Association Between Bietti Crystalline Fundus Dystrophy and Retinitis Pigmentosa

Bietti Kristalin Fundus Distrofisi ile Retinitis Pigmentosa Birlikteliği

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Case Report *Olgu Sunumu*

ABSTRACT

We described a case of Bietti's Crystalline Fundus Dystrophy (BCFD) who was also diagnosed with Retinitis Pigmentosa (RP). A full ophtalmologic examination was performed to a 29 years old female whose night vision has been worsening over the past few years. She was positive for RP65 mutation and yellow sparkling crystals and peripheric bony specules have been detected in her retina. According to her fundus fluorescein angiography, electroretinogram and visual field results, the patient was diagnosed with both BCFD and RP. We recommend to keep in mind that although RP may be seen associated with BCFD, BCFD may also present with RP signs and symptoms.

Key Words: Bietti's crystalline dystrophy, retinitis pigmentosa.

ÖZ

Çalışmamızda Retinitis Pigmentosa ve Bietti'nin kristalin fundus distrofisi (BKFD) tanısı konulan bir olgu sunulmuştur. Son yıllarda kötüleşen gece görüşü şikayetiyle kliniğimize başvuran 29 yaşında kadın hastanın RPE65 gen mutasyon pozitifliği mevcuttu. Hastanın yapılan tam oftalmolojik muayenesinde retinada parlak sarı kristaller ve periferik kemiksi çıkıntı şekilli pigmentasyonlar tespit edildi. Fundus floresan anjiyografi, elektroretinogram ve görme alanı sonuçlarına göre hastaya RP ve BKFD birlikteliği tanısı koyuldu. RP'nin BFKD ile beraber görülebileceği gibi, BFKD'nin de RP semptomları ve bulguları ile prezante olabileceği akılda tutulmalıdır.

Anahtar Kelimeler: Bietti'nin kristalin distrofisi, retinitis pigmentosa.

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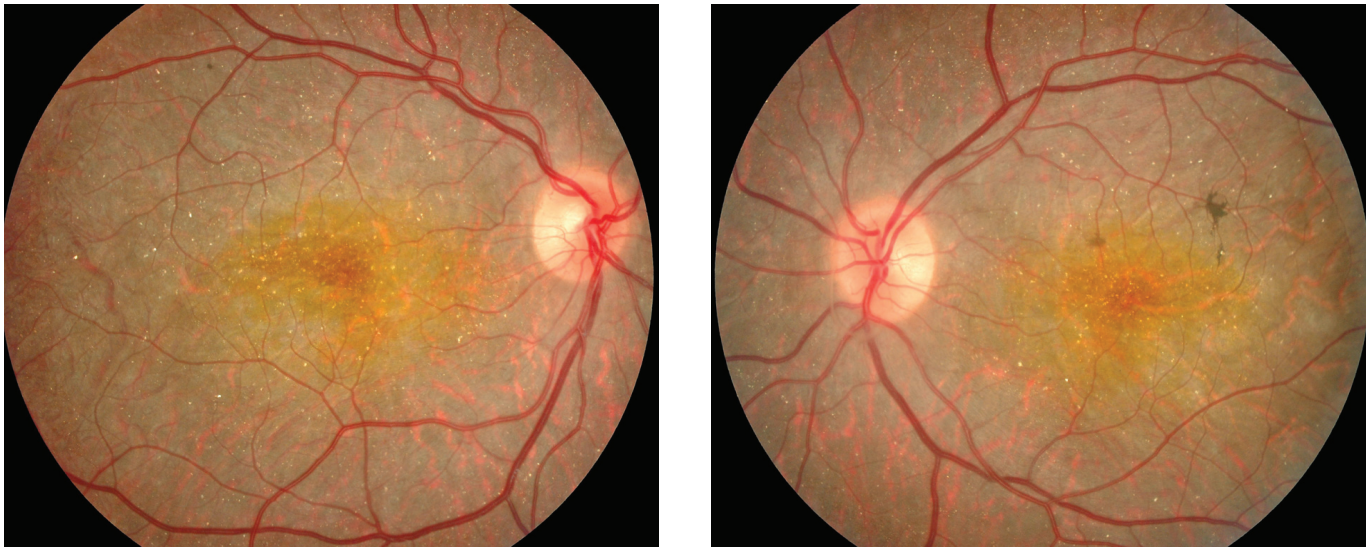

Figure 1,2: Right and left colour fundus photos revealing intraretinal sparkling yellow crystals distributed in the posterior pole, choriocapillaris atrophy, pigmentary clumping in the form of bone spicules and salt-pepper like appearance in peripheral retinal.

