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Cerebellar Ataxia, Myoclonus, Cervical Lipomas, and MERRF Syndrome. Case Report

Mitochondrial DNA (mtDNA) accounts for only 1% of the total cellular nucleic acid content, encoding for 13 polypeptides that are essential for aerobic metabolism. Defects of the mitochondrial genome are an important cause of human disease, including encephalopathies.[1] One such example is myoclonic epilepsy with ragged-red fibers (MERRF), in most cases due to an A to G transition at position 8,344 in the tRNA Lys gene of mtDNA.[1–3] Adding to the classical description, several variants of MERRF have been described including signs such as cognitive impairment, sensory hearing loss, optical atrophy and peripheral neuropathy.[1,3] Here, we report a patient with an unusual presentation of genetically proven MERRF including cerebellar ataxia, myoclonus, and cervical lipomas, compatible with Ekbom's syndrome.

A 52-year-old man had a 15-year history of slowly progressive dysarthria, dizziness, and gait disturbances. Two years after initial symptoms onset, short-term memory deficits developed, progressing to disorientation for time and place. In the last 4 years there wzas progressive worsening of gait ataxia and dysarthria as well as cognition. Family history was positive for a maternal cousin with a diagnosis of a mitochondrial disorder (MERRF). General examination revealed symmetrical, posterior, cervical lipomas. Neurological examination revealed cognitive dysfunction (MMSE: 18/30), moderate scanning dysarthria with slow but understandable speech. Eye movements were full with bilateral horizontal nystagmus on lateral gaze. Remaining cranial nerves were normal. Moderate, intermittent segmental action myoclonus was present in the upper extremities. Tone was slightly reduced in the upper and lower limbs and rebound was present in the upper limbs. Synergy, trajectory, and placement of the limbs were abnormal with dysmetria and dysdiadocokinesia that were moderate in the upper and mild in the lower extremities. Strength was 4/5 throughout and stretch reflexes were hypoactive but symmetric. Plantar responses were flexor. Vibration and position senses were normal. Gait and stance were ataxic and only two to three steps were possible with tandem gait.

A head CT scan showed cerebellar atrophy and extensive symmetrical lipomas in the posterior cranio-cervical area. MRI demonstrated cerebellar atrophy (see Fig. 1). CSF analysis (including lactate level), EEG (with photostimulation), electromyography, and nerve conduction studies were normal. Serum creatine-kinase was 376 (normal $<$ 146 UI/dL) and lactic acid 21.1 (normal $<$ 2.2 mmol/L). Muscle biopsy with histochemistry showed both ragged-red fibers and cytochrome oxidase-negative fibers, compatible with mitochondrial myopathy. Molecular genetic analysis of mtDNA from peripheral blood lymphocytes showed a point mutation (an A to G transition at position 8,344) of the L-strand (heteroplasmic $tRNA^{Lys}$ A8344G).

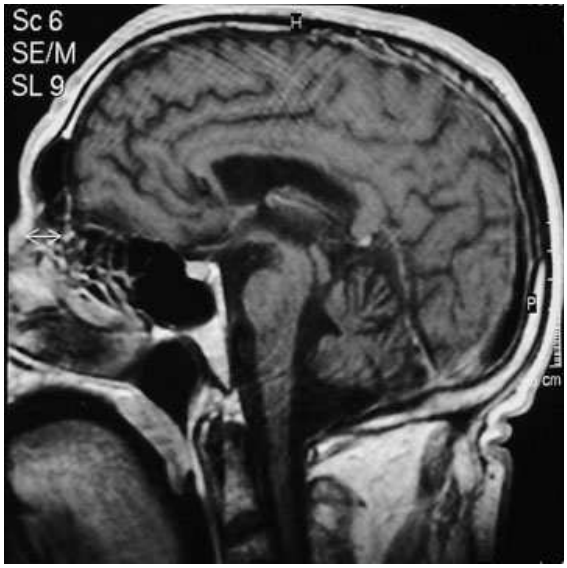

FIG. 1. Brain MRI (T1-weighted sagital image) of the patient shows cerebellar atrophy.

More than 120 point mutations in mtDNA genes have been associated with a wide spectrum of disorders that can affect virtually every body tissue, although brain and skeletal muscle are most frequently involved.[1] MERRF, one of the most common mitochondrial encephalomyopathies is usually attributed to the $tRNA^{Lys}$ A8344G mutation, although two rarer mutations in the same gene have also been associated with this disorder.[3]

Clinical features of MERFF syndrome classically include myoclonic and tonic-clonic seizures, ataxia, and mitochondrial myopathy. Other symptoms variably present include dementia, peripheral neuropathy, sensoneural hearing loss, and optic atrophy, while recurrent strokes, ophthalmoplegia, diabetes mellitus, short stature, and lipomas have been rarely described in single case reports.[2,3]

Multiple symmetric lipomatosis (Morbus Madelung) is characterized by typical lipomatosis, the presence of ragged-red fibers on muscle biopsy, and multiple deletions of the mtDNA. Some patients show cerebellar ataxia and axonal polyneuropathy.[2–7]Additionally in 1975 Ekbom described a hereditary syndrome of cerebellar ataxia, photomyoclonus, skeletal deformities, and lipomas[8] with occasional patients presenting with dementia and pes cavus. Since then, it has been referred to as Ekbom's syndrome,[2,4] and later studies showed an association with the same $tRNA^{Lys}$ A8344G mutation in mtDNA responsible for MERRF syndrome.[1–3]

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Our case, with its distinct phenotypical presentation of mitochondrial encephalopathy, MERRF, symmetrical lipomas, cerebellar ataxia, upper extremities action myoclonus, and dementia, is compatible with the description of Ekbom's syndrome. Our case also highlights aspects of possible overlapping clinical features between this syndrome and other disorders related to mtDNA mutations, particularly MERRF.

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