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Gerstmann-Straussler-Scheinker Disease - A Review

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Abstract

Gerstmann-Straussler-Scheinker Disease (GSS) is an extremely rare, usually familial, fatal prion disease. Such disease affects our one of the most important part of our body that is responsible for our thoughts and coordination of our sensory information, the Nervous System. Some particular variations in the PNRP gene leading to the atypical shape of the prion protein give rise to this disease. PRNP encodes a protein called prion protein (Prp). We are unaware of its functions but we do know that Prp plays a very significant role in the functioning of the human brain and other parts of the human nervous system. The destruction of neural cells due to the clumping of abnormal proteins is one of the characteristic features of this disease. The continuous deterioration of the section of our brain responsible for the motor control in a human body, the cerebellum, and different degrees of dementia are the main characteristics of GSS. Weakness in the legs, diminished reflexes, cognitive decline, ataxia including slurred speech and reduced coordination, and spasticity are some of the main symptoms seen in a person suffering from GSS. The median survival time from onset to death of GSS patients ranges from two to ten years after its diagnosis. The objective of this paper to gather all the data and information available about this rare disease so that future researchers who are interested in this field can refer to this paper without having to curate it all by themselves saving time and increasing their efficiency towards solving this mystery. We are very behind in the understanding of the pathophysiological processes that underlie this disease. Through this paper, we have analyzed and reviewed all the literature on this topic to summarize what is our current understanding of this disease and the possible treatments to cure it or alleviate its symptoms. Through a thorough literature review, we can conclude that research on this topic has potential. With mostly case reports on this disease, the research for its cure and treatments for alleviating its symptoms are not yet advanced.

Keywords: Cerebellar ataxia; Prion disease; Gerstmann-Sträussler-Scheinker disease; PRNP gene; Neurodegeneration

Abbreviation: GSS: Gerstmann-Straussler-Scheinker Disease; MRI: Magnetic Resonance Imaging; CSF: Cerebrospinal Fluid; PrP: Prion Protein; TSE: Transmissible Spongiform Encephalopathy

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Introduction

With less than ten people out of an approximate population of 100,000,000, suffering from this disease that is a mere 0.00001%, GSS is a very rare disease. There are no available treatments to alleviate the symptoms or cures for this disease. With only a few cases documented around the world, cerebral ataxia and dementia are one of the most important characteristics of this TSE, **Gerstmann-Straussler-Scheinker Disease (GSS)**. TSE is a set of rare neurodegenerative diseases characterized by tiny holes in the human brain giving it a spongy appearance. (TSE) is distinguishable from other neurodegenerative diseases due to the build-up of an atypical configuration of a regular protein (PRPC) called scrapie prion protein (PrPSc).

According to Keuss SE et al. the MRI, EEG, and CSF analysis of patients suffering from GSS might not show us the characteristics of GSS leading to its diagnosis and sometimes may even come out as a scan of a normal human being even in a highly progressive and advanced case which makes the diagnosis of this disease extremely hard. They underline the difficulties they faced so that others might learn from their mistakes [1].

The amyloid clusters in the brain are one of the pathological characteristics of GSS. The proteins that have undergone mutations arise from the PrP- immuno-reactive amyloid accumulation in the tissues of the cerebral cortex and the basal ganglia of the human brain. As per Bugiani O et al. the clinical and pathological variability observed in GSS families is related to both mutations and the M/V polymorphism at codon 129 of the mutated gene [2].

Literature Review

According to Smid J et al. p.Pro102Leu is one of the most usual variations of this rare prion disease which is genetically inherited due to DNA abnormality. In their paper, they outline the clinical and neuropathological data of seven Brazilian patients with different heritage carrying the p.Pro102Leu variation [3]. Amino acids like valine or methionine are the common polymorphism at residue 129 of the human prion protein (PrP). This polymorphism at residue 129 increases the chances of prion diseases like TSE, GSS being susceptible [4]. But their findings and conclusions disprove the hypothesis that variation in the phenotypic character is accredited to polymorphism at codon 129 [3].

As per Zhao MM et al. This rare inherited TSE is classified under prion diseases and one of the main identifiable symptoms is progressive cerebral ataxia. But doctors often could misdiagnosis this disease for some other disease that may also cause cerebral ataxia. Therefore, in their paper, they outline the importance of ataxia patients be diagnosed with this disease through genetic testing [5].

According to Cracco L et al. despite the differences among the characteristics of their phenotype, most human prion diseases are categorized into Creutzfeldt-Jakob disease (CJD) and Gerstmann-Sträussler-Scheinker disease (GSS). Although we have a better understanding of CJD's connection with the prion protein that is resistant to proteinase, the linkage between this protein and GSS's underlying pathological processes is still a mystery to us. According to their findings, they are the first to establish resPrPD aggregate formation mechanism in prion diseases. As per Cracco L et al's findings, in GSSA117V and GSSF198S the two most common variants of GSS, they found multimer of an internal fragment forming during the aggregation of prions. They have also reported the development of multimers which are covalently linked to each other in GSS and other neural disorders characterized by neuron degenerations [6].

