Case Report

ANNALS OF MEDICINE & SURGERY

OPEN

A 30-year-old man with Bietti crystalline dystrophy: a rare case report from Syria

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Introduction: Bietti crystalline dystrophy (BCD) is a rare, inherited eye disease that causes progressive damage to the back of the eye (chorioretinal atrophy), characterized by sparkling crystals in the cornea and retina.
Case presention: A 30-year-old man presented with gradual vision loss in both eyes. Fundus photography revealed retinal crystals and retinal pigment epithelium atrophy, consistent with BCD. Enhanced depth imaging optical coherence tomography confirmed retinal and choroidal abnormalities, supporting the diagnosis. Genetic testing was not performed due to financial constraints.
Clinical discussion: Subretinal rAAV2/8-hCYP4V2 gene therapy for BCD is safe and effective, but COVID-19 or AAV8 antibodies may hinder its efficacy. VFQ-25 correlates with visual acuity improvement. Hypertriglyceridemia and hypercholesterolemia were observed as potential side effects.
Conclusion: Health care professionals should be vigilant in recognizing rare eye diseases like BCD, even in uncommon regions. Further research is crucial to understand BCD, develop treatments, and improve the quality of life for affected individuals.

Keywords: Bietti crystalline dystrophy, fundus autofluorescence, optical coherence tomography, retinal pigment epithelium

Introduction

Bietti crystalline dystrophy (BCD) is a chorioretinal degeneration characterized by the presence of yellow-white crystals and/or complex lipid deposits in the retina and (to a variable degree) the cornea. Progressive atrophy and degeneration of the retinal pigment epithelium (RPE)/choroid lead to symptoms similar to those of other forms of retinal degeneration that fall under the category of retinitis pigmentosa (RP) and allied disorders, namely: reduced visual acuity, poor night vision, abnormal retinal electrophysiology, visual field loss, and often impaired color vision. Marked asymmetry between eyes is not uncommon. First described by Bietti in 1937, the condition typically manifests between the second and fourth decades of life, causing significant central vision impairment, night blindness (nyctalopia), and constricted visual fields. Crystalline deposits have also been observed in skin fibroblasts and lymphocytes[1,2].

Recent advancements in genetics and diagnostic imaging, including optical coherence tomography (OCT) and optical coherence tomography angiography[3]. Treatment of manifestations: Referral to low-vision specialists and organizations/professionals trained to work with the visually impaired.

Surveillance: Periodic ophthalmologic examination to monitor disease progression and periodic visual field testing particularly as it relates to the determination of driving eligibility and eligibility for government programs and/or disability. we report a rare case of a 30-year-old man with BCD.

Case presentation

A 30-year-old man presented to the ophthalmology department with complaints of an unclear and gradual onset of decreased vision in both eyes over the past year. He also had a history of night blindness for 6 years. The visual acuity at the time of presentation was 6/60 in the right eye and 3/60 in the left eye. There are no details in the main complaint other than that; he did not suffer from any accompanying symptoms. A fundus photograph was taken, which revealed the notable presence of crystals within the retina located at the posterior pole, alongside dispersed areas of RPE atrophy. These areas are evident as filling defects in the accompanying fluorescein angiographic image (inset). Observed findings are characteristic of BCD (Fig. 1). Enhanced depth imaging optical coherence tomography (EDI-OCT) revealed disorganization of the RPE, photoreceptors, and choriocapillaris at the macula, except for the presence of a small central island of

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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Annals of Medicine & Surgery (2025) 87:2417–2420