INTRODUCTION

Bietti's crystalline dystrophy is first described by Bietti in 1937 as a tapatoretinal degeneration characterized by crystalline deposits in limbus and retina.[1] It is a progressive disease where yellow sparkling crystal deposits consisting of complex lipid inclusions in limbal keratocytes, retina with greater amount in its posterior pole, choroidal, conjunctival and limbal fibroblasts and atrophy in retina pigment epithelium (RPE), choriocapillaris and choroid.[1-4] It causes symptoms like paracentral scotomas, night blindness, visual field constriction and progressive vision loss in 2nd-4th decades and causes legal blindness in 5th-6th decades.[5-9] It is seen commonly in asian patients and has an autosomal recessive inheritance pattern.[3,6,8] The diagnosis of BCFD is based on clinical findings; biomicroscopic and ophthalmoscopic appearance are usually sufficient to make diagnosis.[6-9]

Retinitis Pigmentosa (RP) is one of the most common forms of inherited retinal degenerations. It is a progressive retinal dystrophy causing deterioration of the night vision in early phase and constriction of the visual field leading to tunnel vision in late phase.[10-12] Hence it causes photoreceptor loss, affected people experience legal blindness in childhood or in some cases in 4th-5th decades. Mottling of the RPE with black bony specule pigmentation seen in peripheral retina is patognomanic for RP. RP can be inherited as autosomal dominant, autosomal recessive, and X-linked manner, digenetic and mitochondrial forms have been also described.[10-13] At least 35 different genes or loci mutation are known to cause nonsyndromic RP. Mutations in RPE65 is well known to cause autosomal recessive RP.[11-13] We represent here a patient with both BCFD and RP.

CASE REPORT

A 29 years old woman referred to our clinic with a complaint of decreased night and day vision that has been worsening over the past few years.

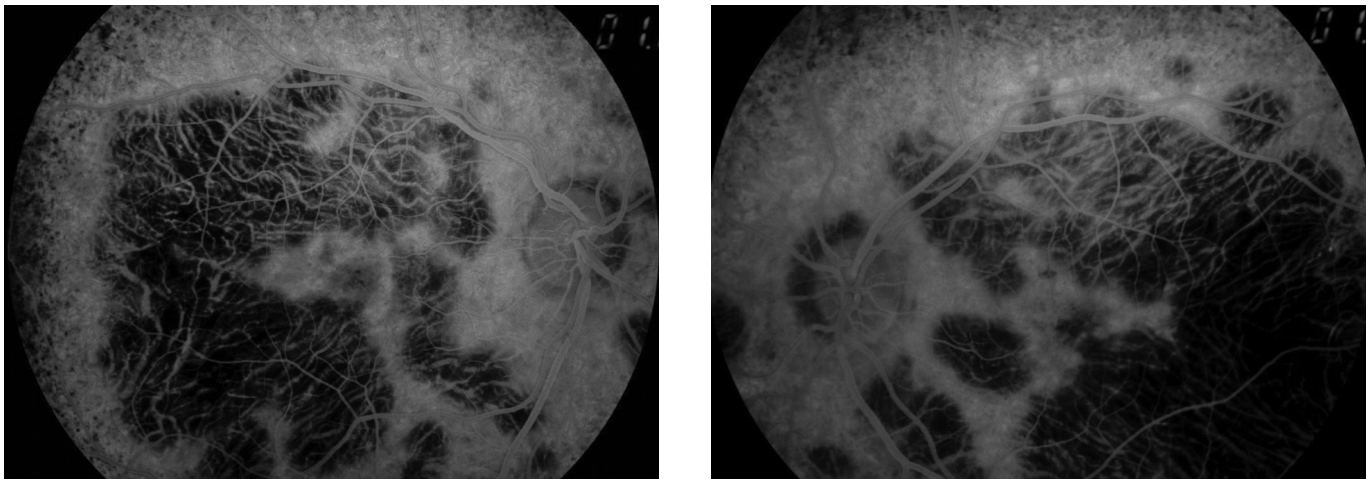

Figure 3,4: FA obtained from right and left eye demostrated focal lobular areas of choriocapillary atrophy with salt-pepper like appearance correspond to concomitant diffuse RPE changes at the peripheral retina.

