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A RARE AND TREATABLE CASE OF SPASTIC PARAPARESIS DUE TO MTHFR GENE MUTATION-CASE REPORT

Neurology

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ABSTRACT

Background: Spastic paraparesis has a diverse etiology, with hereditary forms, such as those caused by mutations in the 5,10-Methylenetetrahydrofolate reductase (MTHFR) gene, being rare but potentially treatable. This case highlights the importance of timely diagnosis and treatment in preventing irreversible neurological damage. **Case Report:** A 21-year-old male presented with a 3-year history of progressive stiffness in both lower limbs, leading to difficulty in walking and performing daily activities such as standing from a squat and wearing footwear. Neurological examination revealed spastic paraparesis with exaggerated deep tendon reflexes, ankle clonus, and a positive Babinski sign, without sensory, cranial nerve, higher mental function, or autonomic involvement. Laboratory investigations were unremarkable except for elevated serum homocysteine levels (112.23 µmol/L). MRI of the brain showed ill-defined T2/FLAIR hyperintensities in the bilateral centrum semiovale and corona radiata. Genetic analysis confirmed MTHFR gene mutation. The patient was treated with Baclofen, methylcobalamin, folic acid, pyridoxine, and dietary modifications, resulting in symptomatic improvement over 6 months. **Conclusion:** MTHFR-associated spastic paraparesis, although rare, is a treatable genetic condition. Early diagnosis using serum homocysteine screening and genetic analysis is crucial to initiating appropriate treatment and preventing irreversible neurological damage.

KEYWORDS

MTHFR, Spastic paraparesis, homocysteine

INTRODUCTION

Spastic paraparesis is a clinical syndrome with varied etiologies. Hereditary forms, such as MTHFR-associated spastic paraparesis, are rare but notable due to their potential treatability.[1] This case illustrates the clinical, radiological, and genetic findings of this condition, emphasizing the need for early intervention.

Case Report

History and Clinical examination: A 21-year-old male presented with progressive stiffness in both lower limbs over three years. Initially, the stiffness caused difficulty in standing from a squatting position and wearing footwear, eventually progressing to significant gait impairment. The patient denied upper limb involvement, sensory deficits, bowel or bladder dysfunction, cranial nerve symptoms, or systemic complaints. The patient had no significant past or family history, normal developmental milestones, and an unremarkable personal history. Clinical examination revealed features of spastic paraparesis, including increased tone, brisk reflexes in both lower limbs, ankle clonus, and a positive Babinski sign, with normal sensory, cranial nerves, autonomic, and cerebellar systems. His higher mental functions were also normal.

Investigations

Routine laboratory tests, including vitamin B12, thyroid function, and autoimmune screening, were normal. VDRL was negative. HIV, HBsAg and HCV were non-reactive. Gas Chromatography and Mass spectrometry (GCMS) and tandem mass spectrometry (TMS) testing were normal. Nerve conduction studies were normal. MRI Brain revealed T2/FLAIR hyperintensities without diffusion restriction or contrast enhancement in bilateral centrum semiovale. Genetic analysis confirmed an MTHFR mutation: c.740del p.Gly247AlafsTer23 and c.304G>C p.Gly102Arg supported by elevated serum homocysteine levels (112.23 µmol/L).

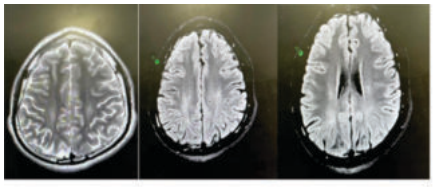

Figure: T2/FLAIR Hyperintensities in bilateral Centrum semiovale and corona radiata

Treatment

The patient was treated with Baclofen (10 mg twice daily), methylcobalamin (1500 mcg weekly for one month, then monthly), folic acid (5 mg twice daily), and pyridoxine (40 mg daily), along with dietary modifications, including a high-betaine diet. At a 6-month follow-up, significant symptomatic improvement was noted.

DISCUSSION

MTHFR-associated spastic paraparesis arises from hypomethioninemia, which impairs myelination and leads to white matter abnormalities. Although rare, adult-onset cases predominantly present with gait disturbances.[2-5] Radiological findings, while nonspecific, can aid in early diagnosis, with white matter abnormalities being the most common feature, observed in 70% of cases.[6] Early intervention with betaine and vitamins can help stabilize symptoms, though complete symptom reversal is uncommon.[1]

CONCLUSION

This case underscores the significance of considering MTHFR-associated spastic paraparesis in patients with chronic non-compressive spastic paraparesis. Serum homocysteine levels serve as a valuable screening tool, and genetic confirmation facilitates targeted therapy, emphasizing the importance of early diagnosis in improving outcomes.

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