Received 16 October 2024; Accepted 17 February 2025

Published online 7 March 2025

http://dx.doi.org/10.1097/MS9.0000000000003102

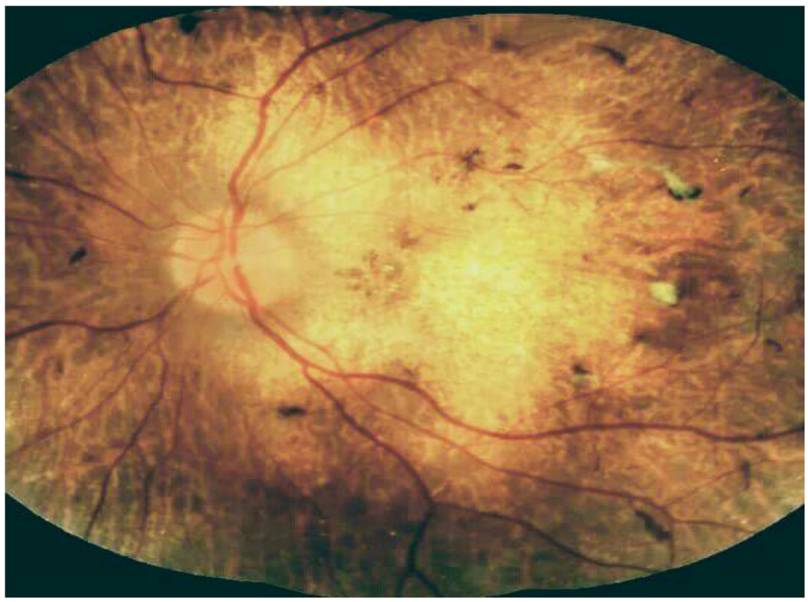

Figure 1. His fundus photograph shows a 30-year-old man with night blindness (nyctalopia) and features consistent with BCD, including intraretinal crystals and RPE atrophy.

preserved structures (Fig. 2). The parents were unavailable for examination, and the siblings exhibited no notable fundoscopic findings. Genetic testing could not be performed due to financial constraints faced by the patient. Due to resource limitations, only imaging studies were executed; no clinical intervention was conducted.

Discussion

BCD is inherited in an autosomal recessive manner. At conception, each sib of an affected individual has a 25% chance of being affected, a 50% chance of being an asymptomatic carrier, and a 25% chance of being unaffected and not a carrier. Carrier testing for at-risk relatives and prenatal testing for a pregnancy

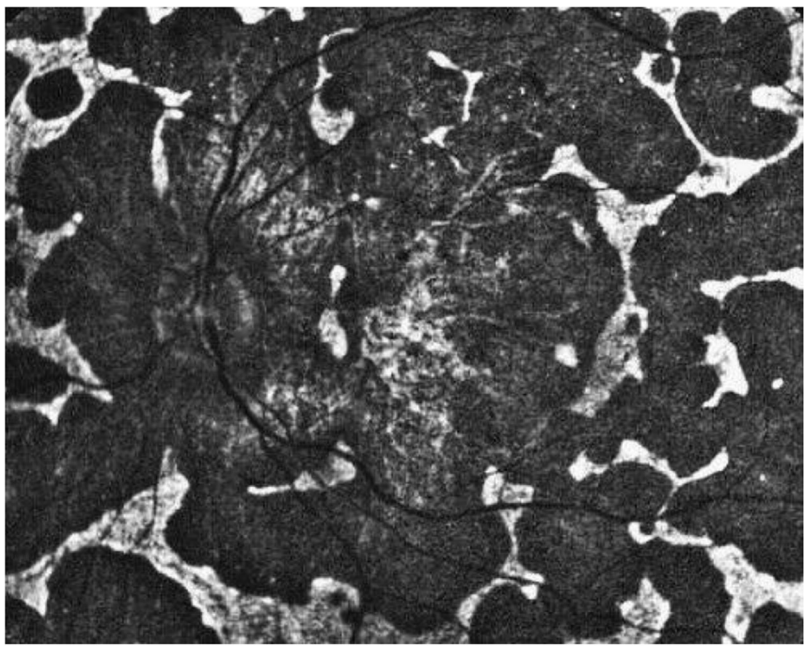

Figure 2. EDI-OCT revealed disorganization of the RPE, photoreceptors, and choriocapillaris at the macula, except for a small central island of preserved structures. A peripapillary ring was also observed. BCD is a rare, inherited chorioretinal dystrophy characterized by sparkling crystals in the cornea and retina. BCD diagnosis in resource limited and geographically unexpected patient. The diagnosis of BCD relies heavily on multimodal imagingtechniques and genetic testing.

at increased risk are possible if the pathogenic variants in the family are known. It was first reported in 1937 by Gian Battista Bietti in three patients, two of whom were siblings. According to Bietti, this uncommon disorder is an autosomal dominant tapetoretinal degeneration identified by yellow-white intraretinal crystals in the posterior pole that contribute to choroidal sclerosis and atrophy of the RPE, along with outer corneal crystals at the limbus which may also be seen[4,5].

