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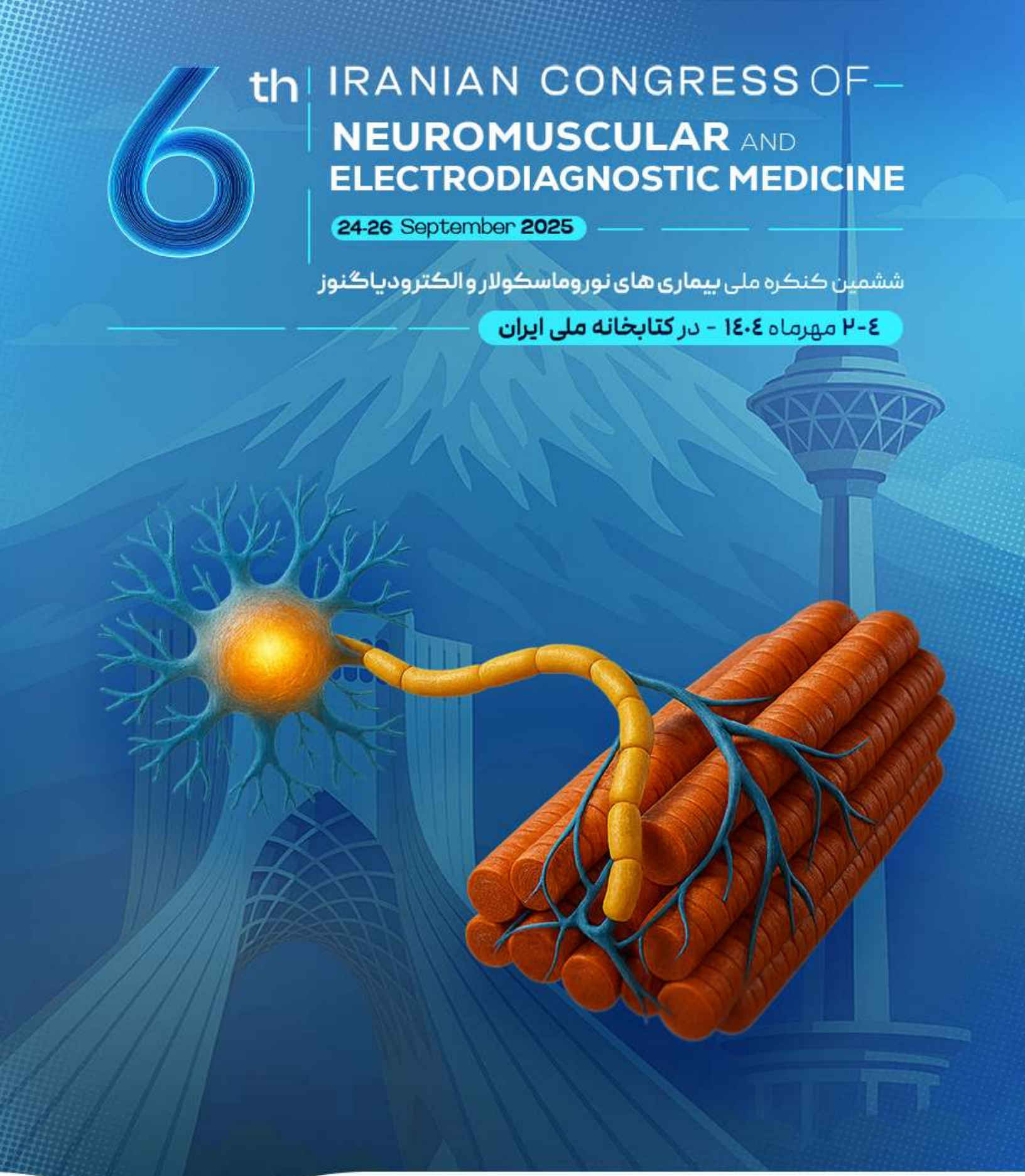

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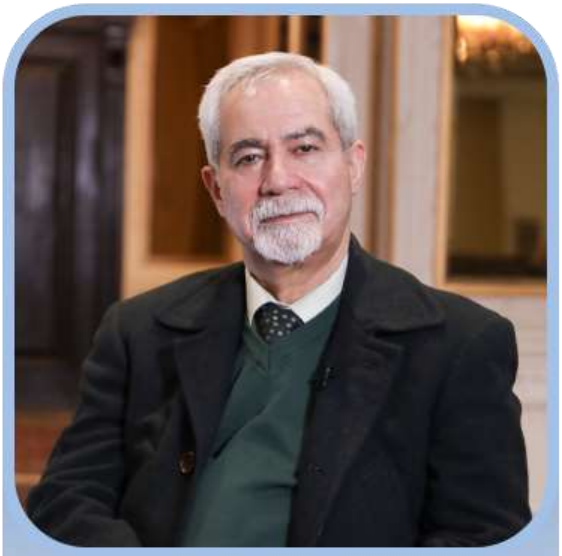

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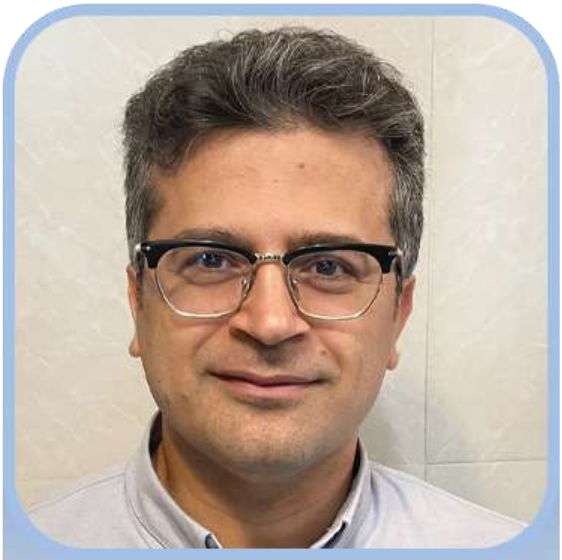

Dr. A Okhovat

Chairperson of Congress

Dear participants, colleagues, and all those interested in the neuromuscular field,

It is our honour to welcome you to the 6th Iranian Congress of Neuromuscular and Electrodiagnostic Medicine. As we come together to share insights, research findings, and best practices, let us unite in our mission to elevate the standard of patient care in the neuromuscular field across Iran. By advancing the diagnosis and treatment of neuromuscular diseases in recent years, using new diagnostic and therapeutic methods, we can improve patient outcomes. We want to thank all the contributors, organisers, and participants for their valuable contributions to this important goal. May the discussions and collaborations during this congress lead us toward a future that will result in better diagnosis and treatment of patients in the neuromuscular field.

Sincerely,

Oral Presentation

Role of physiotherapy in neuromuscular diseases

Dr. Laleh Abadi Marand, Neuromusculoskeletal Rehabilitation Research Center, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran.

