Editorial
Volume 11:4, 2022

Journal of Metabolic Syndrome

ISSN: 2167-0943 Open Access

Editorial on Patients with Hereditary Spastic Paraplegias

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Editorial

Hereditary Spastic Paraplegias are a group of neurodegenerative diseases that affect the corticospinal pathways and cause lower-limb stiffness and paralysis. HSP is estimated to affect approximately 1.8/100,000 patients in both autosomal dominant and autosomal recessive forms. HSP is classified using the inheritance pattern. Clinical phenomenology and molecular pathophysiological processes the most common neuropathological symptom is axonal degeneration affecting the lateral corticospinal pathways in both the cervical and thoracic spinal cords. The purpose of this review paper is to provide a comprehensive understanding of the HSP classification, neuropathology, and differential diagnosis. Hereditary spastic paraplegias (HSPs) are a group of neurological disorders distinguished by severe lower-extremity spasticity caused by a length-dependent axonopathy of corticospinal upper motor neurons.

HSPs are classified as "pure" or "complex," with additional neurologic and extraneurologic characteristics. HSPs are one of the most genetically diverse neurologic diseases, with more than 70 different genetic loci and more than 60 mutant genes previously identified. Many studies on the molecular pathophysiology of HSPs have highlighted the importance of basic cellular activities in axon growth and maintenance, such as membrane trafficking [1-3], mitochondrial function, organelle shape and biogenesis, axon transport, and lipid/cholesterol metabolism. A surprisingly small number of converging cellular pathogenic motifs have been discovered for the most common HSPs, and some of these pathways suggest promising future targets.

Hereditary spastic paraplegia (HSP) is a group of inherited neurodegenerative diseases characterised by increased lower-limb stiffness. It can be difficult to distinguish HSP from other genetic illnesses associated with spasticity because the pathogenic mechanism, associated clinical symptoms, and imaging abnormalities vary greatly depending on the afflicted gene. Despite the fact that next-generation sequencing-based gene panels are now widely available, they have limitations, and the majority of suspected cases do not receive a molecular diagnosis. Symptomatic treatment is still in its early stages, but with a better understanding of the pathophysiological underpinnings of specific HSP subtypes, targeted molecular therapeutics and tailored therapy are becoming more feasible. Hereditary spastic paraplegia refers to a group of hereditary neurodegenerative and neurodevelopmental disorders caused by primary retrograde malfunction of the corticospinal tract's long descending fibres [4,5].

Although spastic paraparesis and urinary dysfunction are the most common clinical manifestations, a complex set of neurological and systemic compromises has recently been identified, as have an increasing number of novel genetic subtypes in the previous decade. Characterizing an individual's and family's medical history is critical in the diagnostic process; however, in many cases, there are few and unspecific data, resulting in a low rate of conclusive diagnosis based solely on clinical and neuroimaging findings. Likewise, a wide range of neurological acquired and hereditary illnesses should be considered in the differential diagnosis and correctly ruled out after a thorough lab, neuroimaging, and genetic examination.

The purpose of this review paper is to provide a comprehensive summary of the primary clinical and genetic characteristics of hereditary spastic paraplegia's traditional and newly identified subtypes (HSP). Hereditary spastic paraplegia (HSP) is a group of genetic illnesses characterised by lower limb weakness and stiffness. HSP has approximately 50 different genetic forms. People from all walks of life are affected by HSP, with prevalence rates ranging from 1.2 to 9.6 per 100,000. The symptoms and signs can appear at any age. Gait disability usually progresses slowly over several years after childhood. Gait disability may not progress significantly if it begins in infancy or early childhood. Post mortem examinations frequently reveal degeneration of corticospinal tract axons (most notably in the thoracic spinal cord) and fasciculus gracilis fibres (maximal in the cervico-medullary region).

HSP syndromes appear to be characterised by motor-sensory axon degeneration, primarily (but not exclusively) affecting the distal ends of long CNS axons.

HSP-encoded proteins perform a variety of functions, including:

- Axonal transport (SPG30/KIF1A, SPG10/KIF5A, and possibly SPG4/Spastin)
- Endoplasmic reticulum morphology (e.g., SPG3A/Atlastin, SPG4/Spastin, SPG12/reticulon 2, and SPG31/REEP1, all of which interact)
- Mitochondrial function (for example, SPG13/chaperonin 60/heat shock protein 60 and mitochondrial ATP6)
- For example, SPG2/Proteolipid protein and SPG42/Connexin 47 are involved in myelin production.
- Protein folding and the ER stress response (SPG6/NIPA1, SPG8/K1AA0196 (Strumpellin), SGP17/BSCL2 (Seipin), "mutilating sensory neuropathy with spastic paraplegia" caused by the CcT5 mutation, and possibly SPG18/ERLIN2).
- Corticospinal tract neurodevelopment (e.g., SPG1/L1 cell adhesion molecule and SPG22/thyroid transporter MCT8)
- SPG28/DDHD1, SPG35/FA2H, SPG39/NTE, SPG54/DDHD2, and SPG56/CYP2U1) are all involved in the metabolism of fatty acids and phospholipids.
- Endosome membrane trafficking and vesicle production are demonstrated by SPG47/AP4B1, SPG48/KIAA0415, SPG50/AP4M1, SPG51/AP4E, SPG52/AP4S1, and VSPG53/VPS37A.

Animal models (including bovine, murine, zebrafish, Drosophila, and C. elegans) are available for several types of HSP, allowing researchers to investigate disease causes and potential therapies. This review focuses on new ideas related to this broad category of clinically related illnesses.

Conflict of Interest

The author declares that there is no conflict of interest associated with this paper.

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Received: 02-Apr-2022, Manuscript No. jms-22-67346; **Editor assigned:** 04-Apr-2022, Pre QC No. P-67346; **Reviewed:** 09-Apr-2022, QCNo.Q-67346; **Revised:** 14-Apr-2022, Manuscript No.R-67346; **Published:** 19-Apr-2022, DOI: 10.37421/2167-0943.2022.11.271.

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How to cite this article: Fink, John. "Editorial on Patients with Hereditary Spastic Paraplegias." J Metabolic Synd 11 (2022): 271.