Clinical, Angiographic, Optic Coherence Tomographic and Electrophysiological Findings in Bietti’s Crystalline Dystrophy

Bietti’nin Kristalin Distrofisinde Klinik, Anjiyografik, Optik Koherans Tomografik ve Elektrofizyolojik Bulgular

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Abstract Objectives: To present the characteristic clinical, angiographic, electrophysiologic and optic coherence tomographic findings in eight patients with Bietti’s crystalline dystrophy. Material and Methods: All patients had detailed ophthalmologic examination, visual field examination, fluorescein angiography, electroretinography, electrooculography recordings, and optic coherence tomography were performed in all patients. Results: Best-corrected visual acuity ranged from 2/10 to 10/10. On fundoscopic examination, the reflective yellow deposits located especially in the posterior pole of the retina with the mottling of retina pigment epithelium were seen in all patients whereas in some of the cases pigment deposition, retina pigment epithelium and choriocapillaris atrophy were also noted. Corneal crystals were observed in the limbus in three cases. Central and paracentral scotomas were detected in perimetric examination. Arden ratios in electrooculography and the results of electroretinography recordings were different. Fluorescein angiography showed island like hypofluorescence corresponding to the geographic areas of retinal pigment epithelium and choriocapillaris atrophy in the posterior pole. In addition to this fluorescein angiographic findings, in diffuse type cases, diffuse hypofluorescence that extended to the midperiphery was detected. Optic coherence tomographic examination disclosed multiple hyperreflective lesions in the retina and acoustic shadowing behind these hyperreflective lesions and a hyperreflective white band. Conclusion: Common characteristics of clinical, angiographic, electrophysiologic and optic coherence tomographic findings in patients with Bietti’s crystalline dystrophy were described.

Key Words: Electrooculography; fluorescein angiography; electroretinography; retinal degeneration; tomography, optical coherence


Anahtar Kelimeler: Elektrookülografisi; floresan anjiyografisi; elektroretinografisi; retinal dejenerasyon; tomografi, optik koherans

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Bietti’s crystalline dystrophy (BCD) is a hereditary condition first described by Bietti in 1937 as a corneoretinal degeneration. It is characterized by numerous, tiny, glistening crystals scattered in the retina and varying degrees of choriocapillary and retinal pigment epithelial loss and in some cases superficial limbal corneal crystals. Bietti’s crystalline dystrophy is a progressive, autosomal recessive retinal degeneration which usually manifests around the third and fourth decade of life. Classically, patients present with nyctalopia, progressive visual loss, constriction of visual fields, and paracentral scotomas leading to legal blindness by the fifth or sixth decades of life. The retinal crystals are found in all retinal layers and the fundus changes can vary from those of a generalized degenerative disorder to those where focal retinal regions are involved. The regions involved will determine the visual acuity, abnormalities of night vision and electroretinography (ERG). Histopathological studies disclosed evidence of advanced choroidal atrophy characterized by a marked loss of the retinal pigment epithelium (RPE) and choriocapillary and mild retinal gliosis.

In this study, we present the findings of ERG, electrooculography (EOG), perimetry, optical coherence tomography (OCT) and fluorescein angiography in eight cases with BCD.

### MATERIAL AND METHODS

The study has been performed in accordance with the Helsinki Declaration of 1975 (as revised in 1983). Between 2005 and 2008, eight patients with common characteristics of BCD were evaluated retrospectively. Informed consent was taken from all patients.

Ophthalmic examination included best-corrected visual acuity (BCVA), slit-lamp biomicroscopy, applanation tonometry, fundus examination, visual field and electrophysiologic examination (ERG, EOG), fluorescein angiography (FA) and OCT. There was no evidence of drug use or a metabolic disorder associated with retinal crystalline deposits. Based on ophthalmoscopic appearance, the cases were categorized into regional and diffuse types, according to the classification of Welch. The regional type, initially confined to the posterior pole, consisted of RPE defects and subsequent choriocapillary atrophy. The diffuse type was characterized by widespread RPE defects with pigment mottling and deposition. Four patients were females (50%) and four patients were males (50%). Case 3, 6, and 7 were members of the same family (3 siblings, two males, one female), and all other cases were sporadic.