Persons with neuromuscular disease should be referred for physiotherapy. The muscle weakness, stiffness, and pain associated with a neuromuscular disease may result in suboptimal compensatory body movements. Physiotherapists have specialist expertise in evaluating the musculoskeletal system and can assess the challenges facing individual patients, as well as their capabilities. They can perform a personalized assessment of movement strategies and patterns and put in place measures to help the individual to use his/her body more effectively in everyday life and during exercise. This evaluation is also integral to making recommendations regarding exercises, aids, activity adjustment, and everyday training load. Problems with balance are common in persons with neuromuscular disease. Balance training can improve bodily awareness and confidence in maintaining balance, and reduce the risk of falls. Walking aids and other activity aids must be evaluated continuously. This often means balancing the wish to maintain activity levels and independent mobility against the risk of falls and injuries. Persons with neuromuscular disease were previously advised to avoid exercise because it was thought to be harmful for weakened muscles, and because it was unclear whether exercise would have any effect. More recently, studies have shown that tailored physical activity, such as aerobic training on a bicycle or moderate strength training, can be beneficial for persons with neuromuscular disease. Therefore, the recommendation is no longer for patients to avoid training, but instead for training to be tailored to each patient in accordance with their diagnosis and functional level. Training aims to maintain existing strength or reduce the progression of muscle weakness, and not necessarily to strengthen the affected muscles. Any increase in muscle strength is probably the result of effects on muscles that are relatively unaffected by the neuromuscular disease, but which may be deconditioned as a result of inactivity. Appropriate training and physical activity is generally safe, but must be tailored to the individual on the basis of his/her diagnosis, functional level, and lifestyle.

Electrodiagnostic Techniques in NMJ Disorders, Choosing the right technique based on clinical scenario, real tracing examples, artifacts and interpretation pitfalls.

Dr Siamak Abdi

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Abstract

Among the available techniques, repetitive nerve stimulation (RNS) and routine nerve conduction studies remain the most practical tools in everyday clinical practice. Selecting the optimal method and interpreting results correctly require close alignment with the clinical scenario and awareness of technical limitations.

This teaching course will provide a case-based overview of electrodiagnostic techniques relevant to NMJ disorders, with an emphasis on RNS and its application in conditions such as myasthenia gravis and Lambert-Eaton myasthenic syndrome. Real tracing examples will be presented to illustrate key findings, while highlighting common artifacts, sources of error, and pitfalls in interpretation.

By the end of the session, participants will be able to:

1. Identify when and how to apply RNS in different NMJ disorders.

2. Recognize and troubleshoot artifacts that may mimic or obscure pathological findings.

3. Avoid common pitfalls that may lead to misinterpretation and diagnostic delay.

This session is designed for neurologists and trainees seeking to refine their electrodiagnostic approach to NMJ disorders and enhance confidence in integrating clinical and electrophysiological data.

Toxin and nutritional neuropathy

Dr. Maryam Afarini

Neurology Department, kashani Hospital, Esfahan University of Medical Sciences)

Abstract:

Vitamin and mineral deficiencies, neurotoxins, are some of the most common causes of peripheral neuropathy.

Nutritional neuropathies are a treatable yet often under recognized group of disorders resulting from deficiencies in essential nutrients such as B vitamins (B1, B6, B9, B12), vitamin E, and copper. These deficiencies commonly arise from malabsorption, alcoholism, bariatric surgery, and inadequate dietary intake

Toxin neuropathies result from numerous causes, including prescribe and recreational drugs, heavy metals, industrial agents and biological toxins. Timely recognition of these neuropathy gives better outcome, as they usually improve or stabilize once the toxin is removed

Scapular winging

A review to straight forward and difficult cases

Shahram AKRAMI MD, EMG Clinic, Tehran, Iran

Scapular winging is a condition where the shoulder blade (scapula) protrudes from the rib cage, resembling a wing. It is caused by weakness or dysfunction of the muscles that stabilize the scapula, particularly the serratus anterior , trapezius, and rhomboid muscles. This can lead to pain, limited arm movement, and difficulty with activities requiring shoulder strength.

Causes:

- Nerve injuries:

The long thoracic nerve, spinal accessory nerve, and dorsal scapular nerve are commonly affected, leading to weakness or paralysis of the serratus anterior, trapezius, and rhomboid muscles, respectively.

- Muscular dystrophy:

Facioscapulohumeral muscular dystrophy (FSHD) can also cause scapular winging due to muscle weakness

- Trauma and musculoskeletal injuries

Injuries to the shoulder or neck can damage the nerves or muscles or bones responsible for scapular stabilization.

Showing simple and difficult cases, a review to causes of scapular cases with discussion will be made.

Chaperon mutation in neuromuscular disease

Behnaz Ansari

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Chaperone Protein Mutations in Neuromuscular Diseases

Molecular chaperones are a group of proteins that assist in the correct folding, stabilization, and degradation of other proteins within cells. They play a crucial role in maintaining proteostasis, especially in highly active tissues such as skeletal and cardiac muscle. Mutations in genes encoding chaperone proteins can disrupt these protective mechanisms and are increasingly recognized as important causes of neuromuscular diseases.

One of the best-known chaperones implicated in neuromuscular pathology is DNAJB6, a member of the HSP40 (DNAJ) family. Mutations in DNAJB6 cause limb-girdle muscular dystrophy type D1 (LGMDD1), characterized by progressive weakness of proximal muscles, abnormal protein aggregation, and impaired autophagy. Similarly, mutations in HSPB8 and BAG3, which function in chaperone-assisted selective autophagy, are linked to distal myopathies and cardiomyopathies. These mutations often lead to accumulation of misfolded proteins, toxic aggregates, and myofibrillar disorganization. Another example is CRYAB (αB-crystallin), a small heat-shock protein highly expressed in muscle. Mutations in CRYAB can result in desmin-related myopathy, where insoluble protein aggregates disrupt the integrity of muscle fibers and lead to both skeletal and cardiac dysfunction. Additionally, mutations in HSPB1 have been associated with certain neuropathies and motor neuron diseases. Overall, chaperone protein mutations contribute to neuromuscular diseases through three main mechanisms: (1) defective protein folding and stabilization, (2) impaired clearance of damaged proteins via autophagy or proteasome pathways, and (3) toxic gain-of-function due to abnormal protein aggregation. Understanding these pathways is essential for developing therapeutic strategies, including pharmacological chaperones, proteostasis regulators, and gene therapy approaches.

Atypical Manifestations of Immune-Mediated Necrotizing Myopathy

Behnaz Ansari

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Immune-mediated necrotizing myopathy (IMNM), traditionally defined by subacute systemic weakness, elevated CK, and necrotic muscle pathology with minimal inflammation, is increasingly recognized to encompass a broader clinical and histopathologic spectrum.

Atypical clinical scenarios include cases with slow, progressive weakness akin to muscular dystrophy, dysphagia, oculobulbar symptoms, FSHD-like patterns, or even completely asymptomatic hyperCKemia. On the histopathological side, IMNM may present with features such as tubular aggregates, myofibrillar changes, mitochondrial pathology, lipid accumulation, and megaconial alterations—findings beyond the classical necrosis and regeneration. One of the most challenging diagnoses is in seronegative patients, so fine granular p62 immunopositivity observed in scattered non-necrotic muscle fibers in the majority of IMNM patients, both seropositive and seronegative can be helpful to diagnosis. Not typically observed in other types of idiopathic inflammatory myopathies, making them potentially valuable for diagnosis. This pattern was at variance with the coarse focal staining pattern mostly confined to rimmed vacuoles in sIBM. Colocalization of p62 with the chaperone proteins HSP70 and αB-crystalline points to the specific targeting of misfolded proteins to the CASA machinery in IMNM was detected as well.

Awareness of these unusual phenotypes is critical for timely diagnosis and treatment, given that IMNM remains a treatable myopathy with improved outcomes when addressed early with immunotherapy.

