New pathogenic variations of mitochondrial DNA in Alzheimer disease!!

Dear Sir,

Alzheimer's disease (AD) is a neurodegenerative disorder characterized by a gradual loss of episodic memory,[1] in which an interplay between genes and environmental factors are involved. A variety of genetic, medical and environmental factors[2] modulate the ageing-related processes leading to the devastation of the brain in AD.[3] Mutations in mitochondrial DNA (mtDNA) are suspected to be causally related, since mtDNA is maternally inherited in a non-Mendelian way.[4,5] In this study (research project number #15), the mtDNA of 24 AD patients and 100 healthy controls from peripheral blood samples collected from Special Medical Center of Tehran, Iran during 2010-2011 were investigated using Plymerase Chain Reaction (PCR)[6] and sequencing methods. The ethical approval and patient informed consent was obtained for the genetic analysis.

Fifteen variations were found in different tRNA mtDNA, where eleven variations were polymorphic mutations. A12308G, a polymorphic mutation (tRNA Leu [CUN]), was found in 8 patients. This mutation was reported in different neurodegenerative diseases as well as in controls. However, four variations {C1631A, T1633A (tRNA Val), T14704C and T14723C (tRNA Glu)} fulfilled the criteria for pathogenic mutations, such as a heteroplasmic state, conserved nucleotides, not reported in previous literature and not found in healthy controls. We believe that these variations may have pathogenic effects in AD or have secondary effects in the disease process. The percentage of heteroplasmic mutations may play a role in the signs and symptoms or age of onset of AD.

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