Maternally Inherited Diabetes and Deafness: A Case Report

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Maternally inherited diabetes and deafness (MIDD) syndrome is a rare disease associated with progressive sensorineural deafness due to a mitochondrial DNA mutation.
Characterized by diabetes mellitus and sensorineural hearing impairment, MIDD is also associated with macular dystrophy, neuromuscular and psychiatric manifestations, cardiomyopathy as well as renal insufficiency. We report the case of a 55-year-old male patient complaining of hearing loss with maternally inherited diabetes and deafness syndrome.

Key words: Sensorineural deafness. Mitochondrial DNA. Maternally inherited diabetes and deafness syndrome.

Síndrome de diabetes de herencia materna y sordera
El síndrome de diabetes de herencia materna y sordera es una causa infrecuente de hipoacusia neurosensorial de origen genético, causado por mutación en el ADN mitocondrial.
Se caracteriza por diabetes mellitus de herencia materna e hipoacusia neurosensorial en relación con distrofia macular, manifestaciones neuromusculares o psiquiátricas, miocardiopatía e insuficiencia renal. Presentamos el caso de un paciente que acude a la consulta por hipoacusia y presenta el síndrome de diabetes de herencia materna y sordera.

Palabras clave: Hipoacusia neurosensorial. ADN mitocondrial. Síndrome de diabetes de herencia materna y sordera.

INTRODUCTION

Mutations in mitochondrial DNA (DNAmt) cause a group of illnesses with very heterogeneous clinical manifestations including hypoacusia, either in isolation or as part of various syndromes.[1] The syndromic forms of hearing loss caused by DNAmt mutation include maternally inherited diabetes mellitus and deafness syndrome (MIDD). The syndrome was first described in 1992 by Ballinger et al.[2] It is characterized by maternally inherited diabetes mellitus and sensorineural hearing loss in connection with macular dystrophy, myocardiopathy, neuromuscular or psychiatric manifestations, and kidney failure. The cause of this syndrome is the substitution of A for G in the tRNA Leu (RUU) gene at position 3243. We report here on the case of a patient who came to the clinic complaining of hearing loss and suffers from this mutation.

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CASE REPORT

Male, 55 years of age, with slowly progressive hypoacusia over the last ten years. Outstanding features of his personal history include insulin-dependent type 2 diabetes mellitus diagnosed 18 years ago and visual impairment (pattern macular dystrophy and severe retinal ischaemia secondary to diabetes). Possible causes of acquired hearing loss (exposure to noise, trauma, ototoxic drugs, infectious diseases of the ear) were ruled out. His mother and a maternal uncle have diabetes and hearing loss, with both of them wearing hearing aids.

The otoscopy result was normal. Pure tone threshold audiometry showed bilateral symmetrical sensorineural hearing loss with a mean threshold of 55 dB (Figure). The verbal audiometry revealed an intelligibility threshold at 60 dB with a discrimination percentage of 100%. The brainstem evoked auditory potentials present normal morphology and amplitude of the waves, inter-wave latency and differences in the interaural latency of the V wave. Assessment of the vestibular function by electronystagmography was normal.

The samples of DNA analyzed by means of bidirectional sequencing confirm heteroplasmy of the A3243G mutation in the mitochondrial gene of tRNA Leu (UUR), compatible with MIDD.

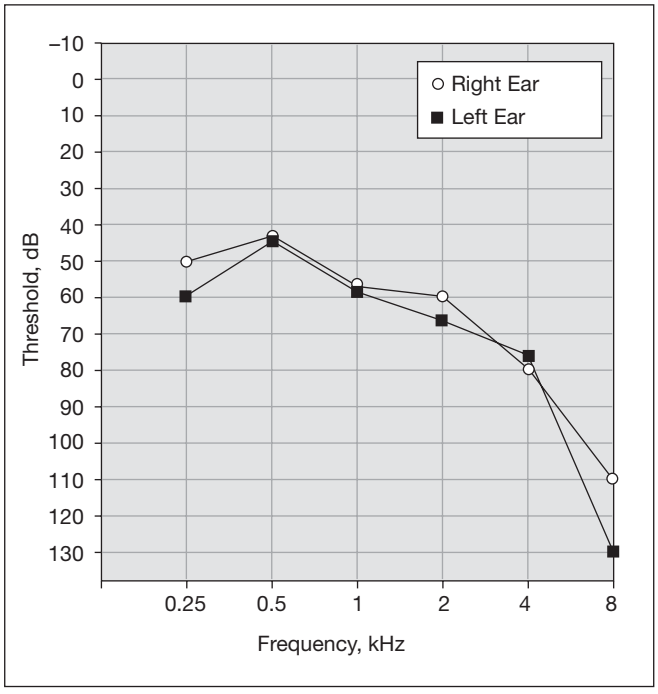

Figure. Patient's tonal audiometry.

