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

Filiz AFRASHİ,[a]
Esat ÇINAR[a]

[a]Department of Oftalmology, Ege University Faculty of Medicine, İzmir

Geliş Tarihi/*Received:* 10.06.2011
Kabul Tarihi/*Accepted:* 30.03.2012

Yazışma Adresi/*Correspondence:*
Filiz AFRASHİ
Ege University Faculty of Medicine, Department of Oftalmology, İzmir, TÜRKİYE/TURKEY
filiz.afrashi@ege.edu.tr

ABSTRACT Objective: 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 hypoflourescence corresponding to the geographic areas of retinal pigment epithelium and choriocapillary 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

ÖZET Amaç: Bietti'nin kristalin distrofisi olan sekiz hastada karakteristik klinik, anjiyografik, elektrofizyolojik ve optik koherens tomografi bulgularını sunmak. **Gereç ve Yöntemler:** Tüm hastalar tam bir göz muayenesinden geçti. Tüm hastalara görme alanı muayenesi, floresan anjiyografi, elektroretinografi, elektrookülografi kayıtları ve optik koherens tomografi yapıldı. **Bulgular:** En iyi düzeltilmiş görme keskinliği 2/10 ile 10/10 arasındaydı. Fundoskopik muayenelerde yansıyan sarı birikintiler özellikle retinanın arka kutbunda yerleşmişti, tüm retinalarda retina pigment epitelinin beneklenmesi görülüyordu, oysa olguların bazılarında pigment birikmesi ve retina pigment epiteli, koriyokapiller atrofi de fark edildi. Üç olguda limbusta korneal kristaller görüldü. Perimetrik muayenede santral ve parasantral skotomlar saptandı. Elektrookülografideki Arden oranları ve elektroretinografi kayıtlarının sonuçları farklıydı. Floresan anjiyografide retinal pigment epitelinin coğrafik alanlarına uyan ada benzeri hipofloresans ve arka kutupta koriyokapiller atrofi görüldü. Bu floresan anjiyografi bulgularına ek olarak, diffüz tip olan olgularda periferin ortasına kadar uzanan diffüz hipofloresans saptandı. Optik koherens tomografi muayenesi retinada çok sayıda hiperreflektif lezyonu ve bu hiperreflektif lezyonların arkasındaki akustik gölgelenme ve hiperreflektif beyaz bir bandı ortaya çıkardı. **Sonuç:** Bietti'nin kristalin distrofisi olan hastalardaki klinik, anjiyografik, elektrofizyolojik ve optik koherens tomografi bulgularının yaygın özellikleri tanımlandı.

Anahtar Kelimeler: Elektrookülografi; floresan anjiyografi; elektroretinografi; retinal dejenerasyon; tomografi, optik koherens

doi: 10.5336/medsci.2011-25237

Turkiye Klinikleri J Med Sci 2012;32(6):1507-11

Bietti's crystalline dystrophy (BCD) is a hereditary condition first described by Bietti in 1937as a corneoretinal degeneration.[1] 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.[2] Bietti's crystalline dystrophy is a progressive, autosomal recessive retinal degeneration which usually manifests around the third and fourth decade of life.[3] 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).[2] 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.[4]

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 benn 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.[5] 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 (0.43º of visual angle) and full field strategy was applied. Medelec Neuropto 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.[6] 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

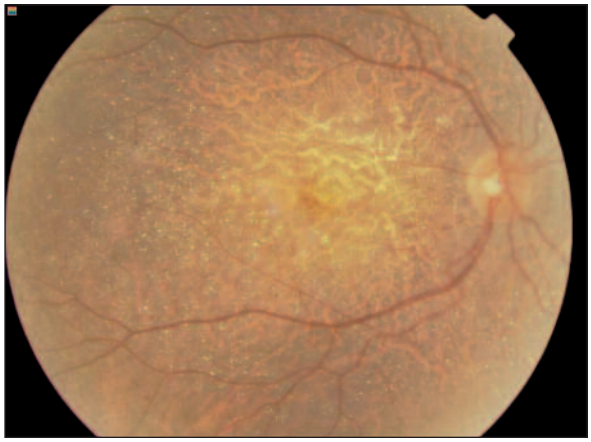

FIGURE 1: Fundus photograph.
(See for colored form http://tipbilimleri.turkiyeklinikleri.com/)

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 hypoflourescence 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 hyperflourescence in the posterior pole as a result of the window defect of the RPE atrophy

TABLE 1: Clinical data.

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

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

TABLE 2: Perimetric and electrophysiologic data.

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

VF: Visual field; ERG: Electroretinography; EOG: Electrooculography.

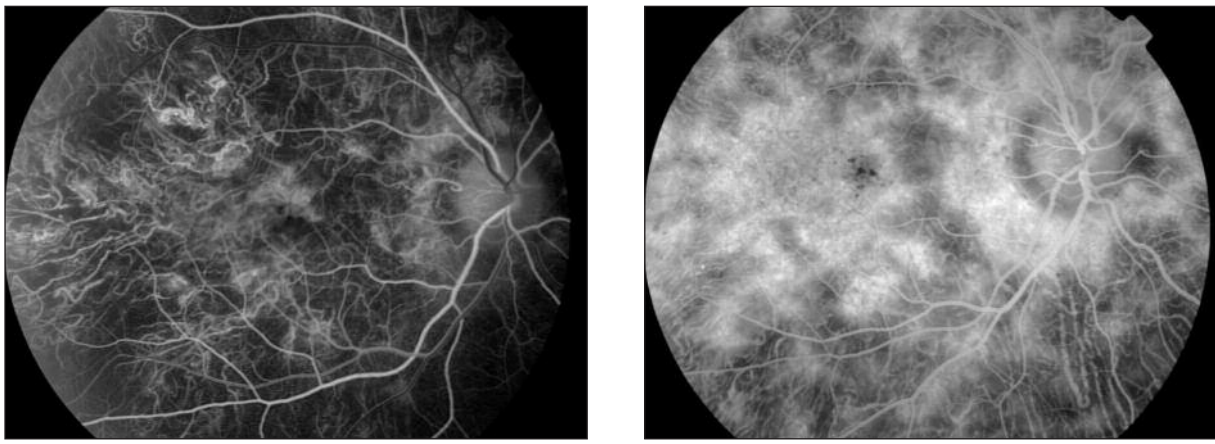

FIGURE 2: Fluorescein angiography, early and late phases

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 hypoflourescence corresponding to the geographic areas of RPE and choriocapillary

