Is there a relationship between outer retinal destruction and choroidal changes in cone dystrophy?

Existe uma relação entre a destruição da retina externa e alterações da coroide em distrofia de cones?

ONDER AYYILDIZ1, GOKHAN OZGE1, MURAT KUCUKCIVILIOGLU1, CEM OzGONUL2, TARKAN MUMCUOGLU1, ALI HAKAN DURUKAN1, FAITH MEHMET MUTLU1

ABSTRACT

Purpose: The aim of the present study was to use enhanced depth imaging optical coherence tomography (EDI-OCT) to investigate choroidal changes in patients with cone dystrophy (CD) and to correlate these findings with clinical and electroretinography (ERG) findings.

Methods: This case-control study included 40 eyes of 20 patients with CD and 40 eyes of 40 age- and refraction-matched healthy individuals. Choroidal thickness (CT) measurements were obtained under the foveal center and at 500 and 1,500 µm from the nasal and temporal regions to the center of the fovea, respectively. EDI-OCT and ERG data were analyzed, and the correlations of CT with the best-corrected visual acuity (BCVA) and the central foveal thickness (CFT) were evaluated.

Results: The mean subfoveal CTs in the CD and control groups were 240.70 ± 70.78 and 356.18 ± 48.55 µm, respectively. The subfoveal CT was significantly thinner in patients with CD than in the controls (p<0.001). The patients with CD also had significantly thinner choroids than the controls at each measurement location relative to the fovea (p<0.001). The subfoveal CT in the CD group correlated with CFT (p=0.012), but no significant correlation was found between the subfoveal CT and BCVA or photopic ERG responses.

Conclusions: The present study demonstrated a significant thinning of the choroid in patients with CD. EDI-OCT is a useful technique for describing the choroidal changes occurring in CD. Future studies investigating the association between choroidal changes and outer retinal destruction or the disease stage may provide a better understanding of the pathophysiology of CD.

Keywords: Choroid; Fovea centralis; Retinal dystrophies; Retinal cone photoreceptor; Tomography; optical coherence, Electroretinography

INTRODUCTION

Cone dystrophy (CD) is an inherited retinal disease characterized by the deterioration of the cone cells responsible for central and color vision10. Progressive vision loss, decreased color vision, photophobia, and nystagmus are common clinical features of CD. Full-field electroretinography (ERG) reveals common reduced single and flicker cone responses under photopic conditions and normal rod responses under scotopic conditions. ERG is a more sensitive technique and can be used to diagnose CD earlier than is possible using current diagnostic techniques11. A variety of mechanisms, such as defective outer segment morphogenesis, protein transport along the cilium, phototransduction, or cellular interaction, have been suggested as being responsible for cone dysfunction12. The retinal pathology of CD occurs mainly between the photoreceptor outer segment and retinal pigment epithelium (RPE) layer13. Alterations in the retinal structure were previously demonstrated in patients with CD using spectral-domain optical coherence tomography (SD-OCT)14, and some investigators have observed reduced neuroretinal thickness in the fovea centralis and macula using SD-OCT15. Enhanced depth imaging (EDI) is a technique that can be utilized to examine both the retina and choroid using specific focusing techniques and an SD-OCT device16. Images acquired with EDI-OCT not only have an improved ability to visualize the deeper ocular structures and the choroid; they also allow the thickness and contour of the choroid to be assessed17.

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1 Department of Ophthalmology, GATA Medical School, Ankara, Turkey.
2 Department of Ophthalmology, Van Military Hospital, Van, Turkey.

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Corresponding author: Onder Ayildiz, Department of Ophthalmology, GATA Medical School, Ankara 06010 - Turkey - E-mail: dronderayyildiz@gmail.com
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Most inherited retinal dystrophies lead to damage of the outer retinal structures and RPE. Several studies have demonstrated that a loss of photoreceptor and RPE cells leads to secondary choroidal thinning and atrophy (3). The pathogenesis of photoreceptor cell deterioration and RPE dysfunction in CD remains unclear, and knowledge on the changes in the choroid in retinal dystrophies is limited. To the best of our knowledge, no published study has yet examined the choroidal changes in cone dystrophy.