Red Flags for ALS Mimics: Avoiding Misdiagnosis

Author: Hormoz Ayromlou

Affiliation: Professor of Neurology, Department of Neurology, Emam Reza Hospital, Tabriz University of Medical Sciences

Abstract: The group of neuromuscular diseases associated with progressive weakness caused by motor neuron degeneration are designated motor neuron diseases (MND). The most common and most severe of these is amyotrophic lateral sclerosis (ALS), characterized by rapid progression, respiratory involvement and short survival.

The differential diagnosis of ALS is potentially wide, but most of these disorders are really of theoretical rather than practical clinical interest; In the past some disorders, such as heavy-metal intoxication, Lyme disease and multifocal motor neuropathies were emphasized, but these are less of a problem in the modern era. Nevertheless, one should be careful to avoid missing a treatable condition. There are a few more relevant disorders, which seem to us to need an update but, in clinical practice, relatively few other conditions merit consideration.

1.‘‘Post-polio syndrome” is a term that was given to the development of progressive weakness, increasing atrophy and more severe cramp and fasciculation in patients with a history of polio, even affecting previously clinically spared segments.

2. Thyrotoxicosis can rarely cause muscle atrophy, fasciculations, weakness and hyper-reflexia. A similar pattern can be observed in patients with hyperparathyroidism and low phosphate levels.

3. Benign fasciculation syndrome: Fasciculations are prominent in ALS, in particular in strong and proximal muscles, and may be the presenting symptom. In addition, patients with ALS often complain of muscular cramps, in general in lower limbs, but sometimes in trunk muscles, which is unusual in benign conditions. Bilateral tongue fasciculation strongly suggests a diagnosis of ALS.

4. Multifocal motor neuropathies are generally associated with a chronic and slowly progressive weakness in the territory of peripheral nerves, mostly affecting upper limbs. Conduction block should be investigated, in particular by stimulating proximal nerve segments. However, in some cases conduction block is not detected, a condition designated as axonal multifocal motor neuropathy.

5. Allgrove syndrome, a genetic disorder presenting like ALS with UMN and LMN signs and bulbar involvement was first described in 1978. This syndrome is characterized by absence of tears, esophageal achalasia, and autonomic disturbance associated with adrenal insufficiency (the four A syndrome).

6. Inclusion body myositis: The most prevalent acquired muscle disease in people older than 50 years is inclusion body myositis, with a prevalence of approximately 4/100,000 in this age group.

7. Multiple sclerosis: Patients presenting with UMN syndromes might be suffering from multiple sclerosis, but this is a diagnosis that is strongly suggested by brain MRI findings, since this technique is exquisitely sensitive in detecting white matter abnormalities.

8. Bulbar-Onset Anti-IgLON5 disease: This a recently described new entity mimicking bulbar-onset ALS, in which patients suffer from progressive dysphagia and sialorrhea, due to marked damage of the trigeminal motor fibers, sometimes associated with facial pain. Cerebral MRI shows enlargement and bilateral T2 fluid-attenuated inversion recovery (FLAIR) hyperintensity of trigeminal nerves. Anti-IgLON5 autoantibodies are detected in and/or CSF, supporting this diagnosis.

Dysphagia Management in Amyotrophic Lateral Sclerosis (ALS)

Jalal Bakhtiyari, PhD in Speech Therapy, Associated Professor in Tehran University of Medical Sciences

Dysphagia is of great concern to patients with amyotrophic lateral sclerosis (ALS) and is the result of a progressive loss of function in bulbar and respiratory muscles. Studies estimate that up to 92% of individuals with ALS experience dysphagia. In neuromuscular diseases like ALS, dysphagia and difficulty in the management of secretions (sialorrhea) are common symptoms. Complications of dysphagia includes aspiration pneumonia, malnutrition, significant weight loss, and dehydration. These complications can increase mortality and reduce the quality of life. Additionally, it can increase general fatigue, eating duration, fear of eating-related complications, eating-related burden, and difficulty with food selection. To prevent and minimize these complications, diagnosis and management of dysphagia must be done as soon as possible by a trained speech therapist. Assessing swallowing includes clinical evaluation and specialized instrumental assessments like videofluoroscopy (VFSS) or fiberoptic endoscopy (FEES).

The current treatment of dysphagia in patients with ALS is the conventional swallowing therapy by a speech therapist. Compensatory approaches and rehabilitative methods are included in this therapy. The best evidence-based swallowing therapies for ALS patients focus mainly on compensatory swallowing techniques, dietary modifications, and specific swallowing exercises that improve muscle strength and coordination.

In summary, evidence-based swallowing therapy in ALS emphasizes compensatory swallowing exercises like the Mendelsohn maneuver, dietary consistency modification, safe medication forms, and early multidisciplinary intervention to reduce aspiration risk and maintain nutrition.

Key Words: Amyotrophic Lateral Sclerosis, Dysphagia, Speech Therapy

Approach to a Patient with Suspected Motor Neuron Disease in the Outpatient Clinic

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Abstract:
Motor neuron disease (MND) is a progressive neurodegenerative disorder that requires timely recognition in order to optimize patient care and referral to specialized centers. However, early presentations in the outpatient setting are often subtle and may overlap with more common conditions such as cervical radiculopathy, peripheral neuropathies, or myopathies, leading to diagnostic delay.

This presentation outlines a structured approach to evaluating patients with suspected MND in the outpatient clinic. Key elements include a detailed clinical history emphasizing symptom onset, progression, and distribution; targeted neurological examination to detect combined upper and lower motor neuron involvement; and the judicious use of ancillary tests, including electromyography and neuroimaging, to support the diagnosis and exclude mimics. Special attention will be given to “red flag” features that should raise early suspicion and prompt expedited referral.

In addition, practical considerations in communicating the diagnostic process, coordinating multidisciplinary care, and integrating supportive interventions from the first encounter will be discussed. By applying a systematic approach, clinicians can reduce diagnostic uncertainty, facilitate earlier access to disease-modifying and supportive therapies, and ultimately improve the quality of life for patients and their families.

Updates in the Treatment of Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

Keivan Basiri MD

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Abstract:

Background: Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) is a heterogeneous immune-mediated neuropathy with variable response to therapy. Advances in pathophysiological insights and therapeutic options have led to important changes in management strategies.

Methods: A review of recent clinical trials, consensus guidelines, and real-world evidence was performed to identify relevant updates in CIDP treatment.

Results: Intravenous immunoglobulin (IVIg), corticosteroids, and plasma exchange remain first-line therapies; however, significant progress has been made in optimizing long-term management. Subcutaneous immunoglobulin (SCIg) has proven effective for maintenance therapy, offering improved convenience and patient satisfaction. FcRn antagonists approved by FDA in June 2024 and have shown promising results in recent randomized trials, with rapid onset of action and favorable tolerability, suggesting a potential role in refractory cases. B-cell–directed therapies, including rituximab, are increasingly considered in selected subgroups, particularly in antibody-positive patients. Updated EFNS/PNS guidelines emphasize early recognition, tailored therapy, and cautious tapering to balance efficacy with long-term safety.

Conclusion: Current evidence indicates a shift from uniform treatment strategies toward individualized, precision-based management of CIDP. Incorporating novel immunotherapies and optimizing maintenance approaches are expected to further improve patient outcomes.