DISCUSSION

A mutation at position 3243 of DNAmt is associated with 2 syndromes: the maternally inherited diabetes mellitus and deafness syndrome and the MELAS syndrome (mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes), described by Pavlakis et al[3] in 1984. Patients with MELAS syndrome suffer from cerebrovascular accidents at a young age, encephalopathy, lactic acidosis, myopathy, recurrent cephalea, deafness, and dementia. The MIDD syndrome is associated with a lower degree of heteroplasmy and less severe clinical manifestations.[4] In both processes, the structures of the ear most affected are the vascular striate and ciliate cells, especially on the basal spira.[5,6]

Patients with MIDD develop insulin-dependent diabetes due to the reduction in acinar insulin secretion.[7] The symptoms of diabetes are manifested in young adults (third-fourth decade of life) and in 80% of cases with a family history in first-degree relatives.

The age of onset of hearing loss is between 14 and 50 years of age and mainly affects high frequencies. The percentage of verbal discrimination ranges from 100% to very severe hearing losses (with thresholds of 80 dB or worse), which also indicates a cochlear origin of the hypoacusia.[8,9] Vestibular function is usually preserved.

It has been calculated that the A3243G mutation in DNAmt has a prevalence of 16.3 cases per 100 000 inhabitants in the general adult population and is observed in 0.314%-1.74% of patients attending clinics due to hearing loss.[1,4] As for the therapeutic options, patients with profound sensorineural hearing loss can benefit from cochlear implants, with good adaptation in most cases.[4]

Although the frequency of mitochondrial illnesses is low, it is possible to encounter patients with hearing loss due to DNAmt mutations at clinics and specialists must remain alert to this diagnosis. Patients with a history indicative of maternally inherited hearing loss, diabetes mellitus or neuromuscular disease (especially with a record of cerebrovascular accidents prior to 40 years of age) must be given a more detailed study including an ophthalmologic examination and DNA analysis.

REFERENCES

1. Usami S, Abe S, Akita J, Namba A, Shinkawa H, Ishii M, et al. Prevalence of mitochondrial gene mutations among hearing impaired patients. J Med Genet. 2000;37:38-40.
2. Ballinger SW, Shoffner JM, Hedaya EV, Trounce I, Polak MA, Koonz DA, et al. Maternally transmitted diabetes and deafness associated with a 10.4 kb mitochondrial DNA deletion. Nat Genet. 1992;1:11-5.
3. Pavlakis SG, Phillips PC, DiMauro S, De Vivo DC, Rowland LP. Mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes: a distinctive clinical syndrome. Ann Neurol. 1984;16:481-8.
4. Sinnathuray AR, Raut V, Awa A, Magee A, Toner JG. A review of cochlear implantation in mitochondrial sensorineural hearing loss. Otol Neurotol. 2003;24:418-26.
5. Yamasoba T, Tsukuda K, Oka Y, Kobayashi T, Kaga K. Cochlear histopathology associated with mitochondrial transfer RNALeu(UUR) gene mutation. Neurology. 1999;52:1705-7.
6. Sue CM, Lipsett LJ, Crimmins DS, Tsang CS, Boyages SC, Presgrave CM, et al. Cochlear origin of hearing loss in MELAS syndrome. Ann Neurol. 1998;43:350-9.
7. Guillausseau PJ, Massin P, Dubois-LaForgue D, Timsit J, Virally M, Gin H, et al. Maternally inherited diabetes and deafness: A multicenter study. Ann Intern Med. 2001;134:721-8.
8. Yamasoba T, Oka Y, Tsukuda K, Nakamura M, Kaga K. Auditory findings in patients with maternally inherited diabetes and deafness harboring a point mutation in the mitochondrial transfer RNA(Leu) (UUR) gene. Laryngoscope. 1996;106:49-53.
9. Tamagawa Y, Kitamura K, Hagiwara H, Ishida T, Nishizawa M, Saito T, et al. Audiologic findings in patients with a point mutation at nucleotide 3,243 of mitochondrial DNA. Ann Otol Rhinol Laryngol. 1997;106:338-42.