>50.0%</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>67</td>
<td>F</td>
<td>OS</td>
<td>NTG</td>
<td>1.0</td>
<td>0.8</td>
<td>Emmetropia</td>
<td>16</td>
<td>2.67 NFL</td>
<td>OCT to near macula</td>
<td>Central</td>
<td>Focal defect</td>
<td>Peripapillary retinoschisis</td>
<td>Myopia</td>
<td>60.0%</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>73</td>
<td>M</td>
<td>OS</td>
<td>NTG</td>
<td>1.0</td>
<td>0.8</td>
<td>Hyperopia</td>
<td>16</td>
<td>16.40 INL, ONL</td>
<td>OCT to near macula</td>
<td>Central</td>
<td>Focal defect</td>
<td>Peripapillary retinoschisis</td>
<td>Myopia</td>
<td>60.0%</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>62</td>
<td>F</td>
<td>OS</td>
<td>NTG</td>
<td>1.0</td>
<td>1.0</td>
<td>Hyperopia</td>
<td>18</td>
<td>4.50 ONL</td>
<td>OCT to near macula</td>
<td>Central</td>
<td>Focal defect</td>
<td>Peripapillary retinoschisis</td>
<td>Myopia</td>
<td>60.0%</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>61</td>
<td>F</td>
<td>OS</td>
<td>NTG</td>
<td>1.0</td>
<td>1.0</td>
<td>Emmetropia</td>
<td>15</td>
<td>Patient 14</td>
<td>OCT to near macula</td>
<td>Central</td>
<td>2 focal defects</td>
<td>Peripapillary retinoschisis</td>
<td>Myopia</td>
<td>60.0%</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>48</td>
<td>M</td>
<td>OS</td>
<td>NTG</td>
<td>0.32</td>
<td>0.32</td>
<td>Hyperopia</td>
<td>22</td>
<td>2.13 NFL, INL</td>
<td>OCT to near macula</td>
<td>Peripheral</td>
<td>2 focal defects</td>
<td>Peripapillary retinoschisis</td>
<td>Myopia</td>
<td>60.0%</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>39</td>
<td>M</td>
<td>OS</td>
<td>NTG</td>
<td>1.0</td>
<td>1.0</td>
<td>Hyperopia</td>
<td>19</td>
<td>1.00 NFL</td>
<td>OCT to near macula</td>
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<td>2 focal defects</td>
<td>Peripapillary retinoschisis</td>
<td>Myopia</td>
<td>60.0%</td>
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</table>

BCVA = best-corrected visual acuity; GCL = ganglion cell layer; INL = inner nuclear layer; LC = lamina cribrosa; MD = mean deviation; NFL = nerve fiber layer; NTG = normal-tension glaucoma; VF = visual field.
of optic disc was observed at the prelaminar region, which appeared to be associated with the peripapillary retinoschisis (Figs 4E and 5A).

**Discussion**

Peripapillary retinoschisis is reported to be more frequently present in glaucomatous eyes compared with normal control eyes. The pathogenic mechanism of retinoschisis in these eyes was supposed to be associated with LC damage, which frequently manifests as an optic disc pit. Recent study data on ONH changes using the EDI technique of SD OCT support this hypothesis. In the current study, we made new observations in patients with glaucoma, which might provide evidence for the contribution of LC defects to the development of peripapillary retinoschisis. The location of the LC abnormalities (central vs. peripheral) appeared to be associated with the involved retinal layers. Inner layer retinoschisis developed in eyes with central focal LC defects. Retinoschisis ranging from the INL to the ONL developed in eyes with peripheral focal LC defects.

In addition, similar involvements were noted in eyes having pachychoroid spectrum diseases with LC disinsertions or peripheral focal LC defects. Retinoschisis in these eyes tended to be involved near the macula or fovea. We observed small retinoschisis cavities or a hyporeflective tract between the LC alteration and the cavity of the retinoschisis in some eyes. The pattern and location of LC abnormalities in these eyes were somewhat different compared with those of the eyes with glaucoma. The most frequent abnormality was LC disinsertion, which develops at the far peripheral region of the ONH, and no eye showed a central focal defect. The clock-hour location in each patient tended to disperse around the temporal side (7–10 clock-hour position in the right eye format). In our cases with glaucoma, the abnormality was a focal defect, either central or peripheral, which was concentrated in the inferotemporal area (7 o’clock-hour position). Lamina cribrosa abnormalities in glaucoma are located in the superotemporal or inferotemporal region where the LC has fewer supporting connective tissues; this may in part reflect a different pathogenic mechanism involved in the development of LC deformity.

