

Hereditary Spastic Paraparesis Mimicking Primary Progressive Multiple Sclerosis Due to CYP7B1 Gene Mutation: A Case Report

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ABSTRACT

The hereditary spastic paraplegias (HSPs) are a group of disorders characterised by progressive lower limb weakness and spasticity. This report presents the a case of a 49-year-old female with spastic paraparesis, initially suspected to be primary progressive multiple sclerosis (PPMS). Genetic testing later identified two mutations in the CYP7B1 gene that was associated with the SPG5 form of HSP. This case highlights the challenge of distinguishing HSP from other chronic spinal cord diseases and emphasizes the role of genetic analysis in rare cases of spastic paraplegia.

Keywords: Hereditary spastic paraplegia, Spastic paraparesis, Primary progressive multiple sclerosis, CYP7B1 gene mutation, Genetic testing.

I. INTRODUCTION

Hereditary spastic paraplegia defines genetically and clinically heterogeneous group of disorders which is mainly characterized by progressive weakness of lower limbs and spasticity. The HSPs can be classified as either 'pure' (uncomplicated) or 'complex' (complicated). Pure forms involve lower limb spastic paraplegia and may include bladder involvement and subtle sensory signs such as impaired vibration sense. Complicated forms include additional neurological and non-neurological manifestations, such as cognitive impairment, dysarthria, optic atrophy and peripheral neuropathy. Due to overlapping clinical features, HSP may sometimes lead to misdiagnosis of other neurodegenerative or neuroinflammatory diseases including primary progressive multiple sclerosis (PPMS). In this case, we report a patient of HSP due to a CYP7B1 gene mutation who presented with spastic paraparesis, initially misdiagnosed as PPMS.

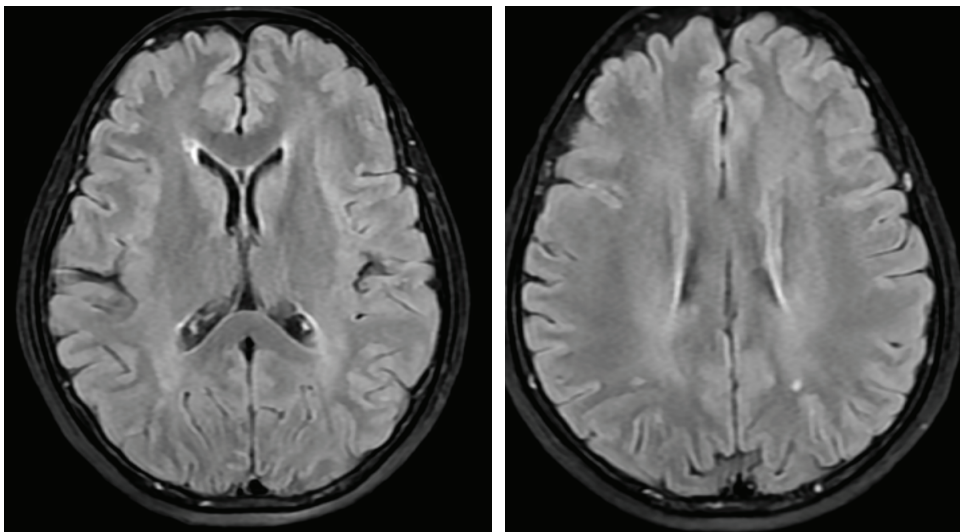


Figure 2. White Matter Lesions on Brain MRI (Lynx Ear Sign)

The brain MRI of the patient shows non-specific white matter lesions in the periventricular region, particularly near the frontal horns of the lateral ventricles. These lesions exhibit the characteristic “ears of the lynx sign”, which is a suggestive feature observed in hereditary spastic paraplegia.

limited to lower limbs beginning at late adulthood and the presence of oligoclonal bands (OCBs) in the cerebrospinal fluid (CSF). Although, the absence of demyelinating lesions as typical MRI features in PPMS, especially in the presence of documented family history gave us a clue to diagnose HSP. The results of genetic testing later confirmed the diagnosis SPG5 form of HSP. It is important to differentiate HSP from other chronic spinal cord diseases, as the management strategies differ significantly.

Although the presence of OCBs in the CSF is typically associated with multiple sclerosis, it has also been observed in a minority of HSP cases, particularly in patients with more severe and chronic presentations. This underscores the need for comprehensive diagnostic approaches, including genetic testing, especially when standard imaging and CSF analysis yield inconclusive results.

However, an increasing number of cases of comorbid hereditary spastic paraplegia (HSP) and possible multiple sclerosis (MS), including the PPMS have been described.

Hereditary spastic paraplegia type 5 (SPG5) is an extremely rare subtype, with an estimated prevalence of 1 per million individuals, usually a pure hereditary spastic paraplegia although complex type features have been reported in some individuals. In addition to spasticity and weakness, people with Hereditary spastic paraplegia type 5 can present deep sensory disturbance, sphincter disorder or high arches of the feet. Symptoms can begin at any age from childhood through late adulthood. Most patients experience onset of symptoms in the second – fourth decades of life.

SPG5 due to mutations in the CYP7B1 gene encoding a distinct microsomal oxysterol-7 α -hydroxylase. This enzyme is involved in the

degradation of cholesterol into primary bile acids. CYP7B1 deficiency results in accumulation of neurotoxic oxysterols, with elevation of 25-hydroxycholesterol (25-OHC) and 27-hydroxycholesterol (27-OHC) in the plasma and a much higher increase of 27-OHC in the CSF. However, it is important to note that two trials have demonstrated a reduction in cholesterol/bile acid biomarkers, but without benefit in terms of clinical, imaging, or electrophysiological outcome measure.

VI. CONCLUSION

This case of HSP type 5 due to mutations in the CYP7B1 gene highlights the clinical challenges in distinguishing hereditary spastic paraplegia from other conditions such as primary progressive multiple sclerosis. Genetic testing plays a crucial role in confirming the diagnosis of rare neurodegenerative disorders and guiding appropriate treatment and management.

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