Management in pregnancy, neonatal MG, CMS in children, and the elderly with comorbidities

Reza Boostani, MD

Professor of Neurology, Neuromuscular Medicine

Mashhad University of Medical Sciences

Myasthenia Gravis (MG) is a common neuromuscular disorder with the immune-medicated nature. Symptomatic therapy (i.e. Acetyl Cholinesterase inhibitors) as well as Immunotherapy by prednisolone, Azathioprine, Mycophenolate Mofetil and rarely methotrexate and cyclosporine.

Above mentioned therapeutic approach should be modified based on Age of onset, status of thymus gland (thymoma or non-thymoma), antibody status, severity and the distribution of disease as well as other medical situations (comorbidities). Moreover, in woman patients with MG, pregnancy is an important condition which requires modification of treatment, before, during and after pregnancy.

The main part of this article is dedicated to the management and treatment of MG in the elderly patients and pregnancy condition, and an attempt has been made to discuss practical clinical points in dealing with these patients.

Finally, a brief overview will made on treatment strategy in congenital myasthenic syndrome.

Anesthesia in patients with Neuromuscular Disorders

Reza Boostani, MD

Professor of Neurology, Neuromuscular Medicine

Mashhad University of Medical Sciences

Neuromuscular disorders are a heterogenous group of muscle, nerve and neuromuscular junction disorders.

People with neuromuscular disorders, like other normal people, may need surgery in certain situations.

Some of these diseases are at the risk of aggravating respiratory muscle weakness during general anesthesia as well as the recovery phase due to baseline respiratory muscle involvement.

Others may experience complications such as malignant hyperthermia and rhabdomyolysis in certain situations due to hereditary defects in muscle fiber proteins.

Others are susceptible to side effects of anesthetic drugs.

The main part of this article is dedicated to the general anesthesia considerations in hereditary myopathies including muscular dystrophies and non-dystrophic congenital myopathies. Moreover, key points in general anesthesia of the patients with myasthenia gravis will be covered in this lecture.

ALS Symptomatic Management

Dr. Masoumeh Cheshmavar

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Abstract:

Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease characterized by progressive degeneration of both upper and lower motor neurons.

In addition to amyotrophy and muscle weakness, patients with ALS may experience spasticity, painful muscle cramps, sialorrhea associated with bulbar palsy, and breathlessness owing to respiratory muscle involvement.

Moreover, a variety of non-motor symptoms, such as cognitive decline, mood disorders, pseudobulbar affect, sleep disturbances, fatigue, and pain, may occur as initial symptoms.

In the absence of cure or any medical intervention which might reverse or stop the progression of ALS, Therefore, the focus on the symptom, rehabilitation and palliation treatment with overall aim of optimizing quality of life is especially important.

Multidisciplinary ALS clinics provide care from neurologists, physical therapists, occupational therapists, speech therapists, respiratory therapists, dietitians, social workers, and nursing care managers.

"Emerging Technologies in the Rehabilitation of Neuromuscular Diseases: A Narrative Review"

Amir Reza Davodi

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Introduction: Neuromuscular diseases create major rehabilitation challenges due to progressive muscle weakness and declining independence. Traditional exercises, often repetitive and monotonous, reduce patient motivation and engagement. With the emergence of novel technologies, new opportunities have arisen to overcome these barriers. This review examines the potential of Virtual Reality (VR), Gamification, and Robotics as empowering tools in NMD rehabilitation.

Methods :This article was conducted as a narrative and analytical review of existing literature. Keywords such as "neuromuscular rehabilitation," "virtual reality," "gamification," and "robotics" were searched in PubMed, Web of Science, and Google Scholar. Given the innovative nature of these technologies and the limited number of large-scale trials, this method enabled the synthesis of evidence from review articles, clinical guidelines, and analytical papers. The aim was to provide a structured overview of how these interventions can improve patient engagement, motivation, and therapeutic outcomes.

Findings: Evidence shows that integrating VR, gamification, and robotics into rehabilitation programs enhances motivation and participation. By creating interactive, immersive, and entertaining environments, they transform therapeutic exercises into engaging experiences that contribute to improvements in motor function, balance, and coordination. Real-time feedback and exercise personalization further promote psychosocial well-being and reduce treatment-related fatigue.

Discussion and Conclusion: VR, gamification, and robotics represent promising approaches for advancing rehabilitation standards in neuromuscular diseases. These technologies make therapy more effective and empower patients to take an active role in recovery. However, further studies are needed to validate long-term effectiveness, standardize protocols, and define best practices for clinical implementation.

NeuroMyology: A Practical Approach to Neuromuscular Medicine

Dr. Hadi Gharebaghian, Dr. Tara Mazaheri, Donya Ebrahimitabar, Zohair Mazaheri

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Abstract

Medical databases and digital health tools are pivotal in enhancing the diagnostic and therapeutic capabilities of physicians while advancing medical knowledge.

Online learning platforms further illustrate how digital resources fill knowledge gaps and promote lifelong learning among primary care doctors, with 86.4% reporting use of e-learning modules for professional practice.

NeuroMyology (https://www.neuromyology.org/) is a specialized medical database focused on neuromuscular medicine, created by Dr. Hadi Gharebaghian, MD (Neuromuscular Fellowship). It serves neurologists, neuromuscular specialists, physical medicine and rehabilitation specialists, and clinical genetics experts.

The platform covers a wide range of neuromuscular clinical and anatomical syndromes, diseases, diagnostic investigations, and genetic abnormalities. Its web-based interface ensures easy access anytime, anywhere and on any smart device.

Effective features include:

- Diseases: Supports rapid differential diagnosis for known common anatomical neuromuscular syndromes.

- Localization: Helps in lesion localization by clinical syndromes within the entire neuraxis. This feature is based on lesion-symptom mapping.

-Investigations: Provides a comprehensive panel of diagnostic tests from different modalities for various neuromuscular syndromes, making it a useful tool for outpatient care.

- Genetics Section: Assists in interpreting genetic test results related to inherited neuromuscular disorders. More than 700 genes and more than 1000 genetic disorders are included in its database and can be reviewed in just a few seconds. Greater genomic coverage (including conditions with both mendelian and non-mendelian inheritance) and faster data interpretation than current databases like “OMIM” and “Gene Table of Neuromuscular Disorders” is a promising superiority.

NeuroMyology is an assistive digital diagnostic tool, developed to enhance neuromuscular patient care by providing high quality and uptodate information for physicians. NeuroMyology can potentially accelerate the diagnosis, improve the diagnostic precision and eventually improve patients’ outcome.

Prospective clinical studies are needed to confirm its reliability, usability and effectiveness and to improve the overall system accuracy and performance.

Rehabilitation in neuromuscular disorders

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Abstract

Neuromuscular disorders (NMDs) represent a heterogeneous group of progressive conditions affecting muscles, peripheral nerves, and the neuromuscular junction. Although significant advances have been made in pharmacological and genetic therapies, rehabilitation remains a cornerstone of management to preserve function, prevent complications, and enhance quality of life. From a physical medicine and rehabilitation perspective, the primary goals include maintaining mobility, reducing contractures and deformities, supporting respiratory function, improving speech and swallowing abilities, and promoting independence in daily activities. Interventions such as tailored physiotherapy, occupational therapy, speech therapy, respiratory support, orthotic management, and multidisciplinary care are essential. However, due to the progressive nature of these disorders, the literature on long-term rehabilitation strategies is relatively limited compared to curative or disease-modifying treatments. This highlights the need for more robust clinical studies and individualized rehabilitation protocols to optimize outcomes in this challenging patient population.

