A Complex Clinical Case in a Patient with Congenital Spastic Tetraparesis: Diagnosis of Relapsing-Remitting Multiple Sclerosis and Hereditary Myopathy with a Novel Variant in the ACTN2 Gene

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OBJECTIVES

We report the complex clinical case of a woman presenting with a multisystemic condition, including congenital spastic tetraparesis, von Willebrand disease, obstructive sleep apnea syndrome (OSAS), restrictive respiratory failure with diaphragmatic elevation and chronic hyperCKemia. She was diagnosed with relapsing-remitting multiple sclerosis (RRMS) and was found to carry a rare variant in the ***ACTN2*** gene, potentially associated with a hereditary myopathy (1, 2).

MATERIALS AND METHODS

The patient, a 37-year-old woman, has had spastic tetraparesis since birth and suffers from multiple comorbidities. Her monozygotic twin sister has been diagnosed with MS. She presented with recurrent episodes of facial hypoesthesia, vertigo, worsening of pre-existing lower limb weakness, and generalized fatigue. Persistently elevated creatine kinase (CK) levels were observed in the patient, her twin sister, and their father. In 2024, the patient was hospitalized for a comprehensive diagnostic workup. This included neurological examination with segmental strength testing, neuropsychological assessment, lumbar puncture for oligoclonal bands, brain and spinal cord MRI, electromyography (EMG), genetic testing for hereditary myopathies, echocardiogram, evoked potentials, and specialist consultations for obesity management.

RESULTS

The clinical relapsing-remitting pattern, radiological findings (periventricular and dorsal demyelinating lesions), and the presence of oligoclonal bands confirmed dissemination in time and space, supporting a diagnosis of RRMS. Elevated CK levels (323 U/L) and EMG findings revealed symmetric signs of active and chronic myopathic involvement. Genetic testing identified a heterozygous c.2648C>T p.(Ala883Val) variant in the *ACTN2* gene.

DISCUSSION AND CONCLUSIONS

This case highlights the diagnostic complexity in patients with congenital motor impairment and multiple comorbidities. Although the identified *ACTN2* variant is not yet described in the literature or major genomic databases, it shows features of rarity and phylogenetic conservation. In silico tools predict a potentially damaging impact on protein structure or function.These findings support the hypothesis of a coexisting hereditary myopathy, which aligns with altered biochemical markers and family history. The clinical overlap between MS and myopathic features further complicates differential diagnosis. In patients with chronic motor deficits and a family history of neuromuscular or biochemical abnormalities, the possibility of coexisting autoimmune and genetic disorders must be considered. *ACTN2* is already associated with various myopathies and cardiomyopathies (3). Genetic testing is ongoing in the family. This case underlines the value of a multidisciplinary approach and the critical role of molecular genetics in clarifying complex clinical presentations.

References:
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