

MELAS: A Rare Cause of Cognitive and Behavioral Disorders for a Sexagenarian

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Abstract

MELAS (Mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes) is a multisystem mitochondrial disorder with a typical childhood onset. The diagnosis is based on clinical findings and molecular genetic testing. We describe a rare presentation of MELAS in a sexagenarian who showed cognitive and behavioral disorders for one year. Four months before admission, he experienced an acute left mowing episode spontaneously resolved in one day. Atypical lesion on cerebral MRI and increased lactate in the cerebrospinal fluid (CSF) lead us to perform genetic analysis that confirmed the m.3243A > G DNA mutation for MELAS. This case illustrates that cognitive and behavioral disorders can obscure a case of MELAS occurring in a relatively advanced age. Moreover, this is the first report of MELAS with late onset of symptoms associated with diffuse atrophy, predominantly hippocampal on MRI.

Keywords: MELAS; Dementia and Behavioral Disorders; Diffuse Atrophy Predominantly Hippocampal

Introduction

MELAS (myopathy, encephalopathy, lactic acidosis, and stroke-like episodes) is a mitochondrial disease characterized by early stroke-like episodes [1] that was first described in 1984 [2]. The most common found mutation (> 80%) is the m.3243A > G in MT-TL1 [3]. Symptoms usually occur during the first decades. Some cases present a delayed onset, up to 40 years but its inception before 2 or after 40 years old is very unusual [4-5].

Case Report

A 66 years old male technicians electromecanicians, having studied up to 18 years old followed by 2 years of military service, was admitted for increasing cognitive and behavioral disorders on one year and progressive dysfluent aphasia for six months actually precluding any formal evaluation (Mini-Mental State Examination (MMSE) [6]: 0/30). His wife described indeed more and more impulsive responses of his part associated with greater apathy than before. He had no significant familial or personal medical history except for an unexplained bilateral hypoacusis since 2008. His wife also related an acute left mowing episode, 4 months ago, spontaneously resolved in the day. During these 6 months, he progressively complained of more and more lack of words and dyscalculia with an MMSE evolving

from 26/30 in April 2014 to 19/30 in October. The patient systematically refused more exhaustive neuropsychological examination. On admission, neurological examination revealed dysfluent aphasia, ideomotor apraxia, bilateral grasping, a right palm-chin reflex and diffuse global hyporeflexia.

Blood tests were normal (Antinuclear factor and anti-neutrophil cytoplasmic antibody were negative). Various serum tests were negative (viral hepatitis, HIV, syphilis). Microscopic urinalysis was negative. Brain FLAIR-MRI revealed a diffuse right temporal high signal and diffuse cortico-sub-cortical atrophy (Figure 1). Lumbar puncture revealed 11 cm H₂O of pressure, 1 white blood cell, 0 red blood cells per mm³ with normal levels of protein and glucose but high lactate raised to 4.1 mmol/l. All microbiological investigations including aerobic-anaerobic cultures and viral PCR (enterovirus, HSV1-2, VZV) were normal. Amyloid-β 1-42 was decreased (161pg/ml). Tau (285pg/ml) and phospho Tau protein (18 pg/ml) were normal. EEG monitoring showed a right slowing without seizures. Genetic analysis confirmed a MTTL1 gene (3243A >G) mutation of mitochondrial DNA causing MELAS disease [4].

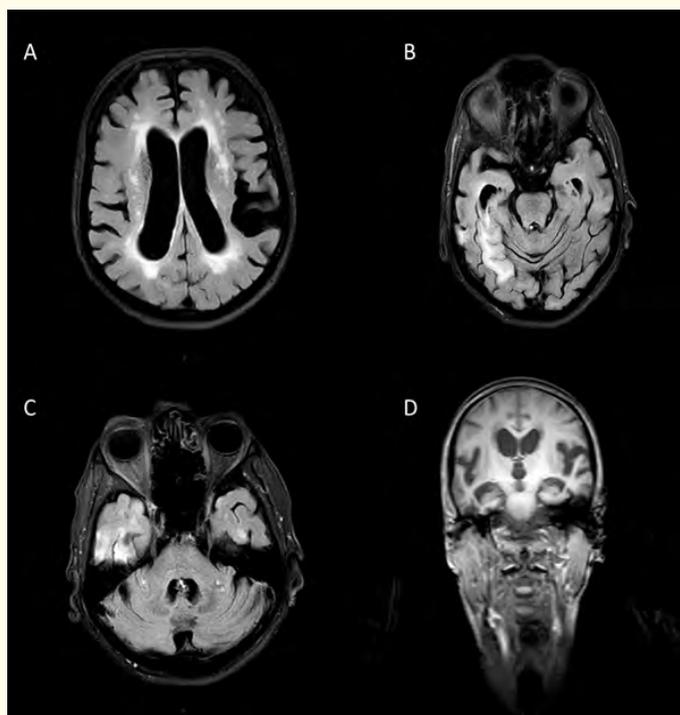


Figure 1: Axial fluid attenuated (FLAIR) images (A-C) and coronal T1 weighted image (D). Hemispheric peri-ventricular hypersignal (A) with cortical inferior temporal involvement (B-C). Diffuse atrophy (A) with predominantly right hippocampal atrophy (B, D).

Discussion

This is the first report of such late cognitive onset of MELAS with cerebral MRI showing diffuse, predominantly hippocampal, atrophies in addition to some classical acute and chronic extensive infarct-like lesions not confined to vascular territories [4-5,7-10]. We should note that a MELAS children radiological follow-up study showed that lesions progressively disappeared, except for a mild cortical atrophy at the site of previous lesions [7].

MELAS is a multisystem mitochondrial disorder caused by mutations in mitochondrial DNA inducing dysfunctional mitochondria that become unable to generate sufficient ATP to meet the energy needs of various organs [5]. The pathogenesis of MELAS is not fully understood and infarct-like lesions in MELAS is presumably due to deficient oxidative phosphorylation or associated with dysfunction of the small endothelium cells of blood vessels due to accumulation of abnormal mitochondria [5,7].

The Diagnosis of MELAS is based on a combination of clinical findings and molecular genetic testing showing mutations in the mitochondrial DNA (mtDNA) gene [4]. The most common mutation in this disease, present in more than 80% of individuals with typical clinical findings, is the m.3243A > G in MT-TL1 [3]. The clinical expression and the age of onset depend on its heteroplasmy (a mix of mutant and normal mtDNAs), the tissue distribution of mutant mtDNAs and the vulnerability of each tissue to impaired oxidative metabolism [4].

In this case, the possibility of a superimposed diagnosis of Alzheimer's disease appeared unlikely considering the fast clinical evolution and the normal levels of Tau/ phosphoTau proteins in the CSF [11,12].

In conclusion, our case reveals that a diagnosis of MELAS must be considered in middle aged patients with isolated cognitive and behavioral disorders of unknown origin. Moreover, diffuse atrophy (predominantly hippocampal) and amyloid decrease in CSF can be associated with a MELAS at this advanced age.

Conflict of Interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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