New Advances in the Diagnosis of Idiopathic Inflammatory Myopathies

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Abstract

Idiopathic inflammatory myopathies (IIMs) comprise a diverse group of autoimmune muscle diseases that traditionally required muscle biopsy for diagnosis. While clinical features, serum creatine kinase (CK), and electromyography remain important, recent advances have reshaped the diagnostic pathway toward a faster, less invasive, and more precise approach.

One of the most significant developments has been the identification of myositis-specific antibodies (MSAs). These markers not only improve diagnostic accuracy but also define distinct clinico-serological syndromes with prognostic and therapeutic implications. For example, anti-MDA5 predicts interstitial lung disease risk, anti-TIF1γ is strongly associated with cancer-related dermatomyositis, and anti-HMGCR identifies immune-mediated necrotizing myopathy often linked to statin exposure. The incorporation of MSAs into diagnostic criteria has reduced reliance on biopsy in many patients.

Magnetic resonance imaging (MRI) is another key advance. STIR sequences detect active muscle inflammation, T1 sequences demonstrate chronic changes, and whole-body MRI reveals characteristic distribution patterns that help distinguish subtypes. MRI also guides biopsy to the most informative sites, reducing false negatives.

Pathology remains relevant but has become more refined. Immunohistochemistry for MHC-I, membrane attack complex, p62, and TDP-43 enhances specificity, particularly for inclusion body myositis and necrotizing myopathies. Finally, molecular approaches, including RNA sequencing and transcriptomic profiling, are beginning to provide disease-specific signatures that may shape future classification systems.

Together, these advances mark a paradigm shift from biopsy-centric diagnosis to a multidimensional strategy integrating serology, imaging, and molecular tools, enabling more rapid, accurate, and personalized diagnosis of IIM.

Stepwise Management of Myasthenia Gravis: From Pyridostigmine to Advanced Targeted Therapies

Bahram Haghi Ashtiani

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Abstract

Background:

The therapeutic landscape of myasthenia gravis (MG) has rapidly evolved. While pyridostigmine and corticosteroids remain foundational, significant advances with immunosuppressants, monoclonal antibodies, complement inhibitors, and FcRn blockers now allow tailored, stepwise approaches.

Case:

We present a 43-year-old man with diabetes who developed fluctuating diplopia and ptosis over three months. He was AChR-antibody positive and initially responded partially to pyridostigmine. Within months, symptoms generalized with bulbar fatigue and mild dysphagia. High-dose prednisone combined with azathioprine improved control but worsened glycemic status, and symptoms recurred when steroids were tapered below 25 mg. Nine months later, he remained significantly symptomatic, illustrating the need for escalation beyond conventional therapy.

Discussion:

Management of MG requires balancing rapid symptom relief with long-term disease control and treatment tolerability. Pyridostigmine provides immediate symptomatic benefit but no disease modification. Corticosteroids act within weeks but are limited by toxicity, particularly in comorbidities such as diabetes. Traditional immunosuppressants (azathioprine, mycophenolate mofetil, calcineurin inhibitors) provide durable steroid-sparing benefits but require months for full effect. Newer targeted therapies address the gap in refractory disease. Rituximab, especially effective in MuSK-MG, complements conventional regimens. Complement inhibitors (eculizumab, ravulizumab, zilucoplan) rapidly improve AChR+ MG within 1–4 weeks, while FcRn blockers (efgartigimod, rozanolixizumab) provide flexible, cycle-based reductions of pathogenic IgG. Thymectomy remains an important long-term intervention in eligible patients.

Conclusion:

This case highlights the importance of a structured, stepwise treatment algorithm in MG, emphasizing early steroid-sparing strategies and timely escalation to biologics. Novel complement and FcRn inhibitors represent a paradigm shift, transforming MG into a controllable, individualized disease.

Paraneoplastic Polyneuropathy: Pathophysiology, Patterns and Pitfalls

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Abstract

Paraneoplastic polyneuropathy is a rare but disabling manifestation of paraneoplastic neurological syndromes, caused by immune responses against shared neuronal and tumor antigens. Pathophysiology is primarily immune mediated, with cytotoxic T-cell activity and onconeural antibodies (anti-Hu, anti-Yo, CRMP5) driving neuronal injury. Neuropathies associated with antibodies to neuronal surface or synaptic proteins may instead cause functional disruption, which can be reversible.

Clinically, distinct patterns include subacute sensory neuronopathy (commonly anti-Hu–related, linked to small cell lung cancer), sensorimotor neuropathies (chronic or rapidly progressive, sometimes CRMP5-associated), autonomic neuropathies, and less common variants such as vasculitic or Guillain-Barré–like presentations. Recognition is critical, as they may precede cancer diagnosis and mimic chemotherapy-induced or idiopathic neuropathies.

Diagnostic pitfalls include false-negative antibody tests, atypical phenotypes, and coincidental neuropathies in cancer patients. Advances in antibody profiling, including novel antibodies (KLHL11, ITPR1, NF186), together with systematic tumor screening (FDG-PET/CT), have improved accuracy and expanded the clinical spectrum, identifying patients more likely to benefit from immunotherapy.

Treatment depends on mechanism: neuropathies from intracellular antigen responses usually progress despite therapy, whereas those mediated by surface antigen antibodies may respond to intravenous immunoglobulin, plasmapheresis, or rituximab, especially with effective tumor control. Recognition of immune checkpoint inhibitor–related neuropathies further illustrates the evolving overlap between oncology and neuroimmunology.

In conclusion, paraneoplastic polyneuropathy involves diverse clinical patterns, complex immune mechanisms, and significant diagnostic pitfalls. Early recognition, comprehensive antibody testing, and vigilant cancer surveillance are essential, while emerging antibodies and checkpoint inhibitor–related complications highlight both challenges and therapeutic opportunities.

Malignancy Workup in Myositis: How and why

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Abstract

According to the EuroMyositis registry, malignancies occurred at any time in 13% of patients with myositis, with most of them being diagnosed in close temporal association with the onset of myopathy. In most cases, cancer develops simultaneously with the onset of myopathy or within the first year of diagnosis, but the risk, although gradually decreasing, remains elevated for several years. In the retrospective study performed by András et al. on a Hungarian cohort of 450 patients with IIM, over 83% of patients with cancer association myositis (CAM) developed cancer within the first year after diagnosis. The course of myositis was reported to be more severe if the cancer was diagnosed concurrently than when the entities emerged at longer time intervals. According to the meta-analysis of five studies on the total group of 4538 patients with myositis, the overall relative risk for developing malignancy was 4.66 (95% CI 3.32–6.52) for patients with dermatomyositis and 1.75 (95% CI 1.37–2.25) for patients with polymyositis. Noteworthy, in patients with antisynthetase syndrome, risk of malignancy seems to be noticeably lower than in remaining types of myositis. Incidence of cancer in the course of inclusion body myositis seems to be inconsistent. Lung, gastrointestinal, ovarian, breast, cervical, bladder, uterine, pancreatic and prostatic tumors, as well as Hodgkin's lymphomas, are listed among the most frequent neoplasms associated with IIM. Anti-TIF1-γ antibodies are of fundamental importance as the most strongly associated with cancer risk. Patients with CAM require dual care—treatment of malignancy and myositis.

