Occult macular dystrophy: brief literature review

Distrofia macular ocular: breve revisão da literatura

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ABSTRACT

Occult macular dystrophy is characterized by a slowly progressive bilateral reduction of visual acuity in patients with normal fundus and fluorescein angiography. We describe a case of a 36-year-old male patient diagnosed with this condition, after extensive investigation with multimodal imaging, electrophysiology tests, and systemic screening.

RESUMO

A distrofia macular oculta é caracterizada por perda visual, lentamente progressiva, em pacientes com fundoscopia e angiografia fluoresceínica normais. Relatamos o caso de um paciente de 36 anos do sexo masculino diagnosticado com essa condição após extensa investigação com exames de imagem multimodais, eletrofisiológicos e rastreio de doenças sistêmicas.

INTRODUCTION

Occult macular dystrophy (OMD) is a slowly progressive macular condition characterized by a progressive bilateral decrease of visual acuity (VA) associated with normal fundus and fluorescein angiography.[1] Although classically described as a dominant inherited retinal dystrophy, currently two forms of OMD are known: hereditary and sporadic. The first one is mostly associated with variants in the RP1L gene (in 50% of the cases).[2-4]

This condition is called occult because patients usually present with a progressive reduction in VA, despite having a normal fundus, fluorescein angiography, and with both the rod and cone components of the full-field electroretinogram (ERG) essentially normal. However, focal macular ERG and multifocal ERG (mERG) are severely attenuated. The optical coherence tomography (OCT) shows structural changes in the outer nuclear and/or photoreceptor layers.

We describe a case of a 36-year-old male patient, complaining of progressive visual loss, without fundoscopic or angiographic findings that could explain his symptoms, who was diagnosed with OMD after extensive investigation.

The patient signed a consent form allowing the description of his case.

CASE REPORT

A 36-year-old male patient was referred to our hospital, complaining of progressive and painless central visual loss, associated with photophobia that had started 3 years before. He referred being evaluated by multiple ophthalmologists, without any diagnosis. At the moment the symptoms started, according to his medical records from previous visits to other hospitals, his best-corrected VA (BCVA) was 20/60 and 20/50 in his right (OR) and left (OS) eyes, respectively, with normal findings on fundus examination, visual field, and OCT. Full-field ERG was also normal.

On his first visit to our hospital, he was complaining of worsening photophobia and VA. His high contrast BCVA was 20/400 and 20/150. However, when tested using his sunglasses, his BCVA improved to 20/80 and 20/60, respectively. Fundoscopy was normal (Figure 1), as well as the fluorescein angiography. A full-field ERG was repeated, with normal results. Nevertheless, mERG showed reduction in the amplitude of P1 in foveal and perifoveal areas in the OR. The left eye showed a reduction of P1 amplitude but was still considered in range of normal values (Figure 2). The patient's past and family histories were unremarkable. He also denied being exposed to laser, radiation, or use of any drugs.

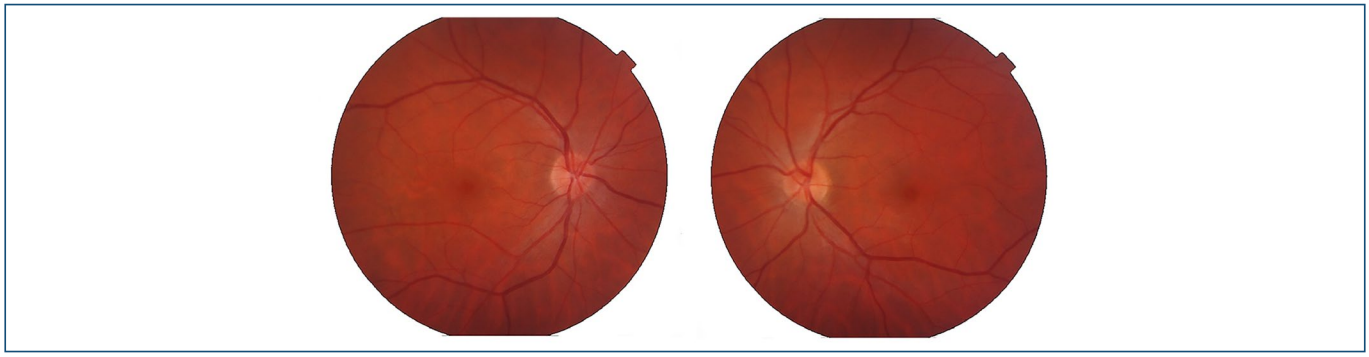

Figure 1. Normal fundus in both eyes.

