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CLINICAL CASE REPORT

Retinal findings in a patient of French ancestry with *CABP4*-related retinal disease

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Abstract

Introduction *CABP4*-related retinal dysfunction is a cone–rod synaptic transmission disorder with electronegative electroretinogram (ERG) waveform. It is a rare retinal dysfunction that can be classified into the incomplete form of congenital stationary night blindness. Absent foveal reflex and overall foveal thinning were previously reported, but in most cases the fundus appearance was described as nearly normal. We report here peculiar macular changes in a patient of French ancestry harbouring *CABP4* mutations.

Methods Complete ocular examination and full-field ERG were performed at the initial presentation and follow-up. Multimodal fundus imagining, including spectral-domain optical coherence tomography, colour, infrared reflectance and short-wavelength autofluorescence photographs, was performed during follow-up visits.

Results A 7-month-old infant was addressed to our department for visual unresponsiveness and nystagmus. ERG had an electronegative waveform, even for light-adapted stimuli, thus supporting the diagnosis of photoreceptor–bipolar cell transmission disorder. Genetic investigations discovered a compound heterozygous mutation in *CABP4:* c.646C > T, p.Arg216*/c.673C > T, p.Arg225*. Multimodal fundus imaging, performed at follow-up visits, showed fine radial folds at the vitreomacular interface and dark foveal dots in both eyes. Optic coherence tomography revealed a focal foveal ellipsoid zone gap.

Discussion Initial presentation was misleading with Leber congenital amaurosis. The electronegative ERG waveform reoriented the genetic investigations and thus establishing a correct diagnosis. To the best of our knowledge, the peculiar fundus changes observed in our patient were never reported before. We

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hypothesized that a foveal ellipsoid zone interruption discovered in our patient could reflect mostly a cone dysfunction. It was unclear whether the fine radial folds in both maculae were linked with high hyperopia or were an intrinsic feature of the retinal disease.
Conclusion *CABP4*-related retinal disease is a cone–rod system disorder with possible foveal abnormalities.

Keywords CABP4 · Electroretinography · Hemeralopia · OCT · Multimodal fundus imaging

Introduction

CABP4-related retinal dysfunction (MIM: 610427) is now recognized as a peculiar ocular disease with distinctive clinical and electrophysiological features [1]. Initially, it was classified as a form of incomplete congenital stationary night blindness (icCSNB) on the basis of a scotopic electronegative ERG waveform [1, 2]. Most of the patients with icCSNB reveal mutations in *CACNA1F*, coding for the α-subunit of the calcium channel localized at the synapse of photoreceptors [3, 4]. *CABP4* codes for a calcium binding protein, similarly also localized at the synaptic terminal of photoreceptors and which is important for modulating voltage-gated calcium channel activity [5]. Later reports outlined cone system abnormalities and proposed to refer it as a congenital cone–rod synaptic disorder [6, 7]. De facto, both scotopic and photopic ERG responses are affected in case of *CABP4* mutations and the clinical picture is dominated by a severe cone system dysfunction [8, 9].

Only few patients with complete clinical and electrophysiological data were reported to this day [1, 6, 8, 9, 11, 14, 18]. Patients suffering from this disease are reported to have no visible fundus changes, except the lack of a foveal reflex [1, 9].

In order to better describe the retinal morphology of *CABP4*-related retinal disease, we report here the ophthalmic findings in a French patient of Caucasian ancestry harbouring *CABP4* mutations.

Methods

A patient with *CABP4*-related retinal dysfunction and his relatives were examined. This retrospective study was approved by our Institutional Review Board and fulfilled the tenets of the Declaration of Helsinki. Informed consent was obtained for all participants to the study.

Clinical data, including best-corrected visual acuities (BCVA) measured with tumbling E at 4 m and 30 cm distance, slit lamp and dilated fundus examinations and eye movements, were collected. Colour vision tests were performed using Farnsworth 15-Hue test.

Spectral-domain optical coherence tomography (SD-OCT) of the macula was performed with both the Zeiss Cirrus HD-OCT (Carl Zeiss Meditec, Jena, Germany) and the Spectralis OCT (Heidelberg Engineering, Inc., Heidelberg, Germany). Colour fundus imaging was performed with a Canon CF-60 UVi Fundus Camera (Canon USA Inc., New-York). Short-wavelength fundus autofluorescence (FAF) and infrared reflectance images (IRR) were obtained using a Heidelberg Retinal Tomograph (Heidelberg Engineering, Inc., Heidelberg, Germany).

Full-field electroretinogram (ERG) was recorded from both eyes following the standards of International Society of Clinical Electrophysiology of Vision (ISCEV) adapted to paediatric purpose. It was done to awakened child without any sedation after local anaesthetic application (04% oxybuprocaine). ERG recording was performed using a hand-held LED stimulator of the MonColor® unit (Metrovision, Perenchies, France). Dark-adapted ERG responses (rod response, maximal response) were obtained after 10 min of dark adaptation and light-adapted responses (cone response, 30-Hz flicker) after 5 min of light adaptation to the background luminance of 50 cd/m^2. To elicit a rod response, we used a blue flash (460 nm) of 0.0175 photopic cd-s/m^2. The strength of standard achromatic flash (maximal response, cone response and 30-Hz flicker) was 3.4 cd-s/m^2.

