CASE REPORT

A CASE OF HEREDITARY SPASTIC PARAPLEGIA- A NEUROLOGICAL CONUNDRUM

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ABSTRACT

Objectives: Hereditary Spastic Paraplegia is a group of rare neurological degenerative disorders with a broad pattern of inheritance and not limited to a specific age group. Around 82 different loci have been identified in the causation of this disease. It may present with weakness limited to lower limbs or maybe a complex disease with extra neurological manifestations.

Case Description: We report a case of a 44-year-old Pakistani male with progressive spasticity and lower limb weakness of 3 years duration with upper motor neuron signs limited to the lower limb. His Baseline investigations were within normal range and his metabolic profile as well as inflammatory markers were normal. His MRI showed Non-specific peri-ventricular intensities on T2W and FLAIR sequences with mild axonal neuropathy on Nerve Conduction Studies. EMG was normal. He was diagnosed with Type 2, Pure Hereditary Spastic Paraplegia after the exclusion of all other possible differentials. He was started on muscle relaxants, statins, and pregabalin.

Discussion: Our diagnosis was supported by previous literature on the disease and the treatment we initiated was also evidence-based. Due to the lack of accessibility to genetic testing in Pakistan, our case highlights the importance of analyzing in detail, a patient's clinical examination and history as well as picking subtle MRI findings.

Key Words: Case Report, Hereditary Spastic Paraplegia, SPG, Inherited

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INTRODUCTION

Hereditary Spastic Paraplegia (HSP) is a rare group of diverse inherited diseases that affect the nervous system with a prevalence of 1–5:100,000. The disease may be inherited through multiple inheritance patterns and may be AD, AR, XR, or even maternal and the patient may not always give a positive family history. They have been classified by their symptoms; pure or complex, the genotypes (more than 82 loci/genes i.e., SPG1-SPG82), and the age of manifestation. The pure form is limited to lower limb spasticity while the complex form may manifest as extra-neurological features in addition to lower limb spasticity. The degeneration in the pure form usually involves the corticospinal tract and manifests as distal axonal neuropathy of the lower limbs. The disease is progressive and to date, there is no drug to slow the progress and we can only alleviate the symptoms of the patients with muscle relaxants and physiotherapy

CASE DESCRIPTION

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A 44-year-old Pakistani male who was employed as a clerk at a factory, presented to the out-patient-department with progressive bilateral lower limb weakness, spasticity, and abnormal gait for the last 3 years. He had no previous comorbidities and no family history of neurological illnesses. He complained of lower limb muscle fatigue and inability to walk for more than 4-5 minutes with associated paresthesia and numbness as well. He also complained of urinary urgency. There were no symptoms of cognitive decline. On examination, he had a wide scissoring gait, there was bilateral hypertonia in lower limbs with hyperreflexia at the knee and ankle. Babinski's Reflex, Chaddock's Reflex, and Gordon's Reflex were all positive. Vibration sense was reduced in the lower limbs and Romberg's sign was positive. Proprioception, pain, touch, and temperature sense were preserved. Power was 5/5 in all limbs and Cranial nerve examination as well as examination for cerebellar signs was unremarkable. Upper limb neurological examination was normal. Laboratory investigations; metabolic profile, inflammatory markers, and auto-immune profile were within normal ranges. Screening for Muscular dystrophy, Myasthenia Gravis, Auto-immune encephalitis, and multiple sclerosis was normal.

Nerve Conduction studies revealed mild axonal neuropathy in bilateral lower limbs. EMG was normal. MRI Brain with contrast showed hyper-intense signals in periventricular white matter and centrum semi-ovale region on T2W and FLAIR sequence. MRI Lumbosacral spine showed a mild disc bulge at LV5-SV1 level with only thecal indentation. See Figure 1 for details. A diagnosis of Pure type of Hereditary Spastic Paraplegia, the adult

variant was made after excluding other possible causes. The patient was started on Baclofen 10mg thrice a day, Pregabalin 50mg once a day, and Atorvastatin 10mg once a day. He was also given multivitamins.

