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CASE REPORT

Electrophysiolocal findings in Mohr-Tranebjærg syndrome

Alterações eletrofisiológicas na síndrome de Mohr-Tranebjærg

Regina Halfeld Furtado de Mendonça[1], Eliana Lucia Ferreira[2], Stefania Abbruzzese[3]

ABSTRACT

Mohr-Tranebjærg syndrome (MTS) is an X-liked recessive rare syndrome also known as deafness-dystonia syndrome. The severity of the symptoms may vary, but they progress usually to severe deafness and dystonia and sometimes they are accompanied by cortical deterioration of vision and mental deterioration. The purpose of this paper is to illustrate a very interesting case of Mohr-Tranebjærg syndrome. A 24-year-old italian man with Mohr-Tranebjærg syndrome underwent full field electroretinography (ERG) and visual evoked potentials (VEPs). Fundus examination showed apparently normal retina with pallor of the optic disc. Pattern reversal VEP and flash VEP responses were non-recordable. ERG showed amplitude reduction of the fotopic, scotopic and 30 Hz flicker responses revealing generalized retinal dysfunction with reduction of cone and rod responses. The progressive neurodegeneration in Mohr-Tranebjærg syndrome can be also associated with a retinal degeneration.

Keywords: Mohr-Tranebjærg syndrome; Deafness-dystonia syndrome;Electroretinography; Visual evoked potentials; Case reports

RESUMO

A síndrome de Mohr-Tranebjærg é rara, com herança recessiva ligada ao X, conhecida também como síndrome da surdez-distonia. A intensidade dos sintomas pode variar e normalmente, evoluem para uma surdez profunda e a distonia, algumas vezes, vem acompanhados por deterioração visual e mental. O objetivo deste trabalho é ilustrar um caso muito interessante dessa doença. Um homem, italiano, de 24 anos, com a síndrome de Mohr-Tranebjærg, foi submetido ao exame de eletrorretinografia de campo total (ERG) e ao exame de potencial evocado visual (PEV) (padrão e flash). No exame do fundo do olho era presente uma palidez do nervo óptico com retina, aparentemente, sem alterações. No exame do eletrorretinografia de campo total ERG detectou-se redução das amplitudes das respostas fotópicas, escotópicas e ao flicker de 30 Hz, demonstrando uma disfunção generalizada da retina, com redução da função dos cones e bastonetes. A progressiva neurodegeneração da síndrome de Mohr-Tranebjærg pode ser também associada à degeneração da retina.

Descritores: *Síndrome de Mohr-Tranebjærg; Síndrome da surdez-distonia; Eletrorretinografia de campo total; Potencial evocado visual; Relatos de casos*

[1]Universidade Federal de Juiz de Fora – Juiz de Fora (MG); Professora convidada Università "La Sapienza" – Roma, Itália;
[2]Universidade Federal de Juiz de Fora – Juiz de Fora, (MG), Brazil;
[3]Università "La Sapienza" Roma, Itália.

Study **c**arried out at Università "La Sapienza" Roma – Italy; Universidade Federal de Juiz de Fora (MG), Brazil.

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Introduction

The Mohr-Tranebjaerg syndrome (MTS), also known as deafness-dystonia syndrome or deafness-dystonia-optic neuronopathy syndrome (DDON), is a rare X-linked recessive neurodegenerative disorder characterized by early-onset deafness, dystonia and further neurological abnormalities such as cortical blindness, spasticity, dementia and mental retardation[1]. The typical initial manifestation is a progressive neurosensorial hearing loss in childhood, with profound hearing loss usually occurring by the age of 10 years[2]. In childhood, color vision and visual fields are normal[3]. These children have prelingual or postlingual sensorineural hearing impairment, with slowly progressive dystonia or ataxia in the teens[4]. Visual impairment may first be evident in the late teens as photophobia, reduced visual acuity, acquired color vision defect, and central scotomas. Ophthalmologic examination in children reveals normal-appearing optic nerves; in adults, the optic nerves become pale[3]. The slowly progressive decline in visual acuity leads to legal blindness around age 30 to 40 years[3]. The onset of dementia is usually around 40 years old[4].

Case Report

A 24-year-old italian man with Mohr-Tranebjærg Syndrome underwent, in 2003, full field electroretinography (ERG) and visually evoked cortical potentials with flash and pattern stimuli. Contact lens electrodes (ERG-jet®) were used for ERG using the ISCEV standard (rod response, combined rod-cone response, oscillatory potentials, cone response and 30 Hz flicker). For the flash VEP, the stimuli were presented in a dimly illuminated room and two averages of 100 sweeps were recorded. The stimulus strength was +0.25 U.L.ott with a frequency of 1 Hz with a background of 20 cd/m^2. For the pattern VEP, the patient was seated 1 meter from a 17-inch monitor (19.5°). Mean luminance of the display was 80 cd/m^2. Check contrast was 90%.The patient underwent a clinical protocol with three check sizes: large checks sizes of 60' (low spatial frequency stimulus), medium checks sizes of 30' (medium spatial frequency stimulus) and small checks sizes of 15' (high spatial frequency stimulus). The responses were amplified 50,000 times with a ½ amplitude bandpass of 1-50 Hz with a 50 Hz notch filter in place. Two averages of 100 epochs of the responses were recorded for each eye. Fixation was monitored by an observer and data collected only when the patient was looking at the pattern.

