ASSOCIATION BETWEEN MULTIPLE SCLEROSIS AND SPG7 INTRONIC MUTATIONS: A CASE REPORT

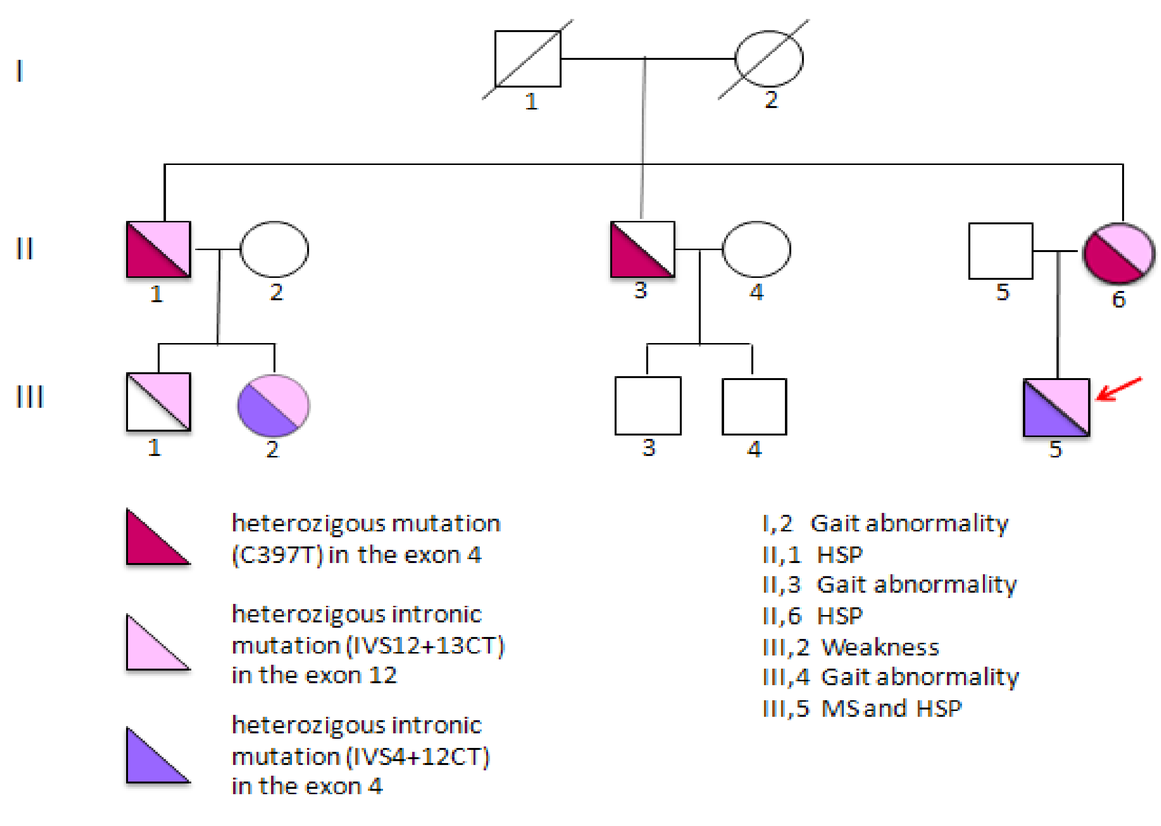
Tempesta I, Introna A, Felica V, Brancasi B, D'Errico E, Tortorella C, Prudenzano MP, Simone IL, Livrea P

Department of Basic Medical Sciences, Neurosciences and Sense Organs, University of Bari "Aldo Moro" – Bari, Italy

INTRODUCTION: Hereditary spastic paraparesis (HSP) is a neurodegenerative disorder showing degeneration of corticospinal tracts as main pathological characteristic and pyramidal signs as main clinical feature. Multiple sclerosis (MS) is characterized by multiple areas of central nervous system inflammation, demyelination and axonal loss. Only few reports described the association between HSP related gene mutations (SPG 4, 11) and MS.

CASE REPORT: A 29 years old male came to our attention showing from several months visual disorders, loss of balance, weakness in the upper limbs and later in the lower limbs, feet paresthesias and sphinteric impairment. His mother and his uncle were affected by spastic paraparesis, both showing an exonic mutation and an intronic mutation in paraplegin gene (figure 1). The genetic analysis previously performed in our patient detected two heterozygous intronic mutations in SPG7 gene that could interfere with exon splicing, suggesting a possible HSP diagnosis. In addition the patient referred a previous episode at age of 21 characterized by visual and urinary disorders and burning pain in back that spontaneously resolved in one month, whereas a weakness in the lower limbs progressively worsened. At neurological examination ataxo-spastic paraparesis, hyperreflexia, weakness in proximal muscles of upper and lower limbs, hypopallesthesia were found. Brain and spinal cord MRI showed multiple hyperintense lesions in the deep and periventricular white matter and cervical-thoracic segments on T2 and FLAIR weighted images (figure 2). At cerebrospinal fluid analysis six oligoclonal immunoglobulin bands were detected. Bacteriological, virological and systemic autoimmune studies were normal. Somatosensory, auditory and visual evoked potentials tests were abnormal. A diagnosis of progressive clinically active MS associated with HSP was performed. He was treated with intravenous methylprednisolone for 5 days (1gr/die) with partial remission of sensory and motor symptoms and signs. Three months later, he complained acute worsening of paraparesis and hypoesthesia in lower limbs. A further MRI scan was unchanged. Further intravenous methylprednisolone was administered for 5 days with benefit. Immunomodulatory treatment was started.