Key words: *Myositis; Cancer, Dermatomyositis, Autoantibodies*

Emerging therapeutics in ALS: from Antisense Oligonucleotides to Gene therapy

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Abstract: Amyothrophic lateral sclerosis (ALS)is an devasting neurodegenerative disorder with involvement of upper and lower motor neurons. About 10% of ALS patients are familial , and so far, more than 30 ALS-related genes have been identified in familial ALS cases . However, the remaining 90% of cases are clearly sporadic . Pathogenic variants in superoxide dismutase 1 (SOD1), TAR DNA binding protein (TARDBP), fused in sarcoma (FUS) and chromosome 9 open reading frame 72 (C9ORF72), the most common ALS-associated genes, account for approximately 60% of familial cases and about 10% of sporadic ALS. Numerous therapeutic approaches have been developed based on the genetic causes and potential mechanisms of ALS . Currently, available treatments for various neurodegenerative diseases can alleviate symptoms but do not provide a definitive cure. Gene therapy, which aims to modify or express specific proteins for neuroprotection or correction, is considered a powerful tool in managing neurodegenerative conditions. To date, antisense oligonucleotide (ASO) drugs targeting the pathological genes associated with ALS have shown promising results in numerous animal studies and several clinical trials. This presentation provides a comprehensive overview of the development, mechanisms of action, limitations, and clinical applications of ASO drugs in ALS.

Key words: Amyothrophic lateral Sclerosis(ALS),Gene therapy, antisense oligonucleotide (ASO) drugs

A strange case with recurrent ataxia responding to plasmaphresis related to SORD gene mutation

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Abstract: The demyelinating hereditary motor and sensory neuropathies (HMSN) are a group of inherited progressive neuropathies with markedly decreased nerve conduction velocity and chronic segmental demyelination in the peripheral nerves. known gene mutation related to it are including PMP22 duplication,point mutation,deletion, in dominant forms and SH3TC2, GDAP1, PLEKHG5, MTMR2, SBF2, NDRG1, EGR2, PRX, FGD4, FIG4 in ressesive forms. on the other side SORD is a biallelic gene mutation related to axonal CMT and distal hereditary motor neuropathy phenotypes.

We introduced a case of hereditary demyelinating polyneuropathy , with prominent ataxia associated with SORD gene mutation with response to plasmaphresis .

Key words: demyelinating CMT, SORD gene mutation, hereditary demyelinating sensory motor polyneuropathy , response to plasmapheresis

Immune Checkpoint Inhibitors-Related Neuromuscular Complications

Dr. T. Khoeini

Background:

Immune checkpoint inhibitors (ICIs) have revolutionized cancer therapy by enhancing antitumor immunity. However, they may trigger immune-related adverse events (irAEs), including rare but potentially severe neuromuscular complications.

Objective:

This session aimed to review the spectrum, clinical presentation, diagnostic challenges, and management strategies of neuromuscular irAEs associated with ICIs, particularly focusing on myositis, myasthenia gravis, and peripheral neuropathies.

Methods & Content:

We presented real-world cases and summarized the latest literature on ICI-induced neuromuscular complications, emphasizing early recognition, multidisciplinary management, and immunosuppressive treatments to prevent morbidity and mortality.

Conclusion:

ICI-related neuromuscular irAEs, though uncommon, can be life-threatening. Prompt diagnosis, close collaboration between oncologists and neurologists, and individualized immunotherapy approaches are crucial to improving patient outcomes.

Atypical presentations in an RTD patient and report of novel SLC52A3 and SLC52A2 mutations

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Background: Riboflavin Transporter Deficiency (RTD) is a rare neurological disorder characterized by pontobulbar palsy, hearing loss, and motor cranial nerve involvement. SLC52A3 and SLC52A2 mutations are causes of RTD. SLC52A2 mutations are usually found in childhood onset cases. Fifteen Iranian RTD diagnosed patients without SLC52A2 mutations have been described.

Objectives: We aimed to identify causative mutations in two childhood cases.

Methods: We recruited patients with diagnosis of BVVL. Comprehensive clinical evaluations were performed on the patients. SLC52A3 and SLC52A2 genes were PCR-amplified and Sanger sequenced. Candidate disease causing variations were screened for segregation with disease status in the respective families and control individuals.

Results: A novel homozygous SLC52A3 mutation (p.Met1Val) and a heterozygous SLC52A2 mutation (p.Ala288Val) were both observed in one proband with typical RTD presentations. The aggregate of presentations in the early stages of disease in the second patient that included weakness in the lower extremities, absence of bulbar or hearing defects, prominent sensory polyneuropathy as evidenced in electrodiagnostic studies, and absence of sensory symptoms including sensory ataxia did not prompt immediate RTD diagnosis. Dysarthria and decreased hearing manifested later in the disease course. A novel homozygous SLC52A2 (p.Val314Met) mutation was identified.

Discussion: A literature search found recent reports of other atypical RTD presentations. These include MRI findings, speech understanding difficulties accompanied by normal hearing, anemia, and left ventricular non-compaction. Knowledge of unusual presentations lessens the chance of misdiagnosis or delayed RTD diagnosis which, in light of favorable effects of riboflavin supplementation, is of immense importance.

Key words: Riboflavin Transporter Deficiency disease (RTD), Brown-Vialetto-Van Laere syndrome (BVVL), atypical presentations, SLC52A3, SLC52A2

Relationship Between Cognitive Impairments, Motor Disorders, and Dysphagia Severity in Patients with Amyotrophic Lateral Sclerosis (ALS)

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Abstract

Objectives:

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disorder affecting both upper and lower motor neurons, and it is frequently accompanied by dysphagia and cognitive impairments. This study aimed to investigate the relationship between cognitive and motor impairments and the severity of dysphagia in patients with ALS.

Materials and Methods:

Thirty ALS patients participated in this cross-sectional study, selected through convenience sampling from the ALS clinic at Imam Khomeini Hospital, Tehran. Swallowing function was assessed using the Mann Assessment of Swallowing Ability (MASA), Cognitive performance was evaluated with the Montreal Cognitive Assessment (MoCA) and motor function was assessed using the ALS Functional Rating Scale–Revised (ALSFRS-R). Data were analyzed using Spearman's rank-order correlation to examine associations between dysphagia severity and cognitive and motor measures.

Results:

Participants had a mean age of 57.9±11.1 years; 46.7% were male. Dysphagia severity was mild in 53.3%, moderate in 36.7%, and severe in 10%. Significant negative correlations were found between swallowing severity and MoCA total scores ($\rho = -0.418$, $p = 0.021$), MoCA memory subscore ($\rho = -0.366$, $p = 0.047$), and ALSFRS-R total score ($\rho = -0.396$, $p = 0.030$). No significant associations were observed with fine or gross motor subscores.

Conclusion:

In ALS patients, more severe dysphagia is associated with lower overall cognitive performance, reduced memory scores, and poorer total motor function. These findings suggest that comprehensive assessment of both cognitive and motor domains is essential for effective clinical management.

EDX pitfall: demyelinating vs. axonal, that is the question

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The distinction between demyelinating and axonal polyneuropathies remains one of the most challenging aspects of electrodiagnostic evaluation. Although nerve conduction studies (NCS) and electromyography (EMG) provide critical information about the underlying pathophysiology, overlapping features often complicate the interpretation. Prolonged distal latencies, conduction block, and temporal dispersion are classical indicators of demyelination, while reduced compound muscle action potential amplitudes and absent sensory responses are typically associated with axonal loss. However, secondary changes such as axonal degeneration in chronic demyelinating neuropathies, or reversible conduction failure in acute axonal disorders, may blur this distinction. Moreover, technical factors, patient-related variables, and atypical disease presentations contribute to diagnostic uncertainty. Recent refinements in electrodiagnostic criteria, along with complementary techniques such as nerve ultrasound and magnetic resonance neurography, have improved diagnostic accuracy but limitations persist. A precise differentiation is essential, as it directly influences prognosis, therapeutic strategies, and patient counseling. This presentation will review the key electrodiagnostic features, highlight common pitfalls, and discuss practical approaches for resolving ambiguities in clinical practice. Emphasis will be placed on integrating electrodiagnostic findings with clinical context and ancillary studies to optimize diagnostic yield and improve patient outcomes.