DNA was extracted from peripheral blood, and direct Sanger sequencing covering exon and flanking regions of genes associated with icCSNB (*CACNA1F,* NM_005183.3*; CABP4,* NM_145200.3*; CACNA2D4,* NM_006030.3) was performed on the affected subject as previously reported [10]. Family segregation was performed using Sanger sequencing.

To predict pathogenic mechanism, a software (Alamut Visual 2.7-1, Interactive Biosoftware) combines prediction program like Sorting Intolerant From Tolerant (SIFT, http://sift.jcvi.org/), Polymorphism Phenotyping v2 (PolyPhen-2, http://genetics.bwh.harvard.edu/pph2/) and Mutation Taster (http://www.mutationtaster.org/) and delivers frequencies in known databases like the Database of Single Nucleotide Polymorphisms (dbSNP, https://www.ncbi.nlm.nih.gov/snp), Exome Aggregation Consortium (ExAC, http://exac.broadinstitute.org/), Exome Variants Server (EVS, http://evs.gs.washington.edu/EVS/), 1000Genomes (http://www.1000genomes.org/) and gnomAD (http://gnomad.broadinstitute.org/). In addition, the Human Gene Mutation Database HGMD® Pro was consulted to investigate for known variants implicated in disease.

Results

The proband (Fig. 1) was examined at age of 7 months for a delayed visual development. He was not visually responsive until the age of 3 months; after this age, his visual behaviour mildly improved (fixed and followed a light source), but a nystagmus was noticed by his parents. He became photophobic at the same time.

He had a horizonto-rotatory nystagmus of low amplitude and high frequency, increasing in lateral and superior gaze, consistent with an infantile nystagmus syndrome. There was also a small-angle right esotropia.

Anterior segment examination found an iris transillumination at the iris root (Fig. 2) without any other anomaly.

Dilated fundus examination (Fig. 3) found a normal appearance of the optic disc, no foveal reflex, a starburst macular aspect with fine radial folds at the vitreomacular interface and a dark red dot lesion in both foveae.

Full cycloplegic refraction was +7.50(−1.0)180° for his right eye (RE) and +8.0(−2.0)10° for his left eye (LE).

Full-field ERG responses (Fig. 4) were markedly abnormal. The first ERG was done at the age of 6 months. The DA 0.01 showed a delayed and severely reduced b-wave. Under scotopic conditions, the DA 0.01 ERG b-wave was severely reduced and delayed, DA 3.0 showed a simplified appearance with

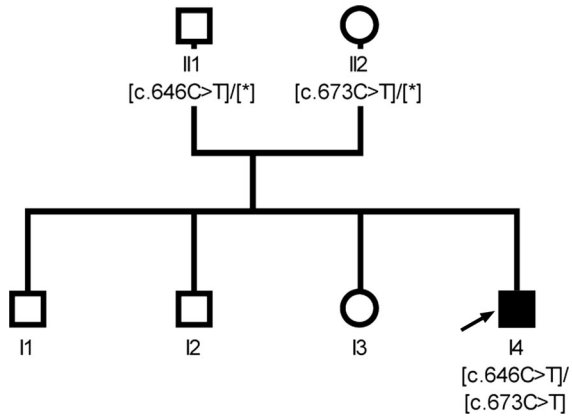

Fig. 1 Pedigree. There was no family history of visual impairment. The parents were not consanguineous. Ophthalmic examination of parents (II1, II2) and siblings (I1, I2, I3) was normal. A compound heterozygous mutation in *CABP4* (c.646C > T, p.Arg216* paternal allele [6] /c.673C > T, p.Arg225*, maternal allele [29]) was discovered in this patient (I4)

a reduced a-wave and a nearly flat b-wave. LA 3.0 ERG and LA 30 Hz were also severely reduced. In the setting of very poor visual behaviour, this "residual" ERG appearance was suggestive of LCA. A repeat ERG was done at 12 months. The DA 3.0 ERG a-wave was reduced and simplified, and the b-wave was delayed and severely reduced (b/a ratio 1.2). After photopic adaptation, the cone-specific LA 3.0 ERG a-wave was present and reduced, the b-wave was more severely reduced compared to DA 3.0 ERG (b/a ratio 0.8). The b/a ratio was 0.8 (normal > 1.4). Thus, an electronegative waveform was found in response to both DA 3.0 and LA 3.0 stimulations. LA 30-Hz flicker was of markedly reduced amplitude. This negative ERG appearance permitted us to target a genetic background research.

There was no family history of visual impairment. The family was of French Caucasian (Picard) ancestry. The parents were not consanguineous. Ophthalmic examination of parents and siblings was normal. A compound heterozygous mutation in *CABP4*(c.646C > T, p.Arg216* paternal allele/ c.673C > T, p.Arg225*, maternal allele) was discovered in this patient.

The patient was re-examined at 7 years of age. He has been attending a specialized school for visually impaired children. He had behavioural problems (autism-spectrum disorder). He complained of photophobia.

