CASE REPORT

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A RARE CASE OF CENTRAL AREOLAR CHOROIDAL DYSTROPHY

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Abstract. *The aim is to present a rare clinical case of central areolar choroidal dystrophy (CACD), confirmed clinically and electrophysiologically. A 49-year-old man underwent a detailed ophthalmological examination, fundus autofluorescence, fluorescein angiography, optical coherence tomography, visual field testing, electrophysiological (EF) studies – full-field ERG and multifocal ERG, thanks to which the diagnosis was established. A classic CACD phenotype with slightly reduced visual acuity, central scotomas, atrophy of the outer layers of the retina and the choroid in the macula and hypoautofluorescence in the macula were demonstrated. EF studies showed absence of diffuse photoreceptor involvement. The local mfERG photopic response was slightly reduced. The relatively good functional results and the pronounced anatomical changes are due to the later, secondary involvement of the photoreceptors in the macular area, characteristic of choroidal dystrophies. The comprehensive clinical and EF testing of patients with rare hereditary retinal dystrophies is essential for the correct diagnosis given the many clinical trials of new innovative therapies for many of these diseases. It is expected that some of them would become curable in the very near future, and we should be prepared when that moment comes.*

Key words: *hereditary retinal dystrophy, central areolar choroidal dystrophy, electrophysiology, rare eye disease*

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INTRODUCTION

Hereditary retinal dystrophies are a heterogeneous group of inherited diseases, characterized by involvement of different retinal layers, most often the complex retinal pigment epithelium (RPE) – photoreceptors and cause severe visual impairment [1, 2].

Choroidal dystrophies (CD) are rare inherited diseases (frequency less than 1:50 000 population cases in Europe), many of which are concentrated in the Scandinavian countries. CD are characterized by progressive degeneration of RPE and choriocapillaris. Recently it is known that the choroid atrophy is a late stage of the disease and does not reflect its etiology. The choroid dystrophies affect more often the retinal periphery. The cases in which the macula is initially affected are very rare, four times rarer than the peripheral CDs [3-5]. The central areolar choroid dystrophies (CACD) are

most commonly caused by mutations in the peripherin-2 (*PRPH2*) gene. To date, seven different mutations in the *PRPH2* gene have been identified to cause the CACD phenotype [5, 6].

The degeneration initially manifests as well-defined, bilateral symmetrical pigmented spots in the macular area which gradually confluent and lead to atrophy of RPE, choriocapillaris and neurosensory retina, exposing the atrophic choroid with the choroidal vessels coursing over the bare sclera. The fovea is preserved for a long time. This condition may be asymptomatic for a long period since the cones are secondary affected which leads to visual acuity reduction, central scotomas and affected color vision [3, 4]. Macular changes usually begin between 20 and 40 years of age and progress gradually leading to severe vision loss between the fourth and seventh decade. The peripheral retina is not affected. Hypofluorescent atrophic areas are found in fluorescein angiography (FA) and fundus-autofluorescence (FAF). Optical coherent tomography (OCT) revealed a thinning of the retina and choroid is detected. The large choroidal vessels traversing the area of involvement are not affected [5, 7-9]. Usually the scotopic ERG is not affected. In the initial stages, the photopic ERG is also normal or slightly decreased. In the advanced stages, the local photopic response is undetectable and the diffuse photopic response is reduced [10, 11].

Four clinical stages of the disease have been described [8].

Stage 1 – Minimal focal parafoveal pigmentary RPE changes which are observed ophthalmoscopically.

Stage 2 – Round to oval area of atrophic hypopigmented area which is poorly demarcated.

Stage 3 – One or more patches of well demarcated area of RPE atrophy which are present outside the central fovea and within the area of mild hypopigmentation.

Stage 4 – Atrophic area which is well-defined and involves the fovea. This causes profound loss of vision [8].

CASE PRESENTATION

Herein, we describe a rare case of CACD, confirmed clinically and electrophysiologically.

We present a 49-year-old man with complaint of slight loss of vision, which he noticed a year ago. There were no known relatives with such complaint. He underwent a detailed ophthalmological examination, including FAF, FA, OCT (Topcon 3D OCT 2000 FA plus), visual field testing (Optopol PTS 920, Optopol Tech), electrophysiological studies – full-field ERG and multifocal ERG (NeuroMEP 4, Neurosoft Company), thanks to which the diagnosis was established.

A written informed consent was obtained from the patient in accordance with the ethics standards defined in the Declaration of Helsinki (2013).