GBS syndrome and other acute inflammatory neuropathies

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Abstract

Acute inflammatory neuropathies, including Guillain-Barré syndrome (GBS), represent a spectrum of immune-mediated disorders targeting the peripheral nervous system. This review provides a comprehensive overview of the current understanding of these conditions, focusing on their pathogenesis, clinical presentation, diagnostic challenges, and therapeutic strategies. GBS, the most common form, is often triggered by an antecedent infection, leading to a rapid-onset, ascending paralysis. Symptoms can vary significantly in how they appear and how severe they are. In addition to weakness and changes in sensation, patients may also experience issues with cranial nerves, difficulty breathing, problems with autonomic functions, and pain. Its varied clinical subtypes, such as Miller Fisher syndrome and acute motor axonal neuropathy (AMAN), highlight the heterogeneity of the disease. While the precise immunological mechanisms remain under investigation, the aetiology involves an autoimmune response targeting Schwann cells or axons, resulting in demyelination or axonal damage.

Early and accurate diagnosis is critical, relying on a combination of clinical features, electrophysiological studies, and cerebrospinal fluid analysis. The primary treatments, intravenous immunoglobulin (IVIG) and plasma exchange, aim to modulate the immune response and reduce nerve damage. However, despite these interventions, a significant number of patients experience residual neurological deficits, underscoring the need for ongoing research into novel therapeutic targets and biomarkers.

Autoantibody Testing and Seronegative myasthenia gravis: interpretation a diagnostic strategies

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Myasthenia gravis (MG) is the most common autoimmune disorder affecting the NMJ characterized by skeletal muscle weakness and fatigability. The AChR are clustered at the NMJ resulting in a localized high density of receptors. Neural agrin, released from nerve terminals, binds to low-density lipoprotein receptor-related protein 4 (LRP4) on the muscle membrane, activating it to form complexes with muscle specific kinase (MuSK). This results in the phosphorylation and activation of MuSK, which in turn leads to rapsyn-mediated AChR clustering at the NMJ.85% of MG patients have autoantibodies against AchR, 6% of MG patients have autoantibodies against the muscle specific kinase (MuSK).

Autoantibodies targeting LRP4 are found in about 2% of MG patients. Patients without detectable autoantibodies are referred to as seronegative (SNMG). Some MG patients have antibodies against a number of other extracellular or intracellular targets.

Herein, I aimed to review Autoantibody Testing including AchR, MUSK, LRP4,Agrin and other nonspecific antibodies and Seronegative myasthenia gravis diagnostic approach.

Autoimmune neuropathies: beyond CIDP or GBS

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Autoimmune neuropathies are a large spectrum of disorders variably named by Descriptive terminology (GBS), Course and pathological features (AIDP, CIDP, CISP), Presence of specific antibodies against myelin-associated glycoprotein (anti-MAG neuropathy), recently antibodies against nodes of Ranvier (NoR) or paranode (PN) of myelinated axons. (Nodoparanodopathy)

2-10% of patients with Paranodal neuropathies are diagnosed with CIDP. Onset is acute/subacute with chronic sever course and axonal involvement and should not be classified as CIDP.

CISP-plus and CISP are both difficult to recognize and diagnose. The diagnosis of CISP is challenging because despite patients having profound sensory deficits, NCS/EMG are normal. CISP-plus is difficult to diagnose because patients' NCS/EMG abnormalities are mild and not severe enough to explain their clinical deficits. They are not in the demyelinating range, and they do not meet the EFNS/PNS criteria for CIDP.

The NCS/EMG findings likely falsely point physicians away from considering an inflammatory demyelinating disorder and towards an axonal pathology.

Herein, I aimed to review the clinical and paraclinical aspects of these groups of inflammatory neuropathies mimicking as CIDP.

Sleep Disorders in Neuromuscular Diseases

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Disorders of sleep are extremely frequent (more than 40%) in NMDs and substantially determine the overall morbidity, quality of life, and survival. Unfortunately insufficient attention is paid to sleep-related issues by neurologists.

Many factors contribute to poor sleep quality and quantity in NMDs. Any kind of motor impairment interfering with the ability to move during the sleep, impairment of cough and swallowing, muscle cramps and spasticity, pain and sensory symptoms, RLS, sleep disordered breathing, abnormal sphincter control, autonomic dysfunction, mood disordes and drugs are factors interfering with good sleep in patients with neuromuscular diseases.

Any process affecting the diaphragm can significantly reduce ventilation and oxygenation during REM sleep. The facial skeletal changes in some genetic NMDs decrease upper airway diameter, increasing its collapsibility during sleep.

Common sleep disorders in patients with NMDs are:

Sleep-related breathing disorders (OSA, NH, CSA)

Insomnia

Sleep-related movement disorders (RLS, PLMS)

Central Disorders of Hypersomnolence

Patients may have nonspecific complaints, such as increased fatigue, daytime hypersomnolence, or disrupted sleep.The slow progression of ventilatory failure may go undetected for some time and, as a consequence, may contribute to increased morbidity and mortality in this population.

As many NMDs currently lack a cure, supportive therapy including appropriate management of sleep-related symptoms is mandatory. Early recognition of sleep disturbances and appropriate treatment can improve both quality of life and survival.

Myasthenic Crisis

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Abstract :

Myasthenic Crisis :

Definition : post-operative MC as a delay in extubation beyond 48 h post-surgery; and MC as the need for hospitalization to monitor respiratory status or severe dysphagia that requires enteral or parenteral nutrition.

In a retrospective study of 577 patients, myasthenia gravis exacerbation or crisis requiring hospitalization with intensive care occurred in 6 percent at a median of 5.3 months from the time of diagnosis.

MC occurs in approximately 15% to 20% of patients with generalized MG, typically within the first 2 to 3 y of the disease course. The mean lead time from MG diagnosis to the first MC episode ranges from 8 to 12 month. The annual incidence of MC is approximately 2.5% among all MG patients.

Age : Elderly patients are more likely to be affected with MC. In several retrospective observational studies, the mean age at MC was approximately 60 to 70 y. In a US claims-based study, the mean age of hospitalization with MC was 56.5 y.

In MG with acetylcholine receptor (AChR) antibodies, muscle weakness tends to initially affect the intercostal and accessory muscles then the diaphragm. In patients with muscle specific kinase (MuSK) antibodies, bulbar and respiratory muscles are preferentially affected.

Mean AChR antibody concentrations are higher in patients with MC when compared to patients with mild disease .A significant elevation of AChR antibody titer over baseline can be associated with the occurrence of MC.

Infections are associated with 30% to 50% of MC, with the most prevalent being bacterial or viral upper respiratory infection, bronchitis and pneumonia.

Another important contributory factor is medication change, which includes initiation of medications that could exacerbate MG or suboptimal MG treatment due to tapering of immunotherapy or medication

nonadherence. However, in up to 30% to 40% of MC cases, no obvious trigger can be identified.