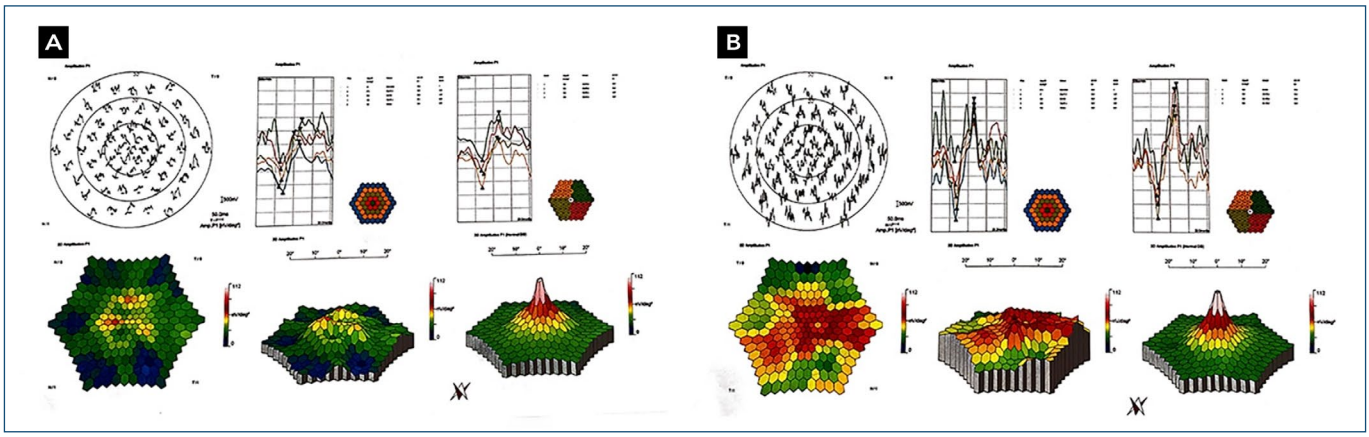

Figure 2. (A) Reduction in the amplitude of P1 in the foveal and perifoveal areas in the right eye. (B) The left eye showed a reduction of P1 amplitude but was still considered in the range of normal values.

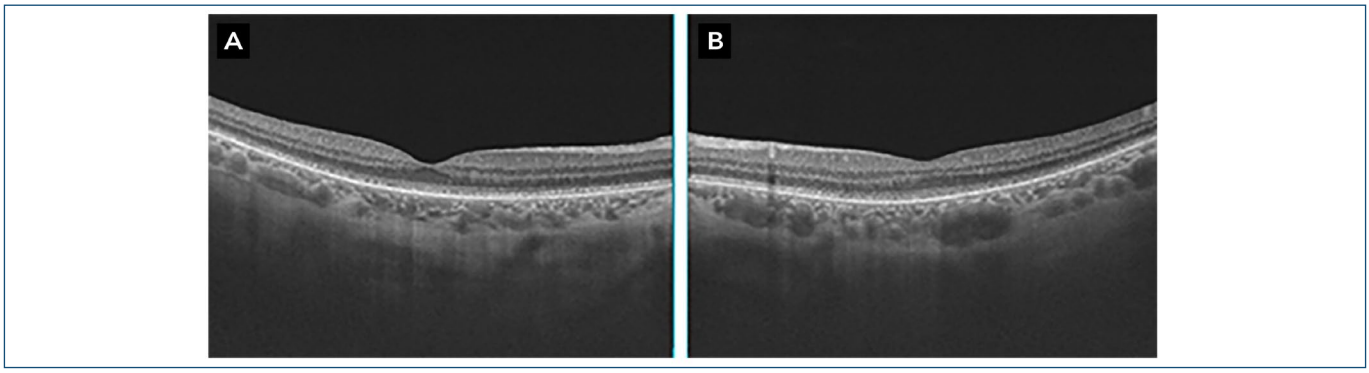

Figure 3. Optical coherence tomography showing blurring of the ellipsoid in both eyes (A: right eye, and B: left eye).