The aims of this case-control study were to image and describe the choroidal changes occurring in patients with CD using EDI-OCT, to compare the results with those from age- and refraction-matched healthy controls, and to correlate these outcomes with the best-corrected visual acuity (BCVA) and ERG responses.

METHODS

This diagnostic case-control study was approved by the institutional review board at GATA Medical School (# 2015-KAEK-45) and was performed at GATA Medical School between March and December 2015. Informed consent was obtained from each subject, and all study procedures adhered to the tenets of the Declaration of Helsinki. Twenty patients with CD were enrolled, and 40 healthy age- and refraction-matched volunteers without CD or other ocular diseases were included for comparison purposes as a control group.

Data recorded for all subjects included Snellen BCVA, intraocular pressure, biomicroscopy, fundoscopy, refractive error, and EDI-OCT (Spectralis OCT; Heidelberg Engineering, Heidelberg, Germany) findings as well as demographic data such as age and sex. The diagnostic criteria for CD were as follows: decreased cone cell function with relatively normal rod cell function in full-field ERG (RetiScan System; Roland Consult, Wiesbaden, Germany); a history of progressive visual loss, photophobia, nyctagmus, or poor color vision; and fundoscopic findings in the macula with non-specific changes to the characteristic RPE lesions of the bull’s eye and reduced neuroretinal thickness in the fovea and macula in OCT. All patients with CD underwent color vision testing and full-field standard ERG. Some of the patients with CD also underwent visual field testing, fluorescein angiography, and fundus autofluorescence imaging.

All subjects were examined using EDI-OCT imaging with pupil dilation. All EDI-OCT images were obtained by the same experienced technician in ambient lighting in the afternoon. The OCT device was positioned sufficiently close to the eye to obtain an inverted image. Each session was obtained using automatic eye-tracking software, and 100 averaged images were taken to improve the signal-to-noise ratio. A horizontal image across the fovea was obtained for each subject. The choroidal thickness (CT) measurement was performed manually in a vertical direction from RPE/Bruch’s membrane interface to the sclerochoroidal interface (Figure 1). The choroid was independently measured by two blinded observers (OA and GO) at the foveal center and at 500 and 1,500 µm from the nasal and temporal regions to the center of the fovea, respectively. The measurement locations were determined according to the cone cell density in the retina (8).

Data analysis was performed using SPSS for Windows 16.0 software package (SPSS Inc., Chicago, IL, USA). The data were expressed as percentage values or as group mean and standard deviation values. The t-test was used to compare continuous variables with normal distribution, and the Mann-Whitney U-test was used to compare non-normally distributed continuous variables. The chi-square test was used for the comparison of discrete variables. Pearson correlations were performed to explore the correlations among BCVA, central foveal thickness (CFT), subfoveal CT, and photopic ERG responses in the CD group. A p-value < 0.05 was accepted as statistically significant.

RESULTS

A total of 20 patients (12 men and 8 women; 40 eyes) with a diagnosis of CD were included in the study. The mean age was 28 ± 11.14 years (range, 18-55 years); the mean spherical equivalent (SE) was -0.70 ± 1.67 diopters (range, -3.50 to +2.50); and the mean BCVA was 0.27 ± 0.19. All patients were phakic with clear lenses. The control group included 40 individuals (21 men and 19 women; 40 eyes) with no abnormalities of the anterior segment and fundus. The mean age in the control group was 24.50 ± 3.50 years (range, 18-32 years); the mean SE was 0.06 ± 0.82 diopters (range, -1.50 to +1.25); and the mean BCVA was 0.95 ± 0.07. The study group and the control group differed significantly in terms of BCVA (p<0.001), whereas the age and SE differences were not statistically significant (p=0.74 and p=0.12, respectively; Table 1).