The patient' best corrected visual acuity (BCVA) was 0.2 (LogMar ETDRS) with -0.75 D sph right eye and 0.0 with -0.75 D sph left eye. His color vision was affected. Symmetrical well demarcated hypopigmented areas in the macula of both eyes were observed in fundus-photography. The left eye was more preserved with changes away from the fovea, which corresponded to the better visual acuity of the left eye. A detailed ophthalmological examination (including fluorescein angiography (FA) and fundus-autofluorescence (FAF)) found absence of fundus autofluorescence and hypofluorescence in FA of the well-defined areas of chorio-retinal atrophy with enhanced visibility of the underlying residual choroidal vessels (Fig. 1). The peripheral retina was normal in both eyes.

Optical coherent tomography (OCT) revealed the characteristic appearance of retinal and choroidal thinning with loss of the outer retinal layers up to the external limiting membrane and thinning of RPE-Bruch's membrane complex in the atrophic areas. They were surrounded by disrupted outer retina with increased irregularity with retinal elevation and loss of reflectivity. There were characteristic plaque-like structures beneath the retinal elevation that can be misdiagnosed as drusen-like deposits (Fig. 2).



Fig. 1. Fundus-photography, FAF and FA (the explanation is in the text)

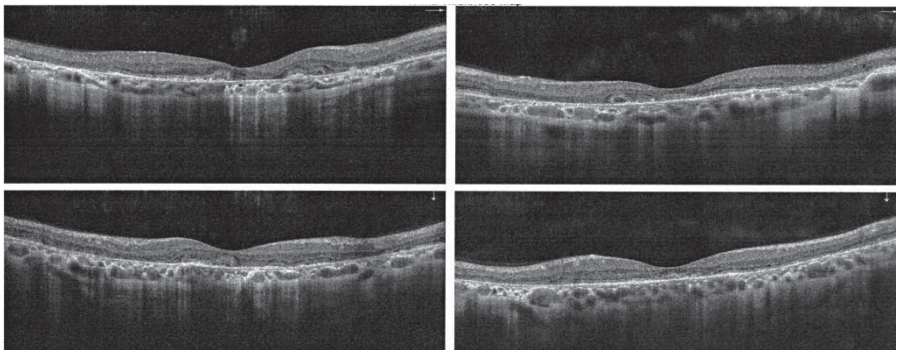


Fig. 2. OCT of the patient (the explanation is in the text)

Central and paracentral scotomas, corresponded to the atrophic areas, were detected in the visual field testing 30º (Fig. 3)

In ffERG which detects the summated response of the cones and rods of the entire retina separately, the diffuse photopic response was very slightly reduced, the diffuse scotopic response of the left eye was slightly reduced also, which corresponded to the more peripheral expansion of the atrophic area in the left eye (Fig. 4).

In mfERG, which allows to assess localized damages, a slightly reduced central response in both eyes was demonstrated, but the results were relatively good considering the severe pictures observed on OCT and FAF (Fig. 5). The EF findings corresponds to the good visual acuity. The explanation is the secondary, later involvement of the photoreceptors.

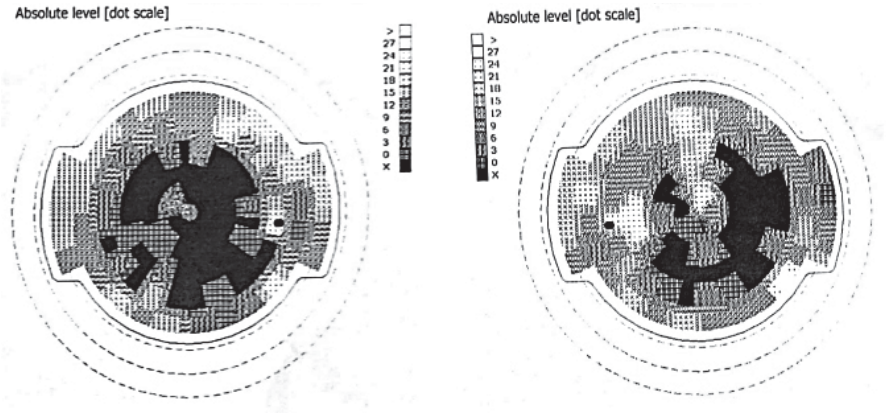


Fig. 3. Visual field testing 30º right eye and left eye (the explanation is in the text)