We speculate that a thickened choroid due to hyperpermeable choroidal vessels is directly involved in the development of LC changes. Choroidal hyperpermeability was noted on ICGA in all 8 cases. In CSC, increased extravasated fluid from the hyperpermeable choroidal vessels exerts mechanical stress on the RPE layer, which frequently elevates the RPE (serous PED) and finally leads to the focal disruption of the RPE manifested as a focal leak on FA. The area of leakage from the RPE on FA, choroidal vascular hyperpermeability on ICGA, and increased choroidal thickness on OCT are commonly co-localized. The increased extravasated fluids and thickened choroid may impose stress not only vertically on RPE but also laterally on ONH. As observed in our images of the ONH, the anterior scleral canal wall is prominent and elongated, perhaps as a result of choroid thickening. This change may displace the LC posteriorly and medially, leading to a break at the weakest point, which is the LC flange where the LC is attached to the sclera and anterior
Figure 2. Images from the right eye of patient 6, a 69-year-old man with a diagnosis of pigment epithelial detachment (PED). A, Fluorescein angiography shows a focal hyperfluorescent spot at the fovea that corresponds to a small PED on optical coherence tomography (OCT), with no definite leakage. B, On indocyanine green angiography (ICGA), choroidal hyperfluorescence was noted at the papillomacular area. C, On macular OCT, peripapillary retinoschisis (yellow arrowheads) was not topographically associated with the subfoveal PED. Macular OCT also showed choroidal thickening and dilated choroidal vessels (green asterisk); however, subretinal fluid was not noted. D, After a single ranibizumab injection, the height of retinoschisis lesion reduced but the lesion persisted. E, Enhanced depth imaging of the optic nerve head of this patient shows a focal laminar defect (red arrow).
Figure 3. Images from the right eye of patient 4, a 48-year-old woman with a diagnosis of chronic central serous chorioretinopathy (CSC). A, Fluorescein angiography showed faint leakage nasal to the fovea, and (B) choroidal hyperfluorescence was noted at the papillomacular area on indocyanine green angiography. C, Macular optical coherence tomography (OCT) showed choroidal thickening and dilated choroidal vessels with large lumens (green asterisk) and peripapillary retinoschisis involving the macular region (yellow arrowheads). The retinoschisis lesion involves the inner nuclear layer and outer nuclear layer. D and E, The enhanced depth imaging of the optic nerve head of this patient shows laminar disinsertion at the temporal side of the disc (red arrow) and retinoschisis cavity connected to this laminar disinsertion (white arrowheads). The peripapillary sclera is displaced posteriorly (orange glyphs) because of the thickened choroid.

Figure 4. Images that represent different clinical courses of peripapillary retinoschisis. Top row: Images from the right eye of patient 2, a 51-year-old man with a diagnosis of chronic chorioretinopathy (CSC). A, The enhanced depth imaging (EDI) of the optic nerve head (ONH) of this patient shows a laminar disinsertion (red arrow). B, The midphase of fluorescein angiography (FA) showed a widespread area of irregular hyperfluorescence with a suspicious leaking point (red arrow). C, Macular optical coherence tomography (OCT) showed diffuse, irregular retinal pigment epithelial (RPE) elevation with subretinal fluid nasal to the fovea and peripapillary retinoschisis involving the inner nuclear layer (INL) and outer nuclear layer (ONL). D, Focal photocoagulation targeted the RPE at the suspicious leaking point. Complete resolution of subretinal fluid was noted at 1 month; however, the retinoschisis lesion remained stable, persisting during the 22-month follow-up period. Middle row: Images from the right eye of patient 5, a 76-year-old man with a diagnosis of chronic CSC. E, The EDI of the ONH of this patient shows a laminar disinsertion (red arrow). A schisis-like change also was noted in the prelaminar lesion of the ONH (green asterisk). F, On FA, late fluorescein staining of the optic disc was observed in the region of the laminar disinsertion. G, Macular OCT showed subfoveal fluid and a small pigment epithelial detachment (PED) temporal to the fovea. Peripapillary retinoschisis lesion involved the INL and ONL. H, After a single aflibercept injection, both subfoveal fluid and peripapillary retinoschisis showed complete resolution. The subfoveal choroidal thickness decreased from 456 to 430 μm. Bottom row: Images from the right eye of patient 7, a 66-year-old man with a diagnosis of polypoidal choroidal vasculopathy (PCV). I, The EDI of the ONH of this patient shows laminar disinsertion (red arrow) from the peripapillary sclera (orange glyphs). J, Indocyanine green angiography revealed multiple polyps with branching vascular network and choroidal hyperpermeability at the macula. K, Macular OCT showed subfoveal fluid that extended temporal to the fovea. Peripapillary retinoschisis involving the INL and ONL were detected apart from the subfoveal PCV lesion. L, After 3 loading injections of intravitreal aflibercept, subretinal fluid decreased and subfoveal choroidal thickness decreased from 394 to 338 μm; however, the peripapillary retinoschisis increased vertically and extended laterally.
scleral canal wall. The possibility of the increased susceptibility of the LC insertion site to deformation by compressive or tensile force has been suggested by others, supporting our hypothesis.28,29