DISCUSSION

Hereditary spastic paraplegias (HSPs) are a group of rare hereditary neurodegenerative diseases characterized by degeneration of the corticospinal tract involving

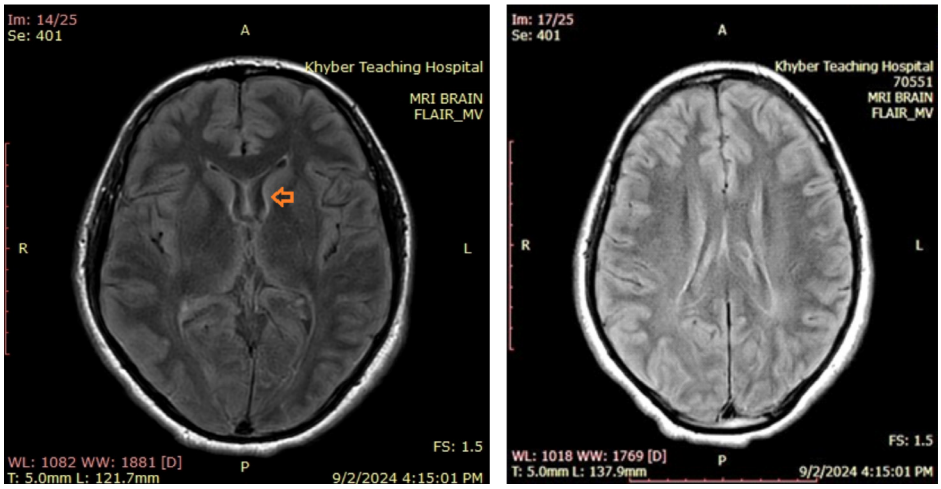

Fig 3: MRI Brain-FLAIR sequence: Shows Few discrete high signal foci in periventricular white matter and centrum semi-ovale region.

the first-order motor neuron but may extend to the second-order motoneuron.[3] Its most prominent clinical manifestation is progressive bilateral lower limb weakness with spasticity. There are two main types identified by Harding based on the clinical manifestations the Pure/uncomplicated type which was the type identified in our patient is characterized by lower limb spasticity, hypertonic bladder, and a mildly decreased vibration sense in the lower limbs. This type is less debilitating and does not decrease the lifespan of the patient. Whereas the complicated type includes symptoms of the pure type with additional symptoms of ataxia, seizures, cognitive impairment, muscle atrophy, extrapyramidal signs, and peripheral neuropathy. Based on the age of onset they can be classified into Type 1 in less than 35 years of age and Type 2 in patients more than 35 years of age.

Genetic diagnosis is the only way to confirm the diagnosis and without it is difficult to estimate the exact prevalence of the disease but a recent study detects the prevalence to be 2.4/100,000 based on genetic/ clinical diagnosis/ both. The diagnosis is usually clinical in the absence of genetic testing facilities but MRI findings can also aid the diagnosis.

Autosomal dominant, autosomal recessive, and X-linked or maternal (mitochondrial) inheritance patterns have all been reported with HSP, therefore, family history is crucial to diagnosis but our patient did not give such a history in immediate family members, distant relatives' history was unknown to him as he was estranged from them. HSP is confused with several disorders such as leukodystrophies, multiple sclerosis, peripheral neuropathies, Parkinson's disease, and even Amyotrophic lateral sclerosis. Therefore, it is essential that we exclude these causes before making a final diagnosis of HSP.

Genetic testing includes Next-generation sequencing of exons and Multiplex litigation probe amplification but unfortunately, it wasn't available in our setting.

MRI Findings are equally important in the diagnosis which may show thinning of the spinal cord, thinning of the corpus callosum, cerebellar atrophy, and Periventricular hyperintensities. In addition, there is the diagnostic "Ears of the Lynx sign" which shows an abnormality at the forceps minor of the corpus callosum appearing hyper-intense on T2-FLAIR-weighted and hypo-intense on T1-weighted images, this was not prominent in our patient but was seen in a similar case in Pakistan. There is no curative or modifying therapy yet available for HSP but symptomatic treatment can improve quality of life. Muscle relaxants such as Tizanidine, Baclofen, and oxybutynin for urinary urgency can be given. Physiotherapy and orthotics may be used for stiffness and deformities. There is currently research being done into gene therapy and tubulin-binding molecules. Lowering cholesterol levels is recommended for the treatment of some HSP phenotypes using atorvastatin.

CONCLUSION

Hereditary Spastic Paraplegia was a clinical diagnosis made after the exclusion of other possible diagnoses in our patient. Based on clinical features and MRI findings of Non-specific periventricular hyperintensities on FLAIR and T2 weighted imaging. The patient had struggled immensely in the 3 years before coming to us and therefore it is essential to focus on the clinical examination and history taking of the patient as well as picking MRI findings and correlating them. We hope that in the future we will have access to genetic testing facilities for this disease so that the patient can be labeled with more certainty.

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Authors	Conceived & designed the analysis	Collected the data	Contributed data or analysis tools	Performed the analysis	Wrote the paper	Other contribution
Qureshi MS	✓	×	✓	×	✓	×
Naeem A	✓	✓	×	✓	✓	×
Naim F	×	✓	×	×	✓	×
Raheem N	✓	✓	✓	×	✓	✓
Shaukat MA	✓	✓	×	✓	✓	×

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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