Central and peripheral nervous system demyelination: a rare case of Multiple Sclerosis and Charcot Marie Tooth type 1B

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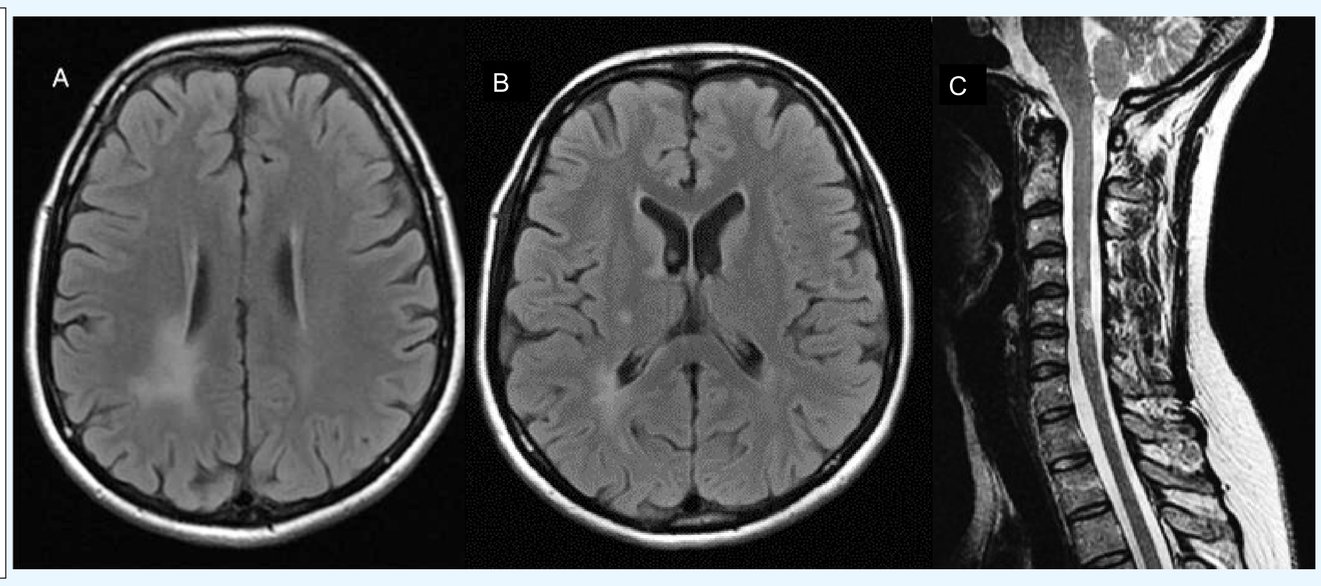
Background - The association between Multiple Sclerosis (MS) and hereditary/sporadic demyelinating disorders of the PNS is rare. Nevertheless, involvement of both central and peripheral myelin could be related to a unique autoimmune pathogenetic mechanism allowed by partial homology among peripheral and central proteins[1]. Herein we describe a case of Charcot-Marie-Tooth disease type 1B (CMT1B) who developed Relapsing Remitting MS.



Case Description - A 40 years old woman was admitted to our hospital complaining of a 10-years history of bilateral progressive weakness and numbness of the lower limbs, followed by loss of strength and difficulty with fine motor skills from a few months before the observation.