Although we observed LC change in our patients, the exact pathogenic mechanism underlying the development of peripapillary retinoschisis is still a matter of speculation. Previous studies have demonstrated that the ONH lacks the

Figure 5. A, Images from the left eye of patient 10, a 42-year-old man with a diagnosis of normal-tension glaucoma. Peripapillary retinoschisis (yellow arrowheads) is involving the nerve fiber layer around the inferotemporal area where a localized retinal nerve fiber layer (white arrowheads) is present. The enhanced depth imaging (EDI) of this patient shows a focal laminar defect (red arrow) in the paracentral region of the optic nerve head (ONH). A schisis-like change is noted in the prelaminar lesion of the ONH (green asterisk), which appears to be connected with the peripapillary retinoschisis. B, Images from the left eye of patient 14, a 61-year-old woman with a diagnosis of normal-tension glaucoma. Peripapillary retinoschisis (yellow arrowheads) involves the nerve fiber layer and ganglion cell layer around the ONH. The EDI of this patient shows a focal laminar defect (red arrow) in the paracentral region of the ONH.

Figure 6. A, Images from the right eye of patient 9, a 60-year-old woman with a diagnosis of normal-tension glaucoma with high myopia. Peripapillary retinoschisis (yellow arrowheads) involves the outer retinal layers and is connected to the laminar defect in the peripheral region of the optic nerve head (ONH) (red arrow). The area with peripapillary retinoschisis is in the region where localized retinal nerve fiber layer (white arrowheads) is located. B, Images from the left eye of patient 11, a 67-year-old woman with a diagnosis of normal-tension glaucoma. Peripapillary retinoschisis (yellow arrowheads) involves the outer retinal layers and the fovea. The enhanced depth imaging of this patient shows a focal laminar defect (red arrow) in the peripheral region of the ONH like a disconnection from the sclera. A hyporeflective tract connecting the peripapillary schisis cavity and the laminar region is observed (white arrowheads).
the near subarachnoid space (pachychoroid spectrum diseases are thought to have distinct worldwide. The clinical characteristics of glaucoma and Thus, these results may not be generalizable to all patients First, only patients from a single ethnic group were included. Study Limitations

classic blood–brain barrier properties. Normally, a small amount of fluid from the choriocapillaris appears to freely diffuse into the ONH, including the prelaminar and LC regions. Tso et al suggested that the glial barrier of Kuhnt between the ONH and the retina prevented proteins and fluid from entering the subretinal space, and this barrier might be absent in a congenital optic pit with serous detachment. In our cases, increased leakage from the hyperpermeable choroidal vessels may lead to greater inflow of fluid to the ONH in eyes with pachychoroid. It is possible that fluid reached the ONH from the subarachnoid space through peripheral LC defects/LC disinsertion or from the vitreous region through central LC defects. This may explain the retinoschisis-like changes of the optic disc at the prelaminar region in our series (Figs 4E and 5A). However, a disruption of the glial barrier, which permits inflow of protein-containing fluid into the interlamellar spaces of the retina, seems to be a prerequisite for the development of retinoschisis, as in a congenital optic pit with serous detachment. Subsequently, additional fluid from any source nearby may move into the retinal tissue to balance the osmotic gradient. In pachychoroid eyes, increased fluid inflow and thickened choroid at the border of ONH may stress the border tissue of Kuhnt. In glaucoma, the blood–brain barrier in the ONH may even be weaker. More severe loss of LC and atrophic changes of inner neural tissue would be apt to cause a disruption of the glial barrier and greater intraretinal penetration of serous fluid. This may be another explanation for the involvement of the RNFL and the ganglion cell layer only in the glaucomatous eyes, and not in the eyes with pachychoroid.

