MATERNALLY INHERITED DIABETES AND DEAFNESS

DIABETES DE HERENCIA MATERNA Y SORDERA

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ABSTRACT

Case report: We described the follow up of a patient with diabetes mellitus type 2 who had a macular pattern dystrophy and bilateral neurosensory hearing loss. Electrophysiological studies revealed abnormal pattern electroretinography and impaired electro-oculogram responses.

Discussion: Maternally Inherited Diabetes, neurosensory Deafness and generally macular pattern distrophy (MIDD syndrome), is a rare mitochondrial disease, responsible for approximately 0.5 to 2.8% of diabetes mellitus (Arch Soc Esp Ofthalmol 2009; 84: 359-362).

Key words: Diabetes, deafness, mitochondrial diseases, mitochondrial DNA, macular dystrophy.

INTRODUCTION

Mitochondrial diseases comprise a group of disorders produced by a failure in the oxidative phosphorylation system, the final route of mitochondrial energy metabolism, with the insulin deficiency in the biosynthesis of adenosin triphosphate (ATP) because a part of the polypeptides making up this system are encoded in the mitochondrial DNA (mtDNA) (1).

The presence of maternally inherited diabetes and neurosensory deafness, to which a pattern macular dystrophy is usually added, constitute the MIDD syndrome, generally produced by a mutation of the mtDNA in position A3243 and which is responsible for 0.5%-2.8% of diabetics (2,3).

RESUMEN

Caso clínico: Se describe el seguimiento de un paciente diabético tipo 2 con una degeneración macular en patrón y sordera neurosensorial bilateral. En la electrofisiología mostraba un electrorretinograma (ERG) patrón anormal y un electrooculograma (EOG) disminuido.

Discusión: La presencia de diabetes de herencia materna y sordera neurosensorial, a los que suele sumarse una distrofia macular en patrón, constituyen el síndrome MIDD (Maternally Inherited Diabetes and Deafness), una rara enfermedad mitocondrial responsable de un 0,5% a 2,8% de los diabéticos.

Palabras clave: Diabetes, sordera, enfermedades mitocondriales, DNA mitocondrial, distrofia macular.
CLINICAL CASE

A 56-year-old patient who attended the practice in 1994 due to diabetes Type II with an 18 year evolution, treated with insulin and regular metabolic control. In addition, the patient exhibited hypoacusia from birth. The ophthalmological exploration revealed a visual acuity of 1 in both eyes (BE) with optical correction, normal intraocular pressure and an ocular fundus without diabetic retinopathy but with pigmentary alteration around the macula. A fluorescein angiography 1999 was performed, showing a grid-shaped pattern degeneration in both posterior poles and severe retinal ischaemia. Accordingly, bilateral photocoagulation was performed in the mean periphery (figs. 1 and 2). Five years later, the patient developed proliferative diabetic retinopathy in the right eye (RE) with pre-retinal haemorrhage, to which photocoagulation in the extreme periphery was added.

The patient was also subjected to cataract surgery in the left eye (LE) in 2006 by means of phakoemulsification without complications. At present, he exhibits a vision of 0.5 in BE, with a cortical cataract in the RE, pseudo-fakia in the LE and ocular fundus with photocoagulated diabetic retinopathy without macular oedema (figs. 3 and 4).

The ear exploration revealed bilateral and symmetric neurosensory deafness with a loss of 73% in the right ear and 63% in the left one. The electrophysiology showed a pattern electroretinogram (pERG) with the absence of response in BE, an ERG Flash (fERG) of decreased amplitude, a diminished electro-oculogram (EOG) and normal visual evoked potentials.

The patient, without family antecedents, was submitted to a genetic study and the DNA samples from peripheral blood analyzed by means of bidirectional sequencing confirmed the presence of a mutation in heteroplasma c. 3243 A>G of tRNA(Leu) of mtDNA, compatible with maternally inherited diabetes and deafness (MIDD).

DISCUSSION

The presence of maternally inherited diabetes mellitus and deafness (MIDD) constitutes a new subtype of diabetes associated to mtDNA mutation A3243G which prevents the admission of leukin to the mitochondria (1). This mutation is also one of the mutations associated to the mitochondrial encephalic myopathy with lactic acidosis and cerebrovascular accident episodes (MELAS), of which MIDD could be a form of partial expression (1).

mtDNA is transmitted almost exclusively through the mother, who transmits a mitochondrial genome to all her children due to the high number of mitochondria which exist in the ovum, since the few which can be provided by sperm are eliminated in an active process. Cellular division can originate cellular lines with some normal and some mutated mitochondria. The combination of both is called heteroplasma. When the mutated DNA...
exceeds a given threshold the disease is expressed because the production of ATP falls below a lower threshold (1).

Clinically, diabetes appears in young adults around 40 years of age, usually in a milder form with tendency towards insulinopenia; typically, the patients are not obese and 80% have first degree familial antecedents (2). Neurosensory deafness appears in 98% and, of these, 25% require hearing aids. Associated diseases comprise myocardiopathy, cardiac conduction disorders and neuropsychiatric symptoms (2). Some patients exhibit muscular pains in the lower limbs with prolonged walking. In these cases, muscular biopsy exhibits the presence of torn red fibres, typical of mitochondrial miopathies (2).

The most frequent ophthalmological alteration is the presence of a pattern macular dystrophy (around 80%), most of the times void of symptoms. Vision is usually maintained in a high percentage of patients although they frequently refer nocturnal blindness, photophobia and visual deficit (2-4). In grade 1, this macular dystrophy exhibits small pigmented lesions located in the macula, while in grade 2 they extend around the macula and the papilla, and in grade 3, in more advanced stages retinal atrophy spots can be observed (2). Recently, a lower prevalence of diabetic retinopathy and high arterial pressure has been described in MIDD-type diabetics vis-a-vis classic diabetics which, on the other hand, exhibit higher rates of nephropathy (5). These are the characteristic macular alterations visible above all in angiograms of diabetic patients, which must warn about the existence of MIDD.

Electrophysiological tests revealed a reduction in the pERG amplitude which mainly measures the central retinal response, and EOG alterations in 50% of cases (4). The coexistence of a decreased fERG in our patient, a diffuse retinal response, would be related to pan-retinal photoacoagulation.

REFERENCES