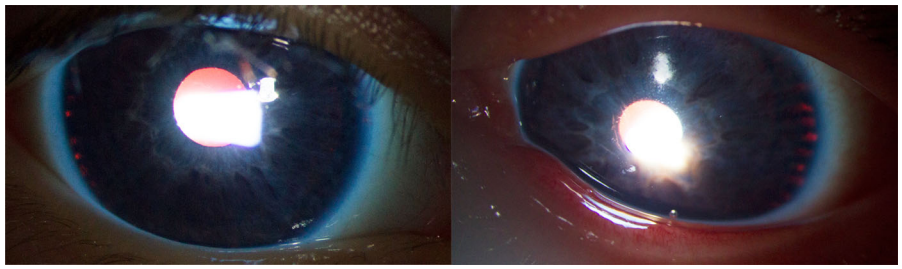

Fig. 2 Iris transillumination defects at the iris root

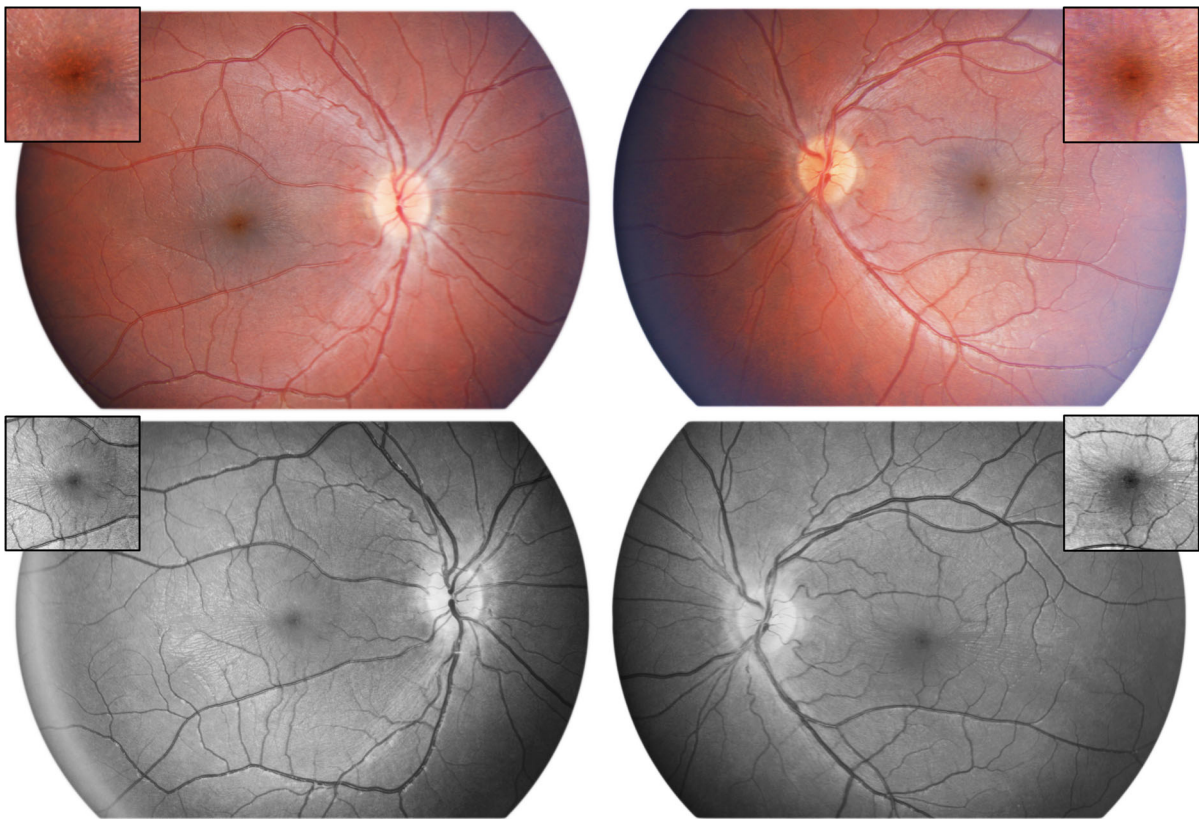

Fig. 3 Fundus photographs. *Top* colour images, *bottom* red-free images. Foveae are zoomed in. Wheel-shaped macular folds and a dark red dot were found in both eyes

Distance visual acuity was 0.008 (decimals, 4/480, logMAR 2.1) in RE and 0.005 (decimals, 4/500, logMAR 2.3) in LE after high hyperopia correction. Near visual acuity was better.

Farnsworth 15-Hue test showed multiple ranking errors without any axis.

An OCT examination (Fig. 5) was performed and revealed a foveal gap in the ellipsoid zone. Parafoveal scans showed a saw-tooth irregularity at the level of inner limiting membrane (Fig. 6).

FAF imaging was normal. IRR fundus imaging (Fig. 7) has enhanced an aspect of a dark foveal dot and radial macular folds already seen at colour fundus photographs.

Other clinical findings were unchanged from previous assessment.

