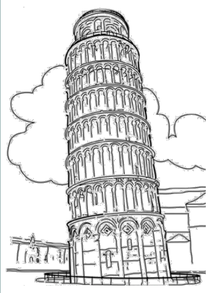
PSEUDOMYOPATHIC COURSE IN A PATIENT WITH CHARCOT-MARIE-TOOTH 2A DISEASE: REPORT OF A NOVEL MFN2 MUTATION



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We describe the case of a 53 years old man with diagnosis of CMT 2A, associated with a novel mutation in *MFN2*.

Background

MFN2 is the most frequent gene mutated in Charcot Marie Tooth type 2A disease (CMT2A). It encodes for a mitochondrial protein involved in mitochondrial structural and functional network for metabolism and intracellular signaling.

Clinical History

Patient family history/medical anamnesis: apparently unremarkable

40 years old: progressive deambulation impairment
widespread muscle fatigue,
(absence of sensory symptoms)

43 years old: muscle weakness proximally at upper limbs, mainly distally at lower ones
muscular hypotrophy (same muscular regions)

Laboratory tests

SERUM: Mildly increased levels of CPK and lactate response to ischemic exercise test

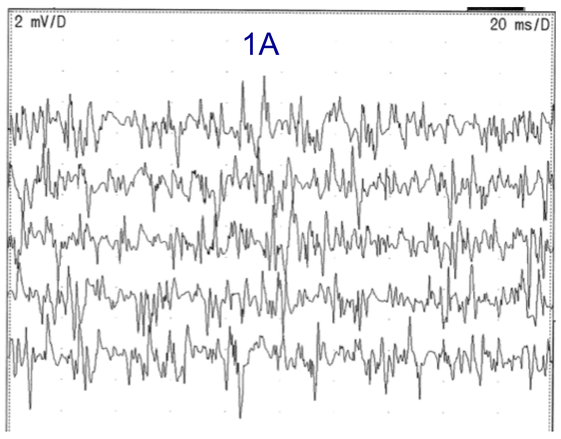
Antinerve antibodies
Acid Maltase Deficiency
Kennedy's disease
SMN-related spinal muscular atrophy
} negative

No evidences of others non-neurological diseases

CSF: normal.

EMG/ENG

widespread myogenic pattern (Fig. 1 A - B) and minimal evidence of reduced motor amplitude potentials



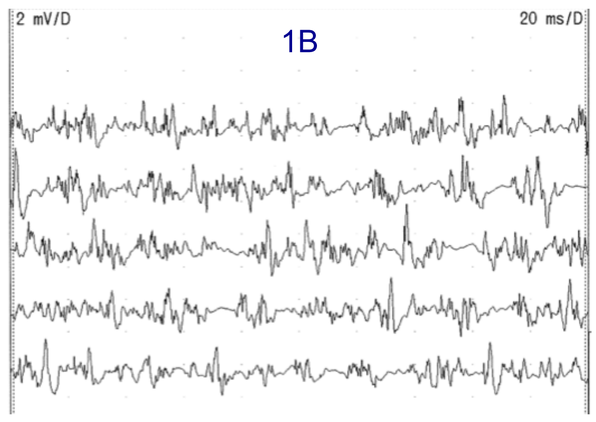


Fig1: A-deltoid on the left
B- tibialis on the right

First Diagnosis

scapulo-peroneal myopathy

Clinical Course

After ten years worsening of the clinical picture

Neurological examination

marked hypotrophy with weakness at the lower limbs,
foot drop gait,
deep tendon hypo/areflexia,
positive Romberg sign
slight sensory ataxia

EMG/ENG

motor and sensitive evoked potentials amplitude reduction distally at four limbs
mixed acute and chronic neurogenic EMG pattern in the lower limbs

WB-CT scan

No thoracic or abdominal lesion

Muscular MRI

massive fatty infiltration of the distal muscles at the lower limbs (especially medial gastrocnemius and soleus muscles), Fig 2 A-B