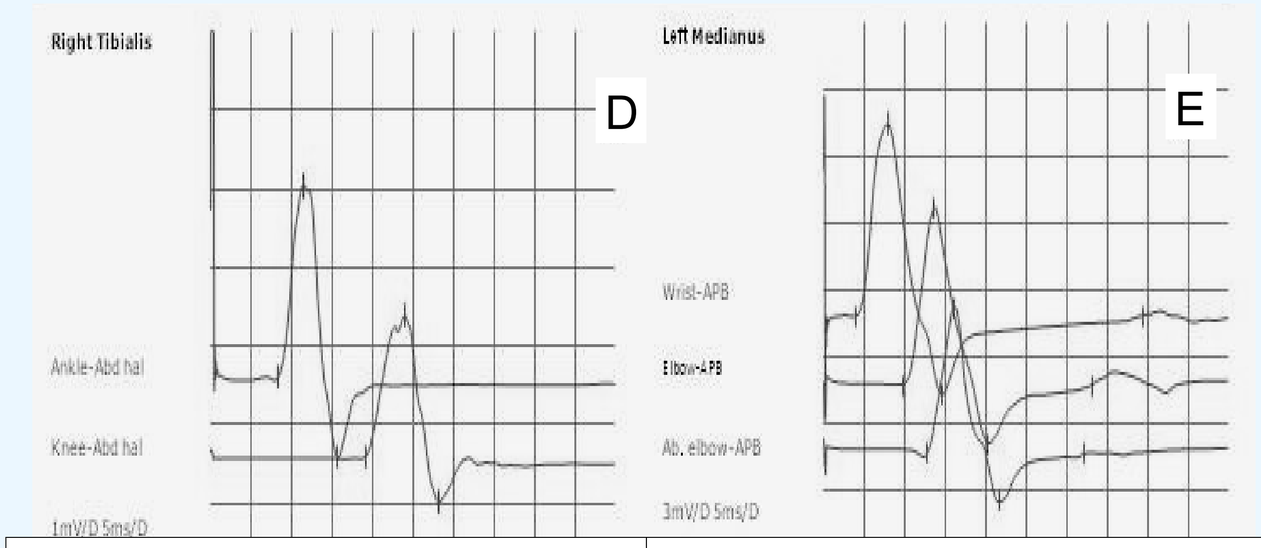
Six years before the admission, the patient developed a bulimic alimentary disturbance. For this reason she underwent a brain MRI that showed T2-hyperintense non-Gd enhancing lesions in right semiovale center and corona radiata, initially interpreted as gliosis (Fig. A).

Neurological examination revealed ataxic gait, impossible on toes and heels, mild distal muscle weakness and wasting of the four limbs more prominent on the right side, with hyper-reflexia and Hoffman and Babinski sign. There were also hypopallesthesia in the four limbs, bilateral pes cavus and urinary incontinence.

A second ***brain MRI*** showed several new T2-hyperintense white matter lesions in corpus callosus and semioval centers (Fig. B), with one of them showing Gd-enhancement. Spinal cord MRI revealed a right side C3-C4 non-Gd enhancing lesion. (Fig. C)

ENG revealed a diffuse reduction of both sensory and motor conduction, with secondary axonal damage (Fig.D-E). ***Cerebrospinal fluid*** showed the presence of 9 oligoclonal bands. A ***genetic study*** of the genes responsible for CMT showed the mutation p.Val 102fs in the exon3 of P0 gene. The same mutation p.Val 102fs has been identified in the proband's brother (43 years) and daughter (18 years), who showed difficulties on gait and bilateral pes cavus. The patient was diagnosed with CMT1B and MS. Treatment with Glatiramer acetate was started. In the following two years the patient didn't develop any clinical relapse and MRI remained stable.

Conclusion - CNS demyelination has been rarely reported in conjunction with CMT disease and most of the cases were related to a PMP22 gene mutation. To our best knowledge - this is the first case described with a Val 102fs mutation in the P0 gene. Association of peripheral and central demyelination has been usually related to chance. A potential explanation may be an autoimmune disorder involving central and peripheral myelin for a potential pro-inflammatory role due to molecular mimicry of mutated P0[2,3]. The evidence of an increasing number of cases with CMT and MS may require larger prospective studies to clarify such a pro-inflammatory role.



Conduction Velocity: 34 m/sec (vn > 40) Amplitude: 3,4 mV (vn 5-15)	Conduction Velocity: 38 m/sec (vn > 40) Amplitude: 12 mV (vn 5-15)

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3) Shy ME et al. "Heterozygous P0 knockout mice develop a peripheral neuropathy that resembles chronic inflammatory demyelinating polyneuropathy (CIDP)". J Neuropathol Exp Neurol. 1997 Jul;56(7):811-21.

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