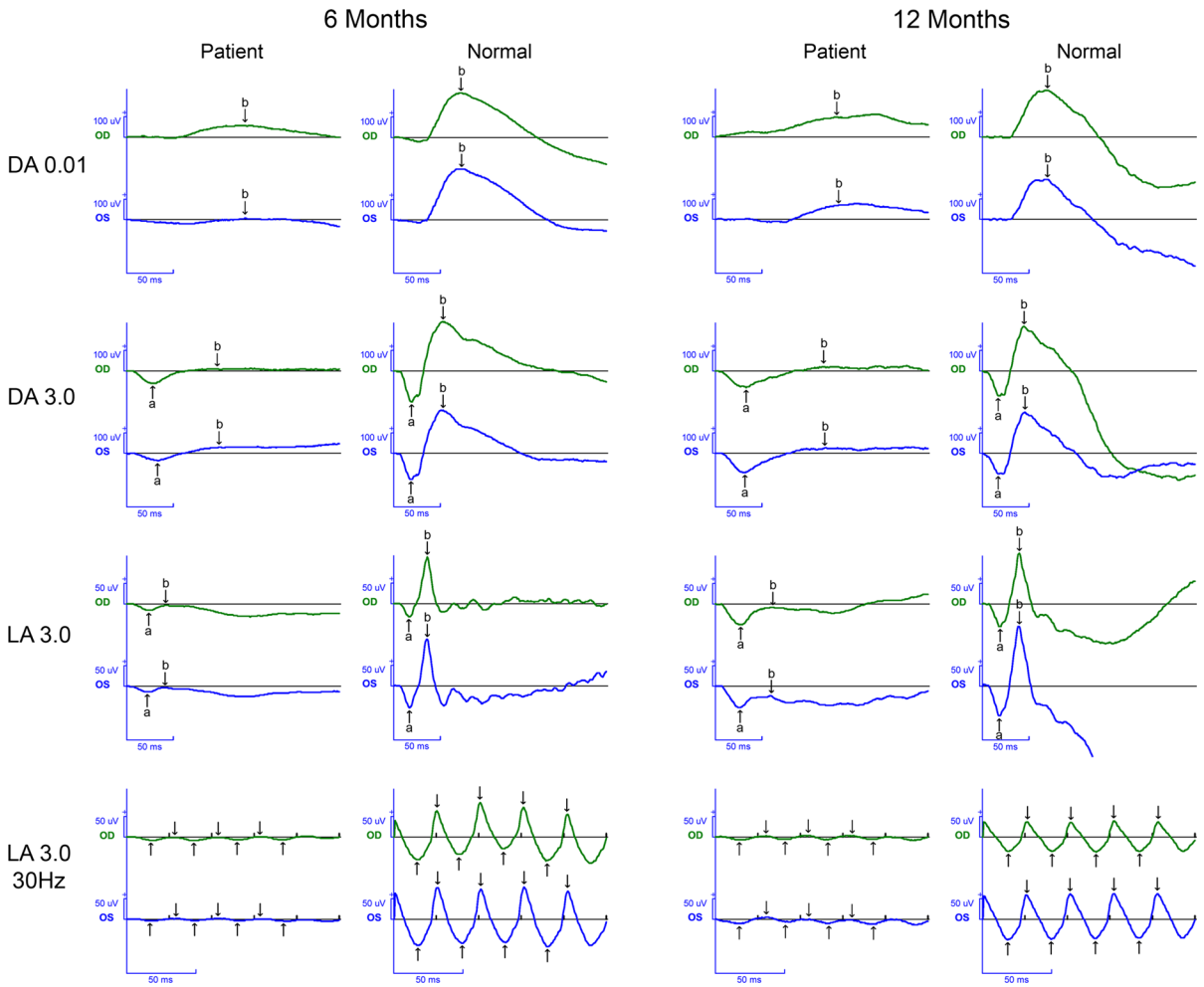

Fig. 4 Full-field ERG at the initial presentation and at the age of 12 months. The rod-specific ERG (DA 0.01) is severely reduced and delayed. Both DA 3.0 and LA 3.0 ERG showed a markedly reduced b-wave with an aspect of electronegative ERG waveform. LA 30-Hz flicker was severely reduced in amplitude

Discussion

The first patients with *CABP4* mutations were characterized as harbouring an incomplete form of congenital stationary night blindness (icCSNB). A slowly progressive course of the retinal disease was suggested [1].

Littink et al. [6] then reported that the patients did not complain of any sign of night blindness but a prominent photophobia. Cone ERGs were most severely affected: under scotopic conditions, the DA 3.0 cone a-wave was absent, rod a-wave was preserved, and the b-wave was severely reduced; under photopic conditions at LA 3.0, all a- and b-wave amplitudes were reduced with normal implicit time; 30-Hz photopic flicker (LA 30 Hz) was also of reduced amplitude. At the basis of these electrophysiological findings, it was proposed to rename the clinical phenotype as a "congenital cone–rod synaptic disorder".