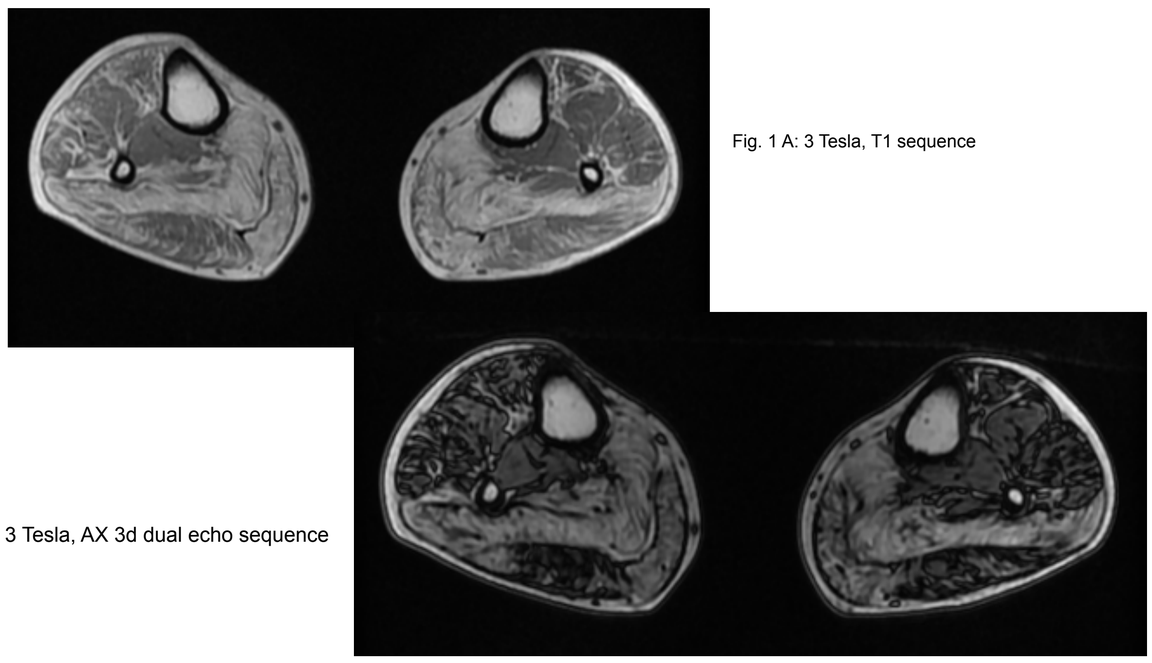


Fig. 1 A: 3 Tesla, T1 sequence

Fig. 1 B: 3 Tesla, AX 3d dual echo sequence

Final Diagnosis

Based on clinical and electrophysiological evidences a diagnosis of CMT2A was supposed

The molecular analysis, searching for mutations of *NEFL*, *GDAP1* and *MFN2*, revealed on exon 8 *MFN2* a heterozygous c.809T>C transition, with p.Met270Thr replacement, not present in health relatives
To date, this mutation is not reported in "The Human Gene mutation Database". In silico analysis in Ensembl database (rs771996573) suggests deleterious effect about SIFT and possibly detrimental effect about Poliphen.
The detection of the mutation in the family members is ongoing..

Conclusion

This new mutation in *MFN2* expands the genetic spectrum of CMT2A phenotype, highlighting the prominent role of the encoded protein in peripheral nerves homeostasis and suggesting extensive sequence analysis should be considered in such patients.

Luigetti M, Fabrizi GM, Bisogni G, Romano A, Taioli F, Ferrarini M, Bernardo D, Rossini PM, Sabatelli M Charcot-Marie-Tooth type 2 and distal hereditary motor neuropathy: Clinical, neurophysiological and genetic findings from a single-centre experience. Clin Neurol Neurosurg. 2016 Mar 9;144:67-71

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