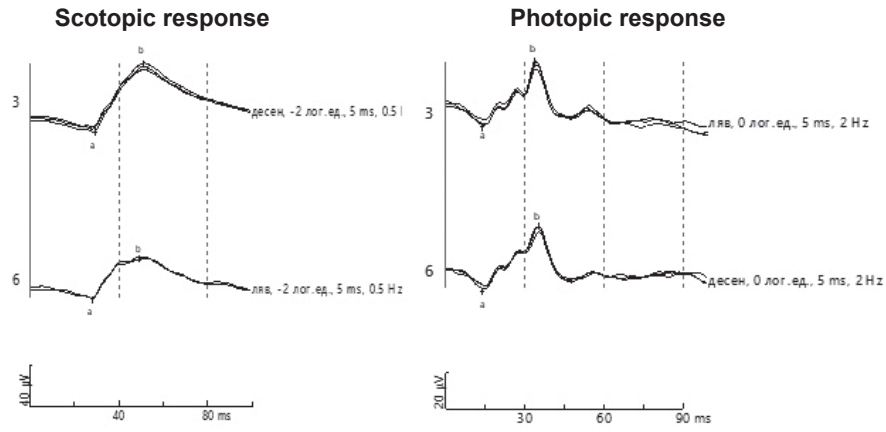


Fig. 4. FfERG scotopic and photopic responses (the explanation is in the text)

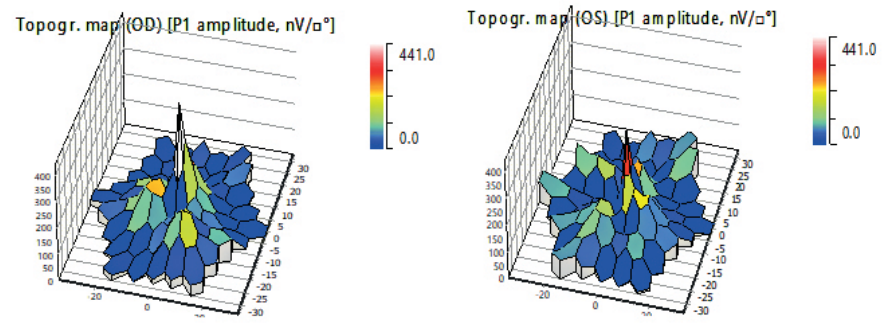


Fig. 5. MfERG (the explanation is in the text)

DISCUSSION

Here we discussed a case of CACD with a long asymptomatic period since the photoreceptors were secondary affected. The macular changes usually begin between 20 and 40 years of age and progress slowly leading to severe vision loss between the fourth and seventh decade. The functional changes in our case were detected by the patient near the age of fifty but the structural changes that we detected were advanced. The disease can be classified as stage 3 since the fovea was still preserved [5, 8]. The differential diagnosis is very important. At this age the condition may be confused with early geographic atrophy in age related macular degeneration (AMD). The difference is that there are no drusen and the atrophic areas are well demarcated and with more regular shape than in AMD. Another difference is that in CACD the atrophic areas are bilateral and more symmetrical than in AMD. In eyes with AMD, the abnormal FAF pattern frequently extends beyond the macula and covers the entire posterior fundus. The genetic testing for PRPH2 screening is very important. Unfortunately in our country it is not reimbursed and is prohibitive for most of the patients [5, 12-17].

It may be challenging to diagnose CACD in the early stages of the disease because of the relative nonspecific RPE abnormalities. The early-onset variant of CACD may be confused with other hereditary retinal dystrophies, more often with Stargardt disease in which the early onset in childhood is characteristic. In Stargardt disease the functional changes occur earlier with severe visual acuity decrease and severe reduction of the central response in mfERG. In the fundus, pigment displacement in the central macula can be observed, which forms a granular appearance of the macula. In FAF small hypoautofluorescent areas in the fovea can be found due to the abnormal RPE. In FA the characteristic “choroid silence” and granular hyperfluorescence of the macula is characteristic. Atrophy of the photoreceptors and RPE layers and accumulation of hyperreflective material in the macular area can be visualized on OCT [8, 18]. All these different features help us recognize the diseases. Very important is also the genetic test.

CONCLUSION

Thanks to the modern diagnostic methods which clearly demonstrate the structural and functional retinal changes in the macula in this case, the clinical diagnosis is relatively easy. Even though the disease is incurable at the moment, many clinical trials investigating experimental therapies are currently underway and it is expected some of them to be effective enough, so we should be prepared to embrace these new therapies in the near future, but more importantly, should be able to diagnose these diseases in the first place [15, 19, 20]. The medico-genetic consultation is also very important, as the disease is hereditary. The comprehensive clinical and electrophysiological testing of patients with rare hereditary retinal dystrophies is essential for the correct diagnosis and the choice of therapeutic strategy.

Disclosure Summary: *The authors have nothing to disclose.*

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