Aldamesh et al. [9] pointed out that the clinical presentation resembled Leber congenital amaurosis in his patients who presented with high hyperopia, infantile nystagmus, low vision and photophobia. Another patient was separated by genetical testing from cohort of LCA [11]. In these patients, the clinical picture and a severely reduced ERG amplitude both under scotopic and photopic conditions were consistent with an LCA-like phenotype. Similar clinical features were found in our patient. Visual

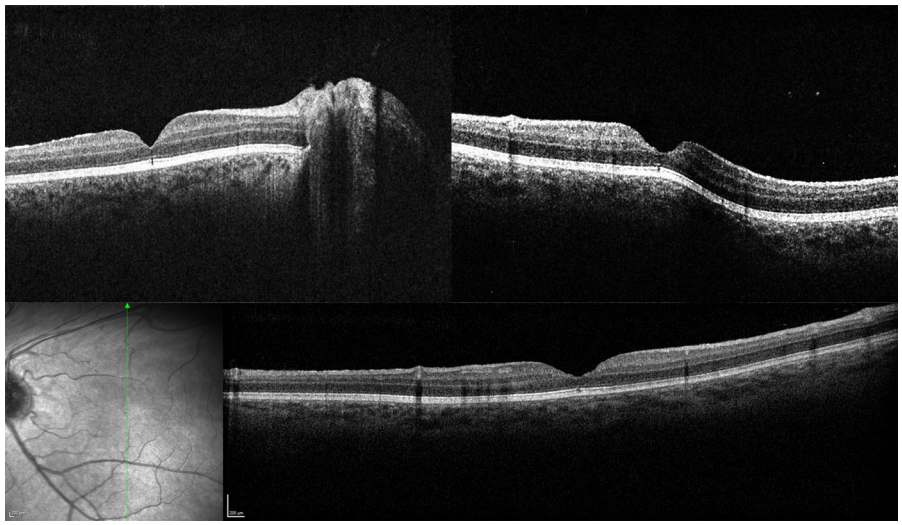

Fig. 5 OCT. *Top right* RE and *top left* LE Zeiss Cirrus HD-OCT. *Bottom* LE Heidelberg Spectralis OCT. A focal foveal interruption of the ellipsoid and interdigitation zones. Note motion artefacts from nystagmus

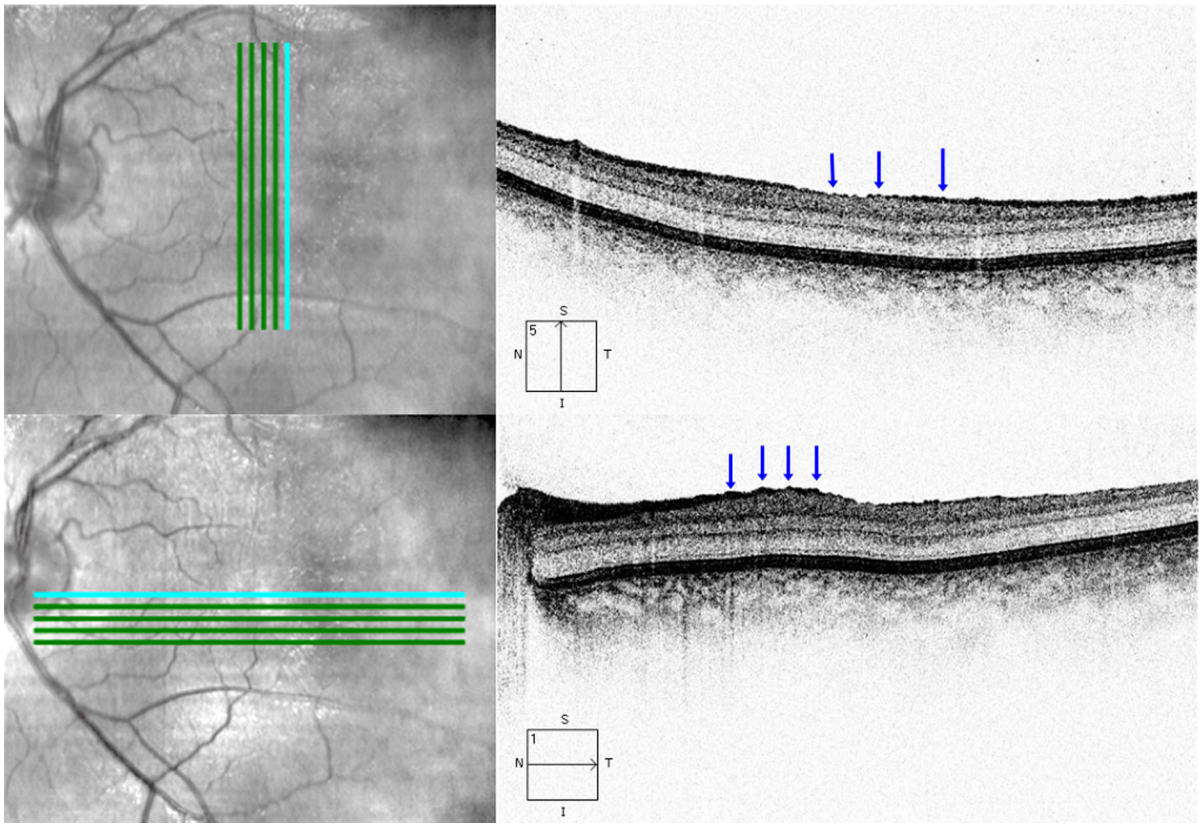

Fig. 6 Parafoveal OCT scans. Fine saw-tooth appearance (arrows) at the level of ILM