Results

Fundus examination showed apparently normal retina with pallor of the optic disc. Pattern reversal VEP and flash VEP responses were non-recordable. ERG showed amplitude reduction of the fotopic, scotopic and flicker responses.

Table 1

Percentage of b-wave reduction compared to the lower response in normal subjects

	Scotopic Rods (%)	Scotopic Massive (%)	Cone (%)	flicker 30Hz (%)
RE	79	62	53	59
LE	78	59	53	59

Discussion

Mohr-TranebjærgSyndrome, progressive neurodegeneration leads to neurosensorial hearing loss, dystonia and a variety of non-obligatory neurological features[1]. In some cases of Mohr-Tranebjærg syndrome, visual loss can be found, while other patients never show signs of visual impairment even in old age[5]. In fact, optic neuronopathy may be subclinical for many years[6]. The concept of "neuronopathy" refers to the destruction of the cell bodies of neurons and is different from "neuropathy," which is defined as a functional disturbance in the peripheral nervous system[4]. The pattern of the clinical features in Mohr-Tranebjærg syndrome suggests a multifocal neurodegeneration affecting distinct areas of the CNS[1]. Usually, the deafness syndromes are associated with progressive visual deterioration, dystonia, dementia, fractures and psychiatric abnormalities[7,8].

In the literature, electrophysiological and neuroimaging investigations are lacking in cases of Mohr-Tranebjærg Syndrome[1]. The correlation of morphological and functional alterations is very important. Positron-emission tomography (PET) and magnetic resonance imaging (MRI) studies revealed a multifocal pattern of neurodegeneration with hypometabolic areas predominantly located over the right striatum and parietal cortex and marked atrophy of the occipital lobes[1]. Whereas the specific mitochondrial dysfunction leading to neuronal loss in Mohr-Tranebjærg syndrome remains to be clarified, the electrophysiological and neuroimaging findings allowed the multifocal manifestation of neurodegenerative lesions in Mohr-Tranebjærg syndrome to be characterized specifically[1].

Optic neuronopathy may be apparent only when prolongation of the P100 wave latency is detected on visual evoked potential (VEP) testing[8]. In the present work, pattern reversal VEP and flash VEP responses were non-recordable. We believe that the severe alteration of the VEP was a consequence of the optic disc and visual cortical strict alterations. According to our findings, optic atrophy and cortical visual impairment were both observed[9]. Neurophysiological investigations showed cochlear dysfunction and disturbance of visual pathways[1]. Abnormal VEP and neuropathological abnormalities included neuronal cell loss in the optic nerve, retina, striate cortex, basal ganglia, and dorsal roots of the spinal cord[8].

In Mohr-Tranebjærg syndrome the appearance of the retina is usually normal, as are night vision and the electroretinogram (ERG)[3]. In the present case, fundus examination showed also apparently normal retina with pallor of the optic disc. In a study of 7 affected males and 2 obligate carriers, only one of 7 affected males had signs of retinal degeneration. The patient had central areolar choroidal dystrophy with visual field alterations (central scotomas) and electroretinographic alterations (reduction of amplitude and prolonged implicit time of the cone b-wave on stimulation with 30 Hz white flicker)[3]. In our patient, although the appearance of the retina was normal, the reduction of cone and rod responses of the ERG demonstrates that in Mohr-Tranebjærg syndrome, the optic and cortical alterations can be associated with retinal damage. It is very important with full-field electroretinography to find out if the blindness was also caused by retinal degeneration or only by optic atrophy and cortical visual impairment.

We are also of the opinion that ophthalmological examination, and electrophysiological exams are very important

in clinically suspected male patients with either progressive hearing impairment, dystonia, or visual disability, in order to establish an early diagnosis and provide appropriate genetic counseling[8].

Although the visual loss is caused predominantly by neurodegeneration of the visual cortex, we agree with authors who point out that the degeneration of the retina and the optic nerve may contribute to visual impairment. The pathological changes in basal ganglia and sensory cortex demonstrate the disintegration of subcortico-cortical circuits and correlate well with the clinical presentation of multifocal dystonia[1].

Neuropathological alterations corresponding to visual loss seem to involve not only the visual cortex but mainly peripheral visual structures, in particular the retinal neurons and the optic nerve fibers[1]. Full-field ERG, in the present case, revealed generalized retinal dysfunction with reduction of cone and rod responses. The progressive neurodegeneration in Mohr-Tranebjærg syndrome can be associated with a retinal degeneration.

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Corresponding author:
Regina Halfeld Furtado de Mendonça
Universidade Federal de Juiz de Fora (UFJF)
Grupo de Pesquisa em Inclusão, Movimento e Ensino a Distância
Campus Universitário s/nº – Martelos
CEP 36036-900 – Juiz de Fora (MG), Brasil
Fone: (32) 2102-3283
E-mail: haldfeld.regina@uab.ufjf.br