Best corrected visual acuity was evaluated by using a Snellen chart. Humphery visual field analyzer (model 750; Humphery-Zeiss, San Leandro, CA) was used for visual field testing. Stimulus size was Goldmann III (0.43° of visual angle) and full field strategy was applied. Medelec Neuropt system was used for ERG and EOG recordings. The ERGs were recorded under conditions that conformed to the standards of the International Society of Clinical Electrophysiology of Vision. The Arden ratios were evaluated in EOG. Topcon TRC-50IX retinal camera was used for FA and Carl-Zeiss (Carl-Zeiss Ophthalmic System Inc., Humphery Division, Dublin, CA, USA) Stratus OCT was used for central retinal evaluation.

### RESULTS

Clinical characteristics of the patients are summarized in Table 1. Three cases were diffuse type and the other five cases were regional type. Four cases were females and four cases were males. Three female patients were categorized into regional type, and one female case was diffuse type. Four male patients were regional type.

The age range of the patients was between 23 and 44 years (mean 30.25±7, median 29). All patients noted decreased visual acuity and six patients noted night blindness. Best-corrected visual acuity ranged from 2/10 to 10/10 (mean 0.58±0.32, median 0.65). All patients were symmetrically affected. In fundoscopic examination, the reflective yellow deposits located especially in the posterior pole of the retina with a RPE mottling seen in all patients, however in some of the cases pigment deposition...
and RPE, choriocapillary atrophy were noted (Figure 1). Corneal crystals were observed at the limbus in three cases (Table 1.)

All patients underwent automated perimetry. Central scotomas in 2 patients, paracentral scotoma in one patient and central and paracentral scotomas in 2 patients were detected. Perimetric responses were not reliable in three cases and not included in the evaluation. The results of ERG recordings were dissimilar. ERG responses were subnormal in 3 cases and nonrecordable in two cases in all test conditions. In one case, ERG responses were nonrecordable in dark-adapted rod ERG, and dark-adapted maximal responses, photopic and flicker responses were subnormal. Arden’s ratio was subnormal in six patients in EOG, indecisive in one case and normal in one case (Table 2).

All patients underwent fluorescein angiography. Fluorescein angiography showed island like hypofluorescence corresponding to the geographic areas of RPE and choriocapillary atrophy in the posterior pole with prominence of medium to large choroidal vessels in the early and mid phase. There was hyperfluorescence in the posterior pole as a result of the window defect of the RPE atrophy.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age</th>
<th>Gender</th>
<th>First symptoms</th>
<th>BCVA (Right-Left)</th>
<th>Corneal crystals</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>30</td>
<td>F</td>
<td>N, DVA</td>
<td>7/10-6/10</td>
<td>(+)</td>
<td>DT</td>
</tr>
<tr>
<td>2</td>
<td>44</td>
<td>F</td>
<td>N, DVA</td>
<td>7/10-10/10</td>
<td>(-)</td>
<td>RT</td>
</tr>
<tr>
<td>3</td>
<td>28</td>
<td>M</td>
<td>DVA</td>
<td>8/10-2/10</td>
<td>(-)</td>
<td>RT</td>
</tr>
<tr>
<td>4</td>
<td>31</td>
<td>F</td>
<td>N, DVA</td>
<td>6/10-3/10</td>
<td>(+)</td>
<td>DT</td>
</tr>
<tr>
<td>5</td>
<td>23</td>
<td>M</td>
<td>DVA</td>
<td>2/10-9/10</td>
<td>(+)</td>
<td>RT</td>
</tr>
<tr>
<td>6</td>
<td>27</td>
<td>F</td>
<td>N, DVA</td>
<td>10/10-5/10</td>
<td>(-)</td>
<td>DT</td>
</tr>
<tr>
<td>7</td>
<td>23</td>
<td>M</td>
<td>N, DVA</td>
<td>10/10-7/10</td>
<td>(-)</td>
<td>RT</td>
</tr>
<tr>
<td>8</td>
<td>36</td>
<td>M</td>
<td>N, DVA</td>
<td>1/10-0.5/10</td>
<td>(-)</td>
<td>RT</td>
</tr>
</tbody>
</table>