An extensive etiological investigation was performed, ruling out rheumatological and infectious causes. The patient was evaluated by a physician, and the imaging of the central nervous system (CNS) was also made, with normal results. Optical coherence tomography was repeated, this time showing blurring of the ellipsoid zone (EZ) in both eyes (Figure 3). Facing the case of a patient with progressive worsening of his VA, with normal fundoscopy, FA, and full-field ERG, but with abnormal mERG, a diagnosis of OMD was made. He was informed about the lack of options for treatment and was requested to inform his family about the possible genetic inheritance. His sister and both of his parents were also evaluated, without any abnormalities. The patient is still being followed up at our hospital, without any changes in his VA or exams in the last 6 months.

DISCUSSION

Occult macular dystrophy was first described by Miyake in 1989,[1] under the title "hereditary macular dystrophy without visible fundus abnormality", in three patients of two generations of the same family - a 29-year-old female patient, her 19-year-old brother, and her 55-year-old father. The term "occult macular dystrophy" was only coined by the same author in 1996.[2] This condition is a form of inherited macular dystrophy, characterized by normal fundus and fluorescein angiography, but progressive decline of VA.

Although originally described as being an autosomal dominant disease, with incomplete penetrance, only 50% of patients with OMD have a detectable genetic cause.[3] In 2010, mutations in the retinitis pigmentosa 1-like (RP1L1) were first identified in two families with autosomal dominant OMD.[4] Since then, multiple reports describing RP1L1 variants in patients with OMD were described. The most common is the c.133.T, p.Arg45Trp in exon 2, and there is another hot spot between amino acid numbers 1194 and 1201 in exon 4.[5] Nowadays, two types of OMD are described: hereditary (also known as Miyake disease) and sporadic.

Patients with this condition usually present with progressive visual loss, with an age of onset that range from 6 to 81 years, and rarely progress after 60 years of age.[6] Fundoscopy is normal – being the reason that this condition is called occult –, as well as full-field ERG. However, mERG is usually attenuated, indicating that the retinal dystrophy is confined to the macula. Autofluorescence (AF) is usually normal, although, in roughly 50% of patients with RP1L1 mutation, a circular area of increased AF signal at the fovea can be noticed.[6] Optic coherence tomography is also an important tool when facing these patients, showing structural changes in outer layers. Nakamura et al.[7] proposed stages of OMD based on the findings on this exam. According to this author, stage I is when no visual symptoms are present, and there are minimal structural changes in the OCT images (Ia when these changes are confined to the fovea, and Ib when parafoveal structures are altered); stage II, in which the interdigitation zone (IZ) is not present and EZ is blurred and dome shaped (IIa when foveal region is impaired and IIb when the entire macular region is impaired). Last, stage III presents a flat EZ (IIIa when the EZ is continuous and IIIb when it is disrupted at the fovea). More recently, a study investigated the progression of the photoreceptor layer damage using ultra-high resolution OCT (UHR-SD-OCT) and showed a cluster of hyperreflective dots between the EZ and IZ, which precedes the damage of outer segments and EZs.[8]

Occult macular dystrophy is diagnosed by clinical history, retinal imaging, and electrophysiological studies. Genetic tests can also be helpful, but not easily accessible in many places. Differential diagnosis includes cone dystrophy, a condition in which some patients also present with a normal fundus; however, with abnormal

or absent full-field cone ERG and an absent focal macular ERG. Congenital stationary night blindness with normal fundus is also a plausible differential diagnosis, although in this condition full-field ERG will show abnormalities. Cancer associated retinopathy can also have an unremarkable fundus; however, the ERG in patients with this condition usually shows global retinal dysfunction, with reduced - or extinct - scotopic and photopic a and B-waves. Amblyopia and optic neuropathy must also be ruled out. Currently, there is no treatment available for this condition.

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