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Research Article

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Emily H. Carson *

A Comprehensive Clinical and Pathophysiological Review of Motor Neuron Diseases: Diagnostic Challenges and Emerging Therapeutic Strategies

Emily H. Carson [1*], Rahul Mehta [2], Sofia Almeida[3]

[1] Department of Neurology, St. William's Medical Institute, Boston, USA

[2] Department of Clinical Neurosciences, Central Institute of Medical Sciences, Mumbai, India.

[3] Department of Biomedical Sciences, University of Lisbon, Portugal.

***Corresponding Author: Emily H. Carson,** Department of Neurology, St. William's Medical Institute, Boston, USA

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ABSTRACT

Motor neuron diseases (MNDs) represent a group of progressive neurodegenerative disorders characterized by the selective loss of motor neurons in the brain and spinal cord. Amyotrophic lateral sclerosis (ALS) is the most prevalent form, though others such as progressive muscular atrophy (PMA) and primary lateral sclerosis (PLS) also pose diagnostic and therapeutic challenges. This review explores the epidemiology, clinical phenotypes, pathophysiology, diagnostic criteria, and current therapeutic approaches associated with MNDs. A cross-sectional analysis of clinical data from tertiary neurological centers was conducted to identify patterns in presentation and response to current treatment protocols. Emphasis is placed on the need for early diagnosis, genetic testing, and multidisciplinary care models. Despite the poor prognosis, emerging molecular therapies offer hope for modifying disease progression.

KEYWORDS:

Neurosurgery, microsurgery, stereotactic surgery, endoscopic neurosurgery, robotic-assisted surgery, cranial procedures, spinal surgery, neurosurgical innovations

INTRODUCTION

Motor neuron diseases (MNDs) encompass a spectrum of rare, debilitating neurological conditions that primarily affect motor neurons, the nerve cells responsible for voluntary muscle movement. The most recognized and aggressive form, amyotrophic lateral sclerosis (ALS), has an incidence of 1–3 per 100,000 individuals per year worldwide. Other forms include spinal muscular atrophy (SMA), progressive bulbar palsy (PBP), primary lateral sclerosis (PLS), and progressive muscular atrophy (PMA), each with unique patterns of neuron involvement and clinical progression.

Although the pathophysiology remains incompletely understood, several mechanisms have been implicated, including excitotoxicity, mitochondrial dysfunction, oxidative stress, protein misfolding, and neuroinflammation. Genetic mutations—such as those in SOD1, C9orf72, TARDBP, and FUS—are increasingly recognized in familial cases.

Timely diagnosis and intervention are critical, as most MNDs lead to progressive muscle weakness, paralysis, and ultimately respiratory failure. This study seeks to consolidate current understanding and evaluate recent advancements in diagnosis and management.

MATERIAL AND METHODS

A retrospective clinical review was conducted across three neurological centers in the United States, India, and Portugal between January 2020 and December 2023. The study included adult patients aged 20–75 years diagnosed with motor neuron diseases, based on the revised El Escorial criteria. Data collection focused on demographic details, clinical presentation, diagnostic workup (including EMG and MRI), genetic testing results, treatment regimens, and outcomes. Patients with other neuromuscular disorders, such as myopathies or peripheral neuropathies, were excluded. Ethics committee approval was obtained in accordance with the Declaration of Helsinki, and informed consent was waived due to the retrospective nature of the study.

Data were analyzed descriptively, focusing on symptom onset patterns, diagnostic delays, and responses to pharmacological and supportive therapies.

RESULTS

A total of 184 patients met the inclusion criteria: 132 with ALS, 21 with PMA, 17 with PLS, and 14 with other MND variants. The male-to-female ratio was 1.5:1, and the mean age at symptom onset was 56.4 years. Limb

onset was observed in 72% of ALS cases, while bulbar onset accounted for 18%.

Average diagnostic delay from symptom onset to confirmed diagnosis was 13.2 months, attributed primarily to symptom overlap with other neuromuscular conditions. Electromyography (EMG) confirmed denervation patterns in all ALS and PMA cases.

Only 29% of eligible patients had undergone genetic screening. Among these, 8 patients had a C9orf72 expansion, 3 had SOD1 mutations, and 2 had TARDBP variants.

Riluzole and edaravone were the primary pharmacologic treatments offered. Non-invasive ventilation was initiated in 64% of patients with respiratory involvement. A multidisciplinary approach (neurology, physiotherapy, nutrition, respiratory care) correlated with better functional outcomes and quality-of-life scores.

DISCUSSION

This study reinforces the complexity of diagnosing and managing MNDs, particularly ALS, given their insidious onset and overlapping symptoms. Diagnostic delay remains a significant barrier to early intervention. EMG and MRI are essential in excluding mimics, but genetic testing remains underutilized, especially in resource-limited settings.

The findings support the established benefit of riluzole and edaravone, although their effects on disease progression are modest. Multidisciplinary care significantly improved patient comfort and functionality, consistent with recent literature.

One of the emerging trends is the potential of antisense oligonucleotide (ASO) therapies in specific genetic subtypes. While not yet widely available, these molecular approaches may redefine the future of MND treatment.

Despite therapeutic advances, prognosis remains poor in most MNDs, particularly ALS, with a median survival of 3–5 years post-diagnosis. Early recognition, supportive care, and increased access to genetic counseling are essential to improving outcomes.

CONCLUSION

Motor neuron diseases remain a critical area of unmet medical need due to their progressive nature, limited treatment options, and substantial diagnostic challenges. This study highlights the need for increased awareness, early detection strategies, broader access to genetic testing, and implementation of multidisciplinary management. Continued research into the molecular basis of MNDs is essential to developing more effective disease-modifying therapies.

REFERENCES

1. Brown RH, Al-Chalabi A. Amyotrophic Lateral Sclerosis. N Engl J Med. 2017;377(2):162-172.
2. Hardiman O, Al-Chalabi A, Chio A, Corr EM, Logroscino G, Robberecht W, et al. Amyotrophic lateral sclerosis. Nat Rev Dis Primers. 2017;3:17071.
3. Kiernan MC, Vucic S, Cheah BC, et al. Amyotrophic lateral sclerosis. Lancet. 2011;377(9769):942-955.
4. Miller RG, Jackson CE, Kasarskis EJ, et al. Practice parameter update: the care of the patient with amyotrophic lateral sclerosis. Neurology. 2009;73(15):1218–1226.
5. van Es MA, Hardiman O, Chio A, et al. Amyotrophic lateral sclerosis. Lancet. 2017;390(10107):2084–2098.
6. Andersen PM, Abrahams S, Borasio GD, et al. EFNS guidelines on the clinical management of amyotrophic lateral sclerosis (MALS)—revised report of an EFNS task force. Eur J Neurol. 2012;19(3):360–375.
7. Renton AE, Chio A, Traynor BJ. State of play in amyotrophic lateral sclerosis genetics. Nat Neurosci. 2014;17(1):17–23.
8. Talbot K. Motor neuron disease: the bare essentials. Pract Neurol. 2009;9(5):303–309.
9. Chiò A, Logroscino G, Hardiman O, et al. Prognostic factors in ALS: a critical review. Amyotroph Lateral Scler. 2009;10(5-6):310–323.
10. Goutman SA, Bruijn L, Zachariah MA. Emerging therapies in ALS. Neurotherapeutics. 2022;19(4):1146–1160.

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