FIG. 1



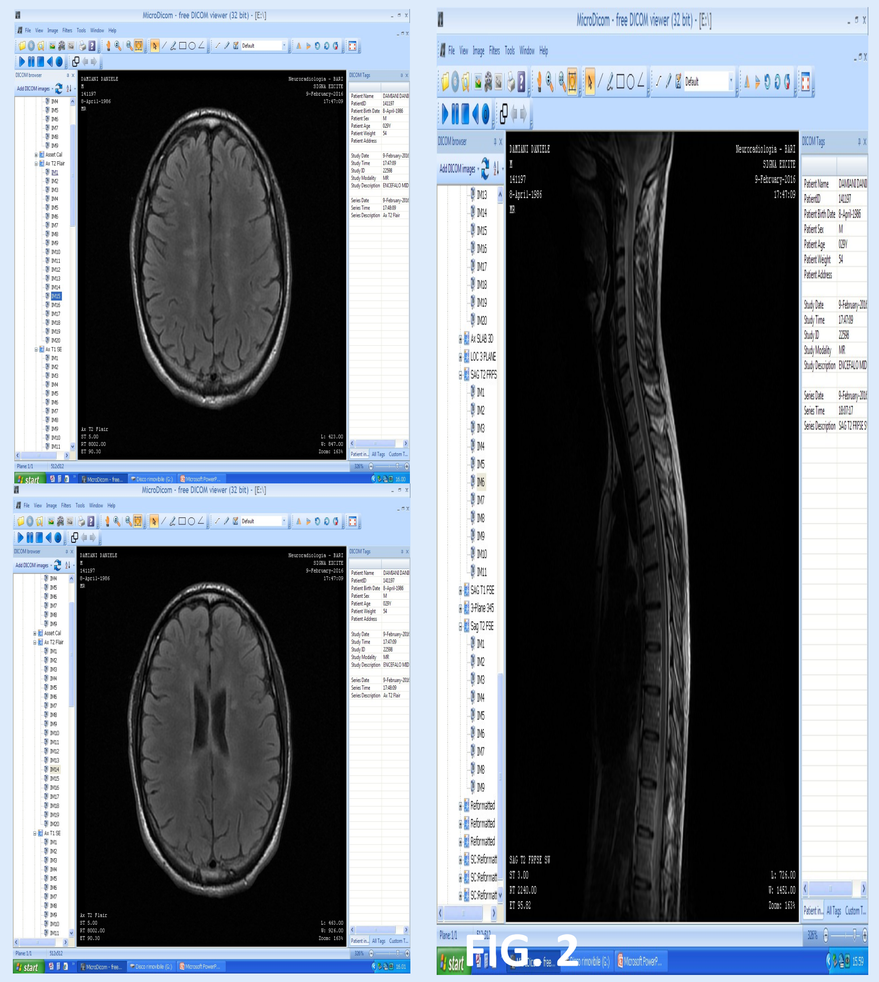


FIG. 2

CONCLUSIONS: To our knowledge this is the first case of association between MS and SPG7 mutation. Loss of function of HSP related genes, which are responsible for the maintenance of axons, could worsen the neurodegenerative process related to MS. Thus these genes could be relevant candidates for studies on the susceptibility to MS and also on disease severity and clinical outcome.

REFERENCES:

1. *Mead S H, Proukakis C, Wood N, Crosby A H, Plant G T, Warner T T. A large family with hereditary spastic paraparesis due to a frame shift mutation of the spastin (SPG4) gene: association with multiple sclerosis in two affected siblings and epilepsy in other affected family members. .J Neurol Neurosurg Psychiatry 2001; 71:788–791.*
2. *Yazıcı I, Yıldırım N, Zorlu Y. The coexistence of multiple sclerosis and hereditary spastic paraparesis in a patient. Neurology International 2013; 5(2):17-9.*
3. *Laurencin C, Rascle L, Cotton F, Grosset-Janin C, Bernard E, Depienne C, Vukusic S, Thobois S. A rare case of SPG11 mutation with multiple sclerosis. Rev Neurol (Paris). 2016 May 11. pii: S0035-3787(16)30019-4.*

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