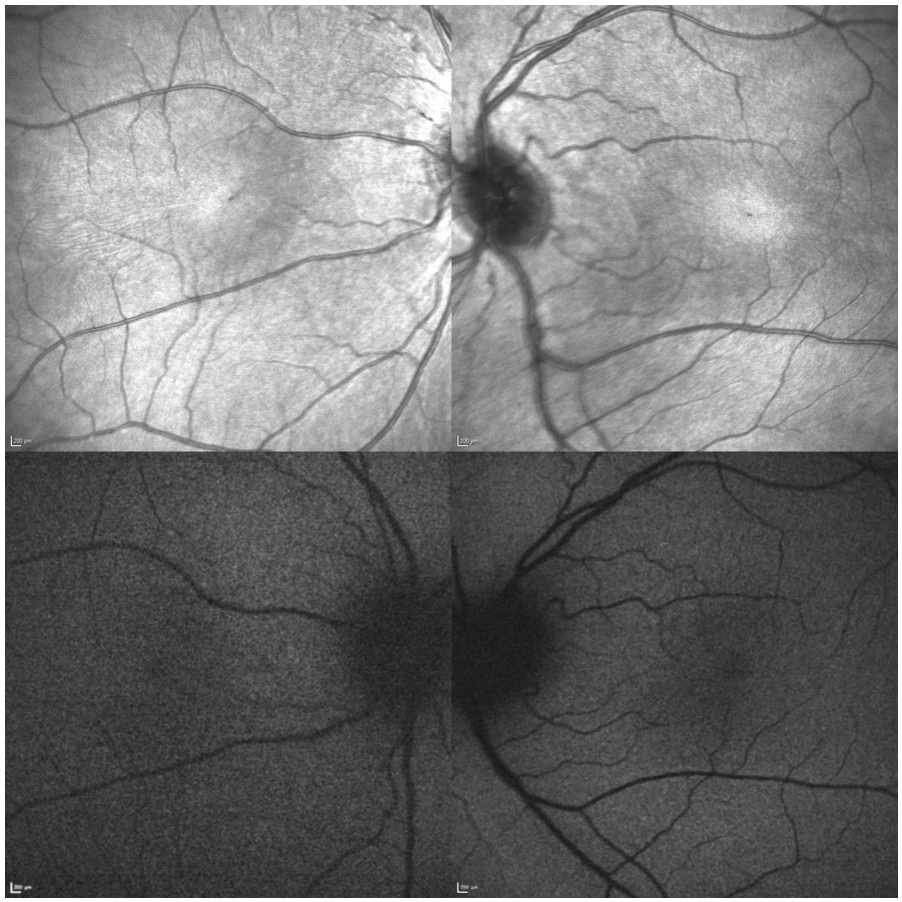

Fig. 7 *Top* infrared reflectance and *bottom* short-wavelength fundus autofluorescence imaging. IRR enhances the aspect of fine radial folds and the dark foveal dot already seen at fundus photographs. FAF shows no macular autofluorescence change

unresponsiveness, nystagmus and few if any visual improvement at follow-up were first confused with LCA. The first ERG was severely reduced but detectable. In some cases of LCA, especially in *AIPL1*-associated LCA, some ERG responses could be obtained in the first year of life but disappeared with progression of retinal degeneration [12, 13]. In our patient, ERG waveforms were always detectable and had become more distinctive at the second ERG, performed at the age of 1 year. A careful analysis of DA 3.0 response displayed an electonegative ERG waveform. This negative aspect was surprisingly persistent under photopic LA3.0 single flash, consistent with a more widespread photoreceptor transmission dysfunction than a simple icCSNB. Therefore, it was this electronegative ERG that motivated a molecular genetic research on the panel of icCSNB-associated genes.

One study points out that a *CABP4*-associated ocular phenotype could be overlapping with those of Aland eye disease (AED, Forsius-Eriksson's albinism, *CACNA1F* mutations) [14], for it is a form of icCSNB with ocular hypopigmentation. Our patient had an iris transillumination defects but no signs of retinal hypopigmentation. Slight iris transillumination could be a feature in AED [15, 16], but also could be frequently seen in healthy infants with lightly coloured iris [17]. We thought it may probably be non-specific in our patient.

Most authors agreed on the "nearly normal" fundus aspect [1, 8, 18]. Absent foveal reflex was pointed out by Zeitz et al. [1]; a granular aspect of peripheral retinal pigment epithelium was also found in one patient by Littink et al. [6]. Wang et al. [11] described their patient having *leopard* fundus, attenuated retinal vessels and normal optic disc. Our patient presented

distinctive retinal phenotype observed at the first examination and then explored by OCT, FAF and IRR imaging. Multiple fine radial folds at the vitreomacular interface and a dark dot foveal lesion were seen. A dark dot corresponded to a focal foveal interruption of ellipsoid zone on the OCT, like it had been reported in patients with cone dysfunction syndromes such as achromatopsia, S-cone monochromatism [19, 20], oligocone trichromacy [21], bradyopsia [22] and Bornholm eye disease-spectrum disorder [23]. In a patient reported by Wang et al. [11], SD-OCT depicted a lack of a foveal pit and a thinning of the surrounding inner retinal laminae; outer retinal layers were intact. A recent multimodal retinal imaging study in *CABP4*-related disorder [18] pointed out an overall retinal thinning at OCT and a normal short-wavelength fundus autofluorescence. This study underlines the difficulty of retinal imaging in case of a high-frequency nystagmus and photophobia. In these settings, we could not realize OCT mapping in our patient.