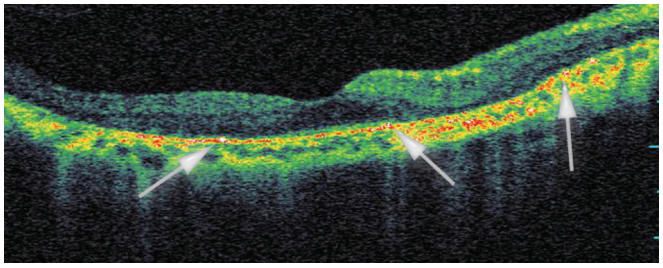

Figure 5: Choriocapillaris atrophy and hyper-reflective nodules at the level of RPE-Bruch's membrane and choriocapillaris complex correspond to crystalline deposits were seen on optical coherence tomography. The white arrows show hyper-reflective area consistent with crystallin deposits.

She denoted that she was using statins because her cholesterol and triglyceryde levels were high. She also explained that she was being followed by another clinic because of atypical RP and she was positive for RP65 gene mutation. It has been noted that her family members have also RP features. She was performed a full ophthalmologic examination. Her intraocular pressure was 16 mmHg in the right eye and 13 mmHg in the left. Her visual acquity was 0.92 log MAR in the right eye and 0.88 log MAR in the left, reaching 0.78 log MAR in both eyes with correction.

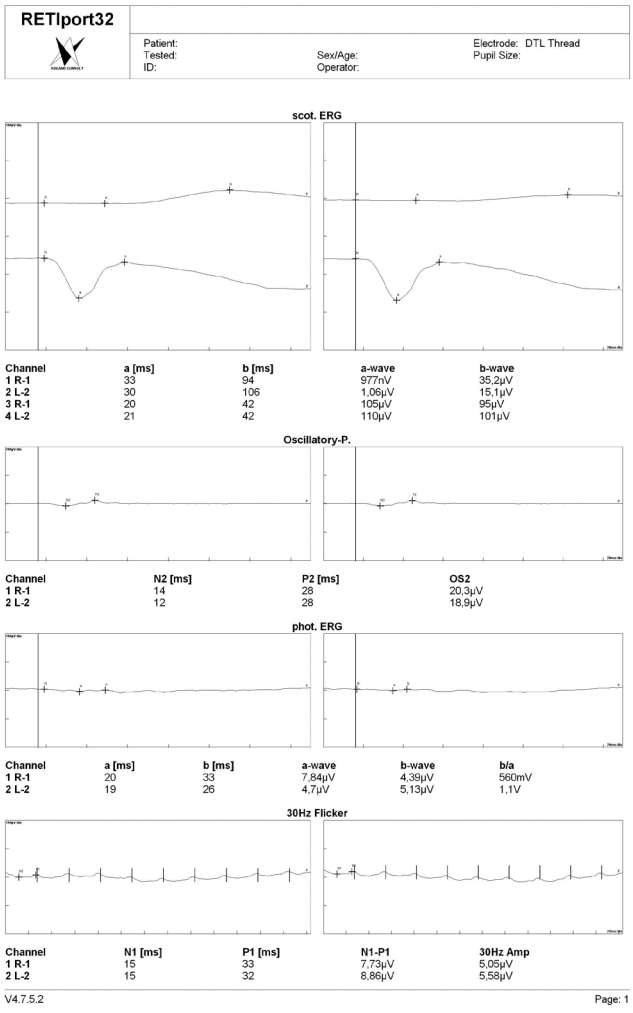

Figure 6: Her electroretinogram showed decreased scotopic a and b-wave amplitudes and the photopic a and b wave, 30 Hz flicker amplitudes were severely attenuated.

On slit lamp examination, the cornea, lens and anterior chamber were normal. There were no limbal, corneal, conjunctival crystalline deposits. She did not have any history of associated other medical conditions or drug usage. Fundus examination showed intraretinal sparkling yellow crystals distributed in the posterior pole and also midperiphery. There was midperipheral RPE and choriocapillaris atrophy, pigmentary clumping in the form of bone spicules and salt-pepper like appearance in peripheral retinal (Figure 1,2).