We now know that a CYP4V2 mutation is the primary cause of BCD, which is primarily a retinal dystrophy[1]. This mutation is thought to impact the activity of an enzyme called fatty acid omega-hydroxylase in the RPE and lead to the accumulation of yellow-white crystalline-like deposits, which may also be present in the peripheral cornea close to the limbus[1,2].

And although this dystrophy is usually inherited in an autosomal recessive pattern, family members who share this disease have occasionally shown evidence of an autosomal dominant pattern, as the example in Bietti's report suggests[1,6,7].

Despite reports from all around the world, BCD is thought to be more prevalent in East Asia, particularly among Chinese and Japanese people. Furthermore, it is estimated that BCD contributes to 10% of nonsyndromic autosomal recessive RP and 3% of all nonsyndromic RP cases. Up to 1 in 67 000 people are thought to have BCD, which translates to about 21 000 people in China alone[2,8,9].

In this case, we report BCD in a middle eastern male, particularly a Syrian, which is to the best of our knowledge the first case in medical literature of a Syrian BCD patient.

BCD usually manifests between the second and fourth decades of life and progresses over time. Patients initially experience diminished vision, nyctalopia, and early-stage visual field constriction. In the fifth and sixth decades of life, patients typically have significant visual impairment, peripheral visual field loss, and legal blindness. In most cases, the progression period of the disease can extend over 5–10 years, or even longer, before vision deteriorates significantly[3,5]. However, it is important to note that patients with BCD vary widely in terms of the severity and progression of their condition. The increased clinical heterogeneity raises the possibility that dietary and genetic variables that impact lipid metabolism might have an impact on how BCD manifests and progresses.

In addition, the high degree of phenotypic variability, along with the fact that medical literature papers reporting this rare condition have mostly studied small numbers of patients, are possible reasons on why no conclusive genotype–phenotype associations have been found regarding this disease yet[3,10].

The 30-year-old male in our case presented with typical BCD symptoms consistent with nyctalopia.

To include a differential diagnosis, conditions such as hereditary syndromes or age-related degeneration or certain forms of hereditary retinitis can be considered[3,4].

However, this is specifically identified as BCD for several reasons. First, this condition is associated with a specific genetic pattern and its underlying mechanisms. Second, patients affected by it exhibit distinctive symptoms, such as progressive vision deterioration that may be accompanied by corneal deposits. Additionally, the clinical findings and diagnostic examinations differentiate them from other conditions, reinforcing the hypothesis that this is indeed BCD rather than other differential diagnoses.

The diagnosis of BCD is based on the finding of numerous small, glistening yellow-white retinal crystals associated with atrophy of the RPE, pigment clumps, and sclerosis of the choroidal vessels; variable crystalline deposits in the corneal limbus; varying degrees of rod and cone dysfunction on electroretinography; visual field defects; and reflective dots visualized by spectral domain OCT. Identification of biallelic pathogenic variants in *CYP4V2* by molecular genetic testing can confirm the diagnosis if clinical features are inconclusive. Fundus autofluorescence and OCT are essential tools for identifying the characteristic intraretinal crystals and RPE atrophy[6,11]. Genetic testing, particularly for mutations in the CYP4V2 gene, can confirm the diagnosis and help differentiate BCD from other retinal dystrophies[12]. However, in this case, genetic testing could not be performed due to financial constraints faced by the patient. This limitation highlights the significant impact of economic barriers on the ability to confirm the diagnosis and provide comprehensive genetic counseling. Despite this, early and accurate diagnosis through available imaging techniques remains crucial for monitoring disease progression and guiding management strategies.

Administering gene therapy to a patient with BCD without conducting genetic testing may be fraught with risks. Accurate diagnosis and confirmation of the presence of the appropriate genetic mutation are essential to ensure that the gene therapy will be effective and safe[2,3,13-14].

Conclusion

Despite the rarity and known regional distribution of BCD, primary care and triaging health care professionals alike should maintain a high level of suspicion for progressive and/or genetic opthalmic disease in young adults reporting vision changes.

Given the progressive nature of BCD in particular, early diagnosis, consistent disease monitoring, and patient counseling have potential to improve the quality of life even in settings with signification resource restrictions. Further research is required to understand the details of this genetic disorder and possibly find a cure for it in the future, or at least ways to reduce the symptoms and rate of progression, and improve the quality of life for patients burdened with this life-compromising condition.