Chorioretinal and full-thickness retinal folds could be seen in patients with high hyperopia (posterior microphthalmos and nanophthalmos) [24, 25]. They are usually papillomacular, solitary and involving inner retinal layers with RPE sparing [26, 27]. In our patient, folds were instead multiple, radial and shallow. Some irregularity and saw-tooth aspect of vitreomacular interface could be seen on the OCT (Fig. 6), so we hypothesized that these folds or mostly "wrinkles" were localized at the level of inner limiting membrane (ILM). Radial folding of ILM was previously reported in the setting of diabetic macular oedema [28] but, to the best of our knowledge, not in association with inherited retinal diseases. It is thus unclear whether these peculiar radial folds in our patient were linked with high hyperopia or were part of the *CABP4*-related retinal phenotype.

Our patient was harbouring a compound heterozygous mutation in *CABP4* (c.646C > T, p.Arg216*/c.673C > T, p.Arg225*). The c.646C > T nonsense mutation in exon 4 of *CABP4* was already reported by Littink et al. [6] in two Dutch siblings. The authors demonstrated that mutant mRNA is not subject to nonsense-mediated mRNA decay but hypothesized that the truncated mutant *CABP4* protein (p.Arg216*) was degraded or non-functional. Clinical phenotype of these patients was quite similar with the one presented by our patient: photophobia, severely reduced visual acuity, nystagmus and high hyperopia. Nevertheless, fundus examination was unremarkable in distinction with our patient. Patients presented not any change for 6 years of follow-up.

The second maternally inherited variant, c.673C > T, p.Arg225*, was recently reported by Carss et al. [29] at the homozygous state in a South Asian female patient with cone dystrophy. This mutation could also lead to a truncated protein which would be either degraded or non-functional. Unfortunately, extended clinical phenotype is unavailable. One may argue that this case of cone dystrophy was in fact a cone–rod inner dysfunction as presented herein.

In conclusion, we describe fine radial folds at the vitreomacular interface, dark foveal dot and foveal ellipsoid gap in a patient with *CABP4*-related retinal disease. Deep phenotyping in additional cases will determine whether this finding is a common feature of the peculiar phenotype associated with *CABP4* mutations.

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Compliance with ethical standards

Conflict of interest None.

Statement of human rights This retrospective study was approved by our Institutional Review Board and fulfilled the tenets of the Declaration of Helsinki.

Statement on the welfare of animals No animals participed in this study.

Informed consent Informed consent was obtained for all participants to the study.

Patient consent Patients' parents have consented to the submission of the case report to the journal.

