



Phenotypic spectrum of MFN2 mutations in the Spanish population

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INTRODUCTION: The most common form of axonal Charcot-Marie-Tooth (CMT) disease is type 2A, caused by mutations in the mitochondrial GTPase mitofusin 2 (MFN2). OBJECTIVE: The objective of our study is to establish the incidence of MFN2 mutations in a cohort of Spanish patients with axonal CMT neuropathy. MATERIAL AND METHODS: Eighty-five families with suspected axonal CMT were studied. All MFN2 exons were studied through direct sequencing. A bioenergetics study in fibroblasts was conducted using a skin biopsy taken from a patient with an Arg468His mutation. RESULTS: Twenty-four patients from 14 different families were identified with nine different MFN2 mutations (Arg94Trp, Arg94Gln, Ile203Met, Asn252Lys, Gln276His, Gly296Arg, Met376Val, Arg364Gln and Arg468His). All mutations were found in the heterozygous state and four of these mutations had not been described previously. MFN2 mutations were responsible for CMT2 in 16% +/- 7% of the families studied and in 30.8 +/- 14.2% (12/39) of families with known dominant inheritance. The bioenergetic studies in fibroblasts show typical results of MFN2 patients with a mitochondrial coupling defect (ATP/O) and an increase of the respiration rate linked to complex II. CONCLUSION: It is concluded that mutations in MFN2 are the most frequent cause of CMT2 in this region. The Arg468His mutation was the most prevalent (6/14 families), and our study confirms that it is pathological, presenting as a neuropathy in a mild to moderate degree. This study also demonstrates the value of MFN2 studies in cases of congenital axonal neuropathy, especially in cases of dominant inheritance, severe clinical symptoms or additional symptoms such as optic atrophy.

Résumé en anglais

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