F: Female; M: Male; N: Nyctalopia; DVA: Decreased visual acuity; BCVA: Best corrected visual acuity; DT: Difuse type; RT: Regional type.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>VF defects (bilateral)</th>
<th>Scotopic ERG (bilateral)</th>
<th>Photopic ERG (bilateral)</th>
<th>EOG (Arden ratio%) right-left</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Central-paracentral scotoma</td>
<td>Subnormal</td>
<td>Subnormal</td>
<td>128-128</td>
</tr>
<tr>
<td>2</td>
<td>Paracentral scotoma</td>
<td>Normal</td>
<td>Normal</td>
<td>220-216</td>
</tr>
<tr>
<td>3</td>
<td>Central scotoma</td>
<td>Normal</td>
<td>Subnormal</td>
<td>170-175</td>
</tr>
<tr>
<td>4</td>
<td>Not reliable</td>
<td>Non recordable</td>
<td>Non recordable</td>
<td>140-135</td>
</tr>
<tr>
<td>5</td>
<td>Central-paracentral scotoma</td>
<td>Non recordable</td>
<td>Subnormal</td>
<td>125-125</td>
</tr>
<tr>
<td>6</td>
<td>Central scotoma</td>
<td>Subnormal</td>
<td>Normal</td>
<td>120-130</td>
</tr>
<tr>
<td>7</td>
<td>Not reliable</td>
<td>Subnormal</td>
<td>Subnormal</td>
<td>160-160</td>
</tr>
<tr>
<td>8</td>
<td>Not reliable</td>
<td>Non recordable</td>
<td>Non recordable</td>
<td>110-110</td>
</tr>
</tbody>
</table>

VF: Visual field; ERG: Electroretinography; EOG: Electrooculography.
in the late phase. In addition to these fluorescein angiographic findings, in diffuse type cases, diffuse hypofluorescence that extended to the midperiphery was detected (Figure 2). All patients were evaluated by OCT. OCT examination disclosed multiple hyperreflective lesions in the neurosensory retina in all cases, and acoustic shadowing behind these hyperreflective lesions were seen in some cases (Figure 3a). The RPE-choriocapillary complex was seen hyperreflective as a white band (Figure 3b).

**DISCUSSION**

In this study, we evaluated clinical and functional findings of eight patients with BCD. Best-corrected visual acuity varied significantly and ranged from 0.05/10 to 10/10. Six patients who were older than the other cases, stated that they have night blindness. Studies in the literature report that the first complaint of nyctalopia is seen around the age of 40.7-11 Fundoscopic examination showed similar findings. Automated perimetry also showed similar results, showing pericentral or central scotomas, in patients who have reliable perimetric responses. Yanagi et al. found similar visual field defects in their series with crystalline dystrophy.7 The results of ERG recordings were different and ranged from normal to undetectable. Arden’s ratio in EOG was subnormal in six patients and was decisive in one case and normal in one case. The variation in the results of ERG and EOG may be due to testing at different stages of the disease. The previous reports have shown similar results.3,7-14 These results imply that the responses of ERG and EOG reflect the degree of retinal involvement.

All patients underwent fluorescein angiography. Fluorescein angiography showed island like hypofluorescence corresponding to the geographic areas of RPE and choriocapillary
atrophy in the posterior pole. Fluorescein angiographic changes occur early in the course of the disease, suggestive of the RPE as the primary site of the disease.\textsuperscript{3,4,9-11} The areas of RPE atrophy progressively enlarge as the disease progresses.

OCT examination showed multiple intraretinal hyperreflective lesions and acoustic shadowing behind these hyperreflective lesions. The RPE-choriocapillary complex was seen hyperreflective as a white band. This OCT findings are similar to previous reports.\textsuperscript{8,15,16} The OCT provides additional data in BCD. We used time-domain OCT which had lower image resolution compared to spectral-domain OCT. Further studies using spectral-domain OCT can provide additional information for BCD.