Acknowledgements

We hope to thank SMSR Team Lab for their efforts and bringing our team together.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images and videos. A copy of the written consent is available for review by the editor of this journal.

Parental consent

Written informed consent was obtained from the patient/legal guardian for publication and any accompanying images. A copy

of the written consent is available for review by the Editor-in-Chief of this journal on request.

Sources of funding

Not applicable.

Author contribution

A.A.O., L.A.O., R.A.S., Z.Z.M., T.A., D.A.S., S.A.A.H., A.A.A. A., M.N.K., M.Y.M.A.A., B.S.: writing-reviewing & editing.

Conflicts of interest disclosure

No conflict of interest.

Research registration unique identifying number (UIN)

Not applicable.

Guarantor

Bilal Sleiay.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Data availability statement

Not applicable.

Methods

The work has been reported in line with the SCARE criteria.[15]

References

[1] Welch RB. Bietti's tapetoretinal degeneration with marginal corneal dystrophy crystalline retinopathy. Trans Am Ophthalmol Soc 1977;75:164–79.

[2] Osman Saatci A, Can Doruk H. An overview of rare and unusual clinical features of Bietti's crystalline dystrophy. Med Hypothesis Discov Innov Ophthalmol 2014;3:51–56.

[3] Hata M, Ikeda HO, Iwai S, *et al*. Reduction of lipid accumulation rescues Bietti's crystalline dystrophy phenotypes. Proc Natl Acad Sci 2018;115:3936–41.

[4] Bietti G. On the familial occurrence of "retinitis punctata albescens" (associated with "dystrophia marginalis cristallinea cornea)," glistening, vitreous humor and other degenerative ocular changes. Augenvera¨Nderungen Klin Monatsbl Augenheilkd 1937;99:737–56.

[5] Bagolini B, Ioli-Spada G. Bietti's tapetoretinal degeneration with marginal corneal dystrophy. Am J Ophthalmol 1968;65:53–60.

[6] Bazvand F, Asadi Khameneh E. Presumed Bietti crystalline dystrophy with optic nerve head drusen: a case report. J Med Case Rep 2022;16:413.

[7] Bocquet B, El Alami Trebki H, Roux AF, *et al*. Retinitis punctata albescens and RLBP1-allied phenotypes: phenotype-genotype correlation and natural history in the aim of gene therapy. Ophthalmol Sci 2021;1:100052.

[8] Furusato E, Cameron JD, Chan CC. Evolution of cellular inclusions in Bietti's crystalline dystrophy. Ophthalmol Eye Dis 2010;2010:9–15.

[9] Ng DS, Lai TY, Ng TK, *et al*. Genetics of Bietti crystalline dystrophy. Asia Pac J Ophthalmol (Phila) 2016;5:245–52.

[10] García-García GP, Martínez-Rubio M, Moya-Moya MA, *et al*. Identification of novel CYP4V2 genotypes associated with Bietti crystalline dystrophy and atypical anterior segment phenotypes in Spanish patients. Acta Ophthalmol 2018;96:e865–e873.

[11] Cheloni R, Clough N, Jackson D, *et al*. Longitudinal structure-function analysis of molecularly-confirmed CYP4V2 Bietti crystalline dystrophy. Nature 2023;623:853–62.

[12] Wang W, Chen W, Bai X, *et al*. Multimodal imaging features and genetic findings in Bietti crystalline dystrophy. BMC Ophthalmol 2020;20:331.

[13] Murakami Y, Koyanagi Y, Fukushima M, *et al*. Genotype and long-term clinical course of Bietti crystalline dystrophy in Korean and Japanese patients. Ophthalmol Retina 2021;5:1269–79.

[14] Zhang Z, Yan B, Gao F, *et al*. PSCs reveal PUFA-provoked mitochondrial stress as a central node potentiating RPE degeneration in Bietti's crystalline dystrophy. Mol Ther 2020;28:2642–61.

[15] Sohrabi C, Mathew G, Maria N, *et al*. The SCARE 2023 guideline: updating consensus Surgical CAse REport (SCARE) guidelines. Int J Surg Lond Engl 2023;109:1136.