FA revealed the focal geographic appearance showing transmission hyperfluorescence in the crystalline retina and characteristic lobuler choriocapillaris atrophy in the adjacent noncrystalline retina (Figure 3,4). Choriocapillaris atrophy and hyper-reflective nodules at the level of RPE-Bruch's membrane and choriocapillaris complex correspond to crystalline deposits were seen on optical coherence tomography (Figure 5). Her electroretinogram (ERG) showed decreased scotopic a and b-wave amplitudes (Figure 6). Furthermore, the photopic a and b wave amplitudes were both severely attenuated. Visual field testing was performed and showed constriction of visual field bilaterally. She was diagnosed with both BCFD and RP on the basis of clinical findings, genetic and diagnostic tests, biomicroscopic and ophthalmoscopic appearance. She refused any further genetic examination or blood or cell culture.

DISCUSSION

Bietti first reported cases of tapetoretinal degeneration characterized by yellow glistering retinal crystals, choroidal sclerosis, and marginal crystalline dystrophy of the cornea.[1-3] Similar cases with no limbal crystalline deposits have been reported and called Bietti crystalline fundus dystrophy or crystalline retinopathy.

BCFD is an autosomal recessive inherited disorder associated with the CYP4-V2 gene polymorphism on 4th chromosome. This gene is responsible for synthesis of cytochrome p450 4 V2 (CYP 4 V2) enzymes functioning in fatty acid synthesis.2,6,8 CYP 4 enzymes are microsomal fatty acid Ω-hydroxylases working with mitochondrial and peroxisomal α-oxidation enzymes to degrade cellular lipids The pathogenesis of crystalline formation in BCFD is not fully understood but assumed malfunction in lipid metabolism of patients like defects in lipid binding proteins or in enzymes. The ocular and peripheral cell cultures of BCFD patients show high amounts of triglyceride and cholesterol deposition.[2-4] The abnormal inclusions are similar to those found in circulating lymphocytes, keratocytes, and conjunctival and skin fibroblasts in electron microscopy. The patient in the present study also had no corneolimbal crystals. Althuogh our patient has high cholesterol and triglyceride levels, she refused to do genetic examination or biopsy of retina for electron microscopy trial or blood sampling.

RP diagnosis is based on visual field findings and genetic analysis. In 1989 a mutation in a gene encoding rhodopsin pigment was found, one of the main proteins of the outer segments of photoreceptors and having an important role in visual transduction cascade. More than 100 other mutations have been demonstrated in the same gene since that date. The main biochemical reason for RP is protein misfolding that is caused by rhodopsin gene mutations.[5] Mutations in RPE65 is well known to cause autosomal recessive RP.[11-13] Visual field and ERG results of RP and BCFD patients are similar.[1,7,10] The visual field demonstrates predominantly a progressive loss of side vision in both of the disorders. Furthermore there may be another signs as blind spot enlargement, paracentral scotomas or altitudinal defects that seem less typical for the said disorders.[11-13]

ERG shows a marked reduction of both rod and cone signals, with general predomination of rod loss in RP patients. BCFD patients' ERG findings are mostly subnormal. Whereas some of BCFD patients have nonrecordable ERG's, patients having recordable ERGs have reduced amplitudes in scotopic, photopic and 30 Hz flicker ERG.[6,7] Our patient's visual field and ERG findings are indistinguishable between an mild stage case of RP or BCFD. An advanced BCFD case shows similarities with a RP case. Mataftsi et al., conducted a research which's aim was to determine the prevalence of BCFD in RP patients.[7] The 207 RP patients included in the study have been ophthalmologicaly examined that incorporated fluorescent and indocyanine green angiography for three years.

The study resulted in 6 patients being diagnosed with BCFD, furthermore it has been established that BCFD has a prevalence rate of 3% in nonsyndromic RP.[8] In Jiao et al., study it is said that BCFD is a form of autosomal recessive RP and accounts for 3% of nonsyndromic RP.[9] Our patient had RPE 65 mutation as an RP spesiphic mutation. Furthermore, FA findings, fundus apperance and high lipid levels in blood lead us to believe that this patient had also BCFD.

Nevertheless, the patient refused to do further genetic examination or biopsy of retina for electron microscopy trial or blood sampling. To the best of our knowledge, this is the first case report showing one patient having both RP and BCFD from Turkey.

We recommend that clinicians should keep in mind that while RP cases may show BCFD manifestations, RP and BCFD may be seen together in same patient. If there is any suspicious condition, genetic analysis should be performed. Further clinic and genetic investigations are needed to evaluate this clinical association.

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