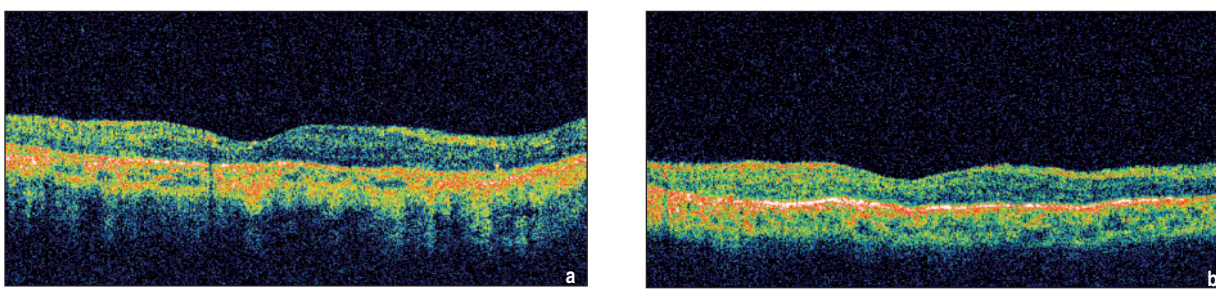

FIGURE 3: OCT images, **a)** Intraretinal hyperreflective lesions, **b)** Hyperreflective white band.
(See for colored form http://tipbilimleri.turkiyeklinikleri.com/)

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.[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.[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.

REFERENCES

1. Bietti GB. [About family with 'Retinitis punctata albescens' (related to 'marginal crystalline corneal dystrophy') glistening vitreus and other degenerative eye changes]. Klin Monatsbl Augenheilkd 1937;99:737-56.
2. Karaçorlu SA. [Bietti's crystalline dystrophy and the other flecked retina syndromes]. Turkiye Klinikleri J Ophthalmol-Special Topics 2009;2(1):12-9.
3. Wilson DJ, Weleber RG, Klein ML, Welch RB, Green WR. Bietti's crystalline dystrophy. A clinicopathologic correlative study. Arch Ophthalmol 1989;107(2):213-21.
4. Kaiser-Kupfer MI, Chan CC, Markello TC, Crawford MA, Caruso RC, Csaky KG, et al. Clinical biochemical and pathologic correlations in Bietti's crystalline dystrophy. Am J Ophthalmol 1994;118(5):569-82.
5. Welch RB. Bietti's tapetoretinal degeneration with marginal corneal dystrophy crystalline retinopathy. Trans Am Ophthalmol Soc 1977;75: 164-79.
6. Marmor MF, Zrenner E. Standard for clinical electroretinography (1999 update). International Society for Clinical Electrophysiology of Vision. Doc Ophthalmol 1998-1999;97(2):143-56.
7. Yanagi Y, Tamaki Y, Takahashi H, Sekine H, Mori M, Hirato T, et al. Clinical and functional findings in crystalline retinopathy. Retina 2004;24(2):267-74.
8. Lai TY, Ng TK, Tam PO, Yam GH, Ngai JW, Chan WM, et al. Genotype phenotype analysis of Bietti's crystalline dystrophy in patients with CYP4V2 mutations. Invest Ophthalmol Vis Sci 2007;48(11):5212-20.
9. Mataftsi A, Zografos L, Millá E, Secrétan M, Munier FL. Bietti's crystalline corneoretinal dystrophy: a cross-sectional study. Retina 2004;24(3):416-26.
10. Fong AMY, Koh A, Lee K, Ang CL. Bietti's crystalline dystrophy in Asians: clinical, angiographic and electrophysiological characteristics. Int Ophthalmol 2009;29(6):459-70.
11. Chen H, Zhang M, Huang S, Wu D. Functional and clinical findings in 3 female siblings with crystalline retinopathy. Doc Ophthalmol 2008;116(3):237-43.
12. Chan WM, Pang CP, Leung AT, Fan DS, Cheng AC, Lam DS. Bietti crystalline retinopathy affecting all 3 male siblings in a family. Arch Ophthalmol 2000;118(1):129-31.
13. Kretschmann U, Usui T, Ruether K, Zrenner E. Electroretinographic campimetry in a patient with crystalline retinopathy. Ger J Ophthalmol 1996;5(6):399-403.
14. Bernauer W, Daicker B. Bietti's corneal-retinal dystrophy. A 16-year progression. Retina 1992;12(1):18-20.
15. Meyer CH, Rodrigues EB, Mennel S, Schmidt JC. Optical coherence tomography in a case of Bietti's crystalline dystrophy. Acta Ophthalmol Scand 2004;82(5):609-12.
16. Ayata A, Tatlipinar S, Unal M, Ersanli D, Bilge AH. Autofluorescence and OCT features of Bietti's crystalline dystrophy. Br J Ophthalmol 2008;92(5):718-20.