As per the research conducted by Baiardi S et al. the finding of accumulated phosphorylated tau protein without a concomitant A-beta protein deposition in the CSF profile of cases with neurodegenerative disorders establishes a neuropathological connection with GSS as secondary tau-positive protein is one of the most important distinctive features of this disease. Their research underlines the importance of diagnosing for the GSS-p. D202N-V129 in cases with unusual Parkinsonism linked to progressive dementia [7].

According to Salsano E et al. the interchange of the amino acid leucine with proline at codon 102 in the Prp gene is the main cause of this rare autosomal dominant neurodegenerative disorder, Pro102Leu (GSS102 of which walking difficulties and dementia are the most common symptoms. Their findings show that areflexia, ataxia, and fragility in lower limbs are the primary symptoms of this prion disease are due to the damage to the hind part of the spinal cord and they outline the importance of the inclusion of GSS102 for the root of ataxia and areflexia. In contrast to Friedreich's Ataxia, the observations in patients with GSS102 show nerve conduction studies give the usual results despite the existence of lower limb areflexia. They conclude that patients struggling to walk due to lower limb areflexia in the absence of usual findings of central and peripheral conduction highly stipulate GSS as the diagnosis. Thus, doctors must be aware of this for the easy diagnosis of GSS102, a rare neurodegenerative disorder [8].

Marino S et al. research is the first to analyze and assess the structural and functional connectivity in GSS using an approach that includes several different modes of occurrences. The diagnosis of GSS was confirmed with the assessment of Genomic DNA. They assessed Somatosensory and Laser evoked potentials with resting-state functional and conventional MRI of a 40-year-old male subject enduring slowly progressive gait disturbance and suffering from cognitive impairment. These assessments showed the disability of the Central Nervous System (CNS) and the Peripheral Nervous System (PNS) to respond to noxious stimuli in the right upper and lower limbs and atrophy of vermis and cerebral hemispheres. They also pointed out the drastic growth in the functional connectivity of the bilateral visual cortex and the decline in functional connectivity of the bilateral frontal pole and percental [9].

Discussion and Conclusion

The research on GSS is not well established yet but through this paper, we have summarized the latest findings related to this disease like; the likelihood of GSS disease to be present on patients with atypical parkinsonism associated with dementia and patients whose muscles do not respond to any stimulus in the lower limbs are specifically indicative GSS102, which would help in the easy diagnosis of this rare disease, and also the findings of small internal fragments in GSS mechanism gives way for new research about the connection between GSS and of neurodegenerative disorders like Parkinson's and Alzheimer's diseases.

There have been advancements in the research of this disease to find better treatments and precise diagnosis methods. This paper underlines all the major advancements and finding in this topic of research. According to me mapping this disease in the brain and finding the root of the problem is the way to start for the

development of cures for GSS. I have collected, analyzed all the literature pertaining to this topic and have reviewed it for future researchers to refer this paper instead of going through tons of literature. Even though there has been a lot of research on this disease, we are still were far away from finding the precise causes and treatments of these diseases.

References

1 Keuss SE, Ironside JW, O'Riordan J (2017) Gerstmann-Sträussler-Scheinker disease with atypical presentation. BMJ Case Rep. bcr-2017

2 Bugiani O, Giaccone G, Piccardo P, Morbin M, Tagliavini F, et al. (2000) Neuropathology of Gerstmann-Sträussler-Scheinker disease. Microsc Res Tech 50: 10-15.

3 Smid J, Studart A, Landemberger MC, Machado CF, Nóbrega PR, et al. (2017) High phenotypic variability in Gerstmann-Sträussler-Scheinker disease. Arq Neuropsiquiatr 75: 331-338.

4 Lewis PA, Tattum MH, Jones S, Bhelt D, Batchelor M, et al. (2006) Codon 129 polymorphism of the human prion protein influences the kinetics of amyloid formation. J Gen Virol 87: 2443-2449.

5 Zhao MM, Feng LS, Hou S, Shen PP, Cui L, et al. (2019) Gerstmann-Sträussler-Scheinker disease: A case report. World J Clin Cases. 7: 389-395.

6 Cracco L, Xiao X, Nemani SK, Lavrich J, Cali I, et al. (2019) Gerstmann-Sträussler-Scheinker disease revisited: accumulation of covalently-linked multimers of internal prion protein fragments. Acta Neuropathol Commun 7: 85.

7 Baiardi S, Rizzi R, Capellari S, Bartoletti-Stella A, Zangrandi A, et al. (2020) Gerstmann-Sträussler-Scheinker disease (PRNP p.D202N) presenting with atypical parkinsonism. Neurol Genet 6: e400.

8 Salsano E, Fancellu R, Di Fede G, Ciano C, Scaioli V, et al. (2019) Lower limb areflexia without central and peripheral conduction abnormalities is highly suggestive of Gerstmann-Sträussler-Scheinker disease Pro102Leu. J Neurol Sci 302: 85-88.

9 Marino S, Morabito R, De Salvo S, Bonanno L, Bramanti A, et al. (2017) Quantitative, functional MRI and neurophysiological markers in a case of Gerstmann-Sträussler-Scheinker syndrome. Funct Neurol 32: 153-158.