Study Limitations

First, only patients from a single ethnic group were included. Thus, these results may not be generalizable to all patients worldwide. The clinical characteristics of glaucoma and pachychoroid spectrum diseases are thought to have distinct racial differences. Second, issues of poor visualization of the LC under the optic disc rim and vessels exist. It is possible that some LC alterations in areas with poor OCT penetration may have been missed. The classification of peripheral and central LC defects was based on the visible portions of the LC. Some central LC defects could have been considered as peripheral LC defects because the peripheral portion of the LC was not captured. To reduce the false-positive detection of focal LC defects, we defined an LC defect as having a diameter of ≥100 μm and a depth of >30 μm. The LC defect also had to be present in 2 neighboring B-scans. The definition of LC defects was based on previous studies and may not be ideal. However, previous studies have mentioned that the definition we used may exclude normal anatomic variations and artifacts. Third, it is possible that the peripapillary retinoschisis that was noted in pachychoroid eyes might be intraretinal edema associated with chronic CSC or PCV. However, most of the peripapillary retinoschisis did not show a topographic relationship with the underlying chronic CSC or PCV lesion, and 1 case demonstrated small PED without any intraretinal or subretinal fluid. Although intraretinal cystoid cavities can be observed in chronic CSC, they tend to occur over areas of RPE atrophy, which were excluded in our cases. The discrepancy of the clinical course of peripapillary retinoschisis and subretinal fluid noted in some cases also suggests that peripapillary retinoschisis is indeed independent of underlying choroidal disease. Finally, we observed CSC cases associated with pachychoroid and peripapillary retinoschisis, but without LC alterations, which were excluded from this study. Pautler and Browning reported a similar case with thickened choroid and hypothesized that a temporal peripapillary crescent may be the site of entry of fluid from the choroid. Because the photoreceptors and RPE are attenuated at that area, serous exudation may extend from the choroid into the extracellular space in the outer neurosensory retina. It is possible that other mechanisms besides alterations of the LC and the ONH blood–brain barrier are involved in the development of peripapillary retinoschisis in pachychoroid eyes.
In conclusion, our results indicate that the LC alteration is associated with peripapillary retinoschisis in glaucoma and pachychoroid spectrum diseases. The mechanism that contributes to the formation of LC abnormalities may be different between the 2 disease categories; however, we suspect that the LC alteration and the disruption of the normal barrier in the ONH seem to have a role in the development of peripapillary retinoschisis. Further studies with larger patient cohorts are required to elucidate the exact pathophysiology.

References

Footnotes and Financial Disclosures

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Abbreviations and Acronyms:
APON = acquired pits of the optic nerve; CSC = central serous chorioretinopathy; EDI = enhanced depth imaging; FA = fluorescein angiography; GCL = ganglion cell layer; ICGA = indocyanine green angiography; INL = inner nuclear layer; LC = lamina cribrosa; OCT = optical coherence tomography; ONH = optic nerve head; ONL = outer nuclear layer; PCV = polypoidal choroidal vasculopathy; PED = pigment epithelial detachment; RNFL = retinal nerve fiber layer; RPE = retinal pigment epithelium; SD = spectral-domain; VEGF = vascular endothelial growth factor.

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Pictures & Perspectives

Epicapsular Stars
A 27-year-old woman was admitted to our hospital for keratoconjunctivitis of her right eye. She had no symptoms in her left eye. Slit lamp microscopic photography of the left eye showed epicapsular stars appearing as several tiny, stellate, brown-pigmented, embroidery-like opacities in the central anterior lens capsule (Fig 1). The epicapsular stars are remnants of the tunica vasculosalentis, a vascular network that surrounds the lens during embryogenesis. As the opacities were not dense, they had no effect on the visual function of the left eye. Accordingly, surgical removal of the deposits was not required, but regular follow-up exams were recommended.

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