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References

1. Zeitz C, Kloeckener-Gruissem B, Forster U et al (2006) Mutations in CABP4, the gene encoding the Ca2 + -

binding protein 4, cause autosomal recessive night blindness. Am J Hum Genet 79:657–667. https://doi.org/10.1086/508067
2. Zeitz C, Robson AG, Audo I (2015) Congenital stationary night blindness: an analysis and update of genotype–phenotype correlations and pathogenic mechanisms. Prog Retin Eye Res 45:58–110. https://doi.org/10.1016/j.preteyeres.2014.09.001
3. Bech-Hansen NT, Naylor MJ, Maybaum TA et al (1998) Loss-of-function mutations in a calcium-channel alpha1-subunit gene in Xp11.23 cause incomplete X-linked congenital stationary night blindness. Nat Genet 19:264–267. https://doi.org/10.1038/947
4. Strom TM, Nyakatura G, Apfelstedt-Sylla E et al (1998) An L-type calcium-channel gene mutated in incomplete X-linked congenital stationary night blindness. Nat Genet 19:260–263. https://doi.org/10.1038/940
5. Maeda T, Lem J, Palczewski K, Haeseleer F (2005) A critical role of CaBP4 in the cone synapse. Investig Opthalmology Vis Sci 46:4320. https://doi.org/10.1167/iovs.05-0478
6. Littink KW, van Genderen MM, Collin RWJ et al (2009) A novel homozygous nonsense mutation in CABP4 causes congenital cone-rod synaptic disorder. Invest Ophthalmol Vis Sci 50:2344–2350. https://doi.org/10.1167/iovs.08-2553
7. Khan AO (2014) CABP4 mutations do not cause congenital stationary night blindness. Ophthalmology 121:e15. https://doi.org/10.1016/j.ophtha.2013.11.005
8. Khan AO, Alrashed M, Alkuraya FS (2013) Clinical characterisation of the CABP4-related retinal phenotype. Br J Ophthalmol 97:262–265. https://doi.org/10.1136/bjophthalmol-2012-302186
9. Aldahmesh MA, Al-Owain M, Alqahtani F et al (2010) A null mutation in CABP4 causes Leber's congenital amaurosis-like phenotype. Mol Vis 16:207–212
10. Neuillé M, Malaichamy S, Vadalà M et al (2016) Next-generation sequencing confirms the implication of SLC24A1 in autosomal-recessive congenital stationary night blindness. Clin Genet 89:690–699. https://doi.org/10.1111/cge.12746
11. Wang S, Zhang Q, Zhang X et al (2016) Clinical and genetic characteristics of Leber congenital amaurosis with novel mutations in known genes based on a Chinese eastern coast Han population. Graefes Arch Clin Exp Ophthalmol 254:2227–2238. https://doi.org/10.1007/s00417-016-3428-5
12. Lorenz B, Gyürüs P, Preising M et al (2000) Early-onset severe rod-cone dystrophy in young children with RPE65 mutations. Invest Ophthalmol Vis Sci 41:2735–2742
13. Pennesi ME, Stover NB, Stone EM et al (2011) Residual electroretinograms in young leber congenital amaurosis patients with mutations of AIPL1. Invest Ophthalmol Vis Sci 52:8166–8173. https://doi.org/10.1167/iovs.11-8298
14. Hove MN, Kilic-Biyik KZ, Trotter A et al (2016) Clinical characteristics, mutation spectrum, and prevalence of Åland eye disease/incomplete congenital stationary night blindness in Denmark. Invest Ophthalmol Vis Sci 57:6861–6869. https://doi.org/10.1167/iovs.16-19445
15. Forsius H, Eriksson AW (1964) A new eye syndrome with X-chromosomal transmission: a family clan with fundus albinism, fovea hypoplasia, nystagmus, myopia, astigmatism and dyschromatopsia. Klin Monatsbl Augenheilkd 144:447–457
16. van Dorp DB, Eriksson AW, Delleman JW et al (1985) Aland eye disease: no albino misrouting. Clin Genet 28:526–531
17. Sjödell L, Sjöström A, Abrahamsson M (1996) Transillumination of iris and subnormal visual acuity–ocular albinism? Br J Ophthalmol 80:617–623
18. Schatz P, Elsayed MEAA, Khan AO (2017) Multimodal imaging in CABP4-related retinopathy. Ophthalmic Genet. https://doi.org/10.1080/13816810.2017.1289543
19. Thiadens AAHJ, Somervuo V, van den Born LI et al (2010) Progressive loss of cones in achromatopsia: an imaging study using spectral-domain optical coherence tomography. Invest Ophthalmol Vis Sci 51:5952–5957. https://doi.org/10.1167/iovs.10-5680
20. Barthelmes D, Sutter FK, Kurz-Levin MM et al (2006) Quantitative analysis of OCT characteristics in patients with achromatopsia and blue-cone monochromatism. Invest Ophthalmol Vis Sci 47:1161–1166. https://doi.org/10.1167/iovs.05-0783
21. Smirnov V, Drumare I, Bouacha I et al (2015) Long-term follow-up of two patients with oligocone trichromacy. Doc Ophthalmol Adv Ophthalmol 131:149–158. https://doi.org/10.1007/s10633-015-9508-8
22. Strauss RW, Dubis AM, Cooper RF et al (2015) Retinal architecture in RGS9- and R9AP-associated retinal dysfunction (Bradyopsia). Am J Ophthalmol 160(1269–1275):e1. https://doi.org/10.1016/j.ajo.2015.08.032
23. Carroll J, Dubra A, Gardner JC et al (2012) The effect of cone opsin mutations on retinal structure and the integrity of the photoreceptor mosaic. Invest Ophthalmol Vis Sci 53:8006–8015. https://doi.org/10.1167/iovs.12-11087
24. Boynton JR, Purnell EW (1975) Bilateral microphthalmos without microcornea associated with unusual papillomacular retinal folds and high hyperopia. Am J Ophthalmol 79:820–826
25. Relhan N, Jalali S, Pehre N et al (2016) High-hyperopia database, part I: clinical characterisation including morphometric (biometric) differentiation of posterior microphthalmos from nanophthalmos. Eye Lond Engl 30:120–126. https://doi.org/10.1038/eye.2015.206
26. Jackson TE, Yang YC, Shun-Shin GA (2012) Spectral domain optical coherence tomography findings in retinal folds associated with posterior microphthalmos. J AAPOS Off Publ Am Assoc Pediatr Ophthalmol Strabismus 16:389–391. https://doi.org/10.1016/j.jaapos.2012.02.020
27. Park SH, Ahn YJ, Shin SY, Lee YC (2016) Clinical features of posterior microphthalmos associated with papillomacular fold and high hyperopia. Clin Exp Optom 99:590–593. https://doi.org/10.1111/cxo.12371
28. Abe S, Yamamoto T, Kashiwagi Y et al (2013) Three-dimensional imaging of the inner limiting membrane folding on the vitreomacular interface in diabetic macular edema. Jpn J Ophthalmol 57:553–562. https://doi.org/10.1007/s10384-013-0275-3
29. Carss KJ, Arno G, Erwood M et al (2017) comprehensive rare variant analysis via whole-genome sequencing to determine the molecular pathology of inherited retinal disease. Am J Hum Genet 100:75–90. https://doi.org/10.1016/j.ajhg.2016.12.003