The mean CFT measured 152.58 ± 57.14 µm in the CD group and 219.35 ± 14.74 µm in the control group. CFT was significantly thinner in patients with CD than in controls (p<0.001; Table 1). In addition to the significant difference in CFT between the groups, the mean subfoveal CTs in the CD and control groups were 240.70 ± 70.78 and 356.18 ± 48.55 µm, respectively. The subfoveal CT was also significantly thinner in patients with CD than in controls (p<0.001; Figure 2). The CT measurements taken at 1,500 and 500 µm from the nasal region, and 500 and 1,500 µm from temporal region to the center of the fovea were, respectively, 190.80 ± 79.17, 235.68 ± 77.66, 243.48 ± 72.24, and 221.13 ± 63.14 µm in the CD group and 325.18 ± 54.28, 336.70 ± 43.31, 330 ± 55.38, and 372.38 ± 41.83 µm in the control group (Figure 2). The patients with CD had significantly thinner CTs compared with the controls at each measurement location relative to the fovea (p<0.001).

The mean BCVAs for the CD and control groups were 0.27 ± 0.19 and 0.95 ± 0.07, respectively (p<0.001). Best corrected visual acuity correlated weakly with CFT in the CD group (Pearson’s r=0.552, p<0.001) and no correlation was found between BCVA and other factors, such as the subfoveal CT and photopic ERG responses (Table 2). In the same group, subfoveal CT correlated weakly with CFT (Pearson’s r=-0.396, p=0.012) and no significant correlation was found between the subfoveal CT and BCVA or the photopic ERG responses.

DISCUSSION

Previous histopathological studies have established choriocapillaris degeneration, photoreceptor loss, and RPE deterioration in eyes with various dystrophies (9). The photoreceptor layer and RPE are the major sites of structural impairment as discerned by SD-OCT in patients with CD. Some investigators have observed reduced neuro-

Figure 1. Measurement of choroidal thickness with enhanced depth imaging optical coherence tomography. The upper yellow line indicates the retinal pigment epithelium/Bruch’s membrane interface, and the lower yellow line indicates the sclerochoroidal interface. (A) Healthy control with a choroid of normal thickness and (B) cone dystrophy patient with choroidal thinning.
Table 1. Characteristics of the individuals

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Gender (M/F)</th>
<th>Visual acuity</th>
<th>SE (Dpt)</th>
<th>Photopic A Amp (mV)</th>
<th>Photopic B Amp (mV)</th>
<th>30 Hz Amp (mV)</th>
<th>CFT (µm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>28.00 ± 11.14</td>
<td>12/8</td>
<td>0.27 ± 0.19</td>
<td>-0.70 ± 1.67</td>
<td>9.72 ± 7.01</td>
<td>28.49 ± 21.77</td>
<td>6.01 ± 5.64</td>
<td>152.58 ± 57.14</td>
</tr>
<tr>
<td>24.80 ± 3.50</td>
<td>21/19</td>
<td>0.95 ± 0.07</td>
<td>0.06 ± 0.82</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>216.35 ± 14.74</td>
</tr>
</tbody>
</table>

Table 2. Pearson correlations in the cone dystrophy group (p values)

<table>
<thead>
<tr>
<th>BCVA</th>
<th>CFT</th>
<th>SCT</th>
<th>Photopic A Amp</th>
<th>Photopic B Amp</th>
<th>30 Hz Amp</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.001</td>
<td>0.770</td>
<td>0.180</td>
<td>0.23</td>
<td>0.77</td>
</tr>
<tr>
<td>&lt;0.001</td>
<td>1</td>
<td>0.012</td>
<td>0.1</td>
<td>0.360</td>
<td>0.27</td>
</tr>
<tr>
<td>0.770</td>
<td>0.012</td>
<td>1</td>
<td>0.360</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>0.230</td>
<td>0.570</td>
<td>0.270</td>
<td>N/A</td>
<td>1</td>
<td>N/A</td>
</tr>
<tr>
<td>0.770</td>
<td>0.770</td>
<td>0.080</td>
<td>N/A</td>
<td>N/A</td>
<td>1</td>
</tr>
</tbody>
</table>

REFERENCES

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