Risk factors for MC : previous MC, oropharyngeal weakness, severe MG symptoms, MuSK antibody positivity, thymoma.

A large series identified thymoma in about one-third of MC patients.

Operative risk factors for POMC : intraoperative blood loss (>1000 mL), long operation time, trans-sternal thymectomy as compared video-assisted thoracoscopic surgery, presence of thymoma.

The main postoperative risk factor for POMC is postoperative pneumonia.

IVIG has been used to optimize myasthenic patients prior to thymectomy, though the time to maximal response is somewhat variable, ranging from 3 to 19 days. Postoperative MC does not occur in well-controlled

MG patients. Preoperative IVIG for MC prevention is not justified when quantitative MG score is less than 8 or VC is more than 70% of predicted.

Three plasmapheresis treatments in patients who need preoperative optimization. The last plasmapheresis should ideally be performed 48 h preoperatively to allow for both repletion of coagulation factors and

hemodynamic stability.

CLINICAL MANIFESTATION AND EVALUATION OF MC : The single breath test is a useful bedside measurement of respiratory function that correlates with VC and NIF.

The patient is asked to take one breath in then count aloud at approximately two counts per second before requiring another inspiration.

Ability to count to 30 with one breath correlates with adequate pulmonary function, and counting to 20 or less indicates significant inspiratory muscle weakness. Another useful measure of diaphragmatic

weakness is a fall in VC in the supine position when compared to a seated VC.

MC MANAGEMENT : Early intubation and mechanical ventilation are perhaps the most important steps in the management of MC, and emergency intubation should be avoided.

Indications for intubation :

(1) signs of respiratory distress with increasing tachypnea and declining lung volume;

(2) severe bulbar dysfunction, weak cough, and difficulty to clear secretions;

(3) progressive hypercarbia on blood gas measurement;

(4) chest X-ray showing significant atelectasis and aspiration.

Disease modifying treatment : IVIG and plasmapheresis : While limited data seemingly indicated that plasmapheresis and IVIG are comparable in terms of efficacy, several studies have suggested that plasmapheresis led to faster and more noticeable clinical improvement and shorter ICU stay. Treatment of MC with plasmapheresis has proven to lead to fast and predictable recovery.

Small-fiber Neuropathy: A diagnostic challenge

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Abstract (Maximum 250 words)

Small fiber neuropathy (SFN) is a disorder characterized by selective damage to thinly myelinated Aδ fibers and unmyelinated C fibers, which are responsible for pain, temperature sensation, and autonomic function. Patients typically present with burning pain, dysesthesia, allodynia, and symptoms of autonomic dysfunction, often in a length-dependent pattern. While routine nerve conduction studies are usually normal, diagnostic confirmation relies on skin biopsy for intraepidermal nerve fiber density measurement and quantitative sensory or autonomic testing. SFN may occur as an idiopathic condition, but it is frequently associated with diabetes, impaired glucose tolerance, autoimmune diseases, genetic mutations, and toxic exposures. Management includes treating the underlying cause when possible, alongside symptomatic therapies for neuropathic pain. Increasing awareness and early recognition of SFN are crucial to improve patient outcomes and to guide research toward targeted therapies.

Primary Lateral Sclerosis and Bulbospinal Variants: Diagnostic and Management Challenges

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Motor neuron disease (MND) represents a heterogeneous group of disorders involving motor neurons. Primary motor neuronopathies are characterized by progressive degenerative loss of the lower motor neurons or upper motor neurons.

The traditional classification of MND subgroups are based in four characteristics: 1/site of onset of the motor symptoms such as bulbar or spinal onset; 2/degree of upper or lower motor neuron involvement with four classical and distinct phenotypes that are primary lateral sclerosis (PLS), amyotrophic lateral sclerosis (ALS), progressive muscular atrophy (PMA) and progressive bulbar palsy (PBP); 3/heritability with sporadic or familial disease; 4/level of certainty of diagnosis according to the criteria.

Amyotrophic lateral sclerosis (ALS) represents the most common and most severe type of adult-onset neurodegenerative MND in clinical practice. But also, there are distinct entities of MNDs that present with either UMN degeneration or LMN degeneration. It is important to emphasize that all phenotypic forms are considered variants of ALS because it was observed that, at autopsy, the probability of finding abnormalities in both upper and lower motor neurons is very high.

These entities are often challenging to distinguish and accurately diagnose given overlapping clinical pictures and overall rarity.

My lecture focuses on aspects of ALS and its variants in an effort to improve the process of diagnosis, therapy and exclusion of mimics of this group of diseases.

Poster Presentation

The Role of Therapeutic Exercise in the Rehabilitation of Myasthenia Gravis Patients

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Introduction: Exercise is a widely accepted therapeutic intervention for many chronic diseases, offering broad benefits for function and quality of life. However, in Myasthenia Gravis (MG), the approach has been cautious due to fluctuating muscle weakness and fatigability. This review examines the existing evidence on the safety and efficacy of exercise in MG patients, proposing a paradigm shift to integrate exercise as a key therapeutic component.

Methods: The scientific literature on exercise in Myasthenia Gravis was analyzed, with a primary focus on studies investigating the safety and effects of resistance and aerobic exercise. The review also considered the impact of key variables such as immunosuppressive medications, comorbidities, and the natural aging process on a patient's ability to engage in physical activities.

Findings: The analysis reveals that MG patients with mild-to-moderate disease activity can safely participate in appropriate exercise programs without the risk of symptomatic exacerbation. The findings indicate improvements in muscle function, motor abilities, and quality of life. Importantly, this review suggests that the management of fatigue, a common and debilitating MG symptom, can be improved through exercise. The effects of comorbidities and aging on exercise response require specific attention.

Conclusion: This review demonstrates that exercise has the potential to become a vital therapeutic intervention in MG management, helping to alleviate symptoms, especially fatigue. Despite encouraging evidence, more extensive research is needed to establish comprehensive and personalized exercise guidelines. This article emphasizes the importance of integrating exercise as an effective complementary treatment strategy.

Occupational therapy interventions for management of fatigue in neuromuscular patients

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Introduction: Fatigue is a common and debilitating symptom in neuromuscular disorders (NMDs), significantly affecting independence and quality of life. It has physiological, psychological, and cognitive dimensions, distinct from weakness and fatigability. This review aims to explore the role and effectiveness of occupational therapy (OT) interventions in managing fatigue in NMDs.

Methods: A Narrative Review design was applied with qualitative data analysis. The search strategy included terms such as "fatigue," "occupational therapy interventions," "neuromuscular diseases," "energy conservation," "activity pacing," and "exercise" in PubMed and Google Scholar. Due to the complexity of OT interventions and the scarcity of high-quality randomized controlled trials, this method enabled synthesis of evidence from reviews, clinical guidelines, and analytical studies.

Results: Neuromuscular fatigue arises from both peripheral and central mechanisms. Recent findings indicate cognitive stress, especially through prefrontal cortex activity, aggravates central fatigue. OT interventions adopt a holistic, patient-centered approach to empower self-management. Core strategies include energy conservation, activity pacing, structured exercise, adaptive equipment, assistive devices, and environmental modifications. These approaches minimize unnecessary energy expenditure, optimize activity performance, and enhance participation in daily and social roles.

Discussion: Despite methodological limitations and the need for further research, current evidence emphasizes the pivotal role of OT within multidisciplinary care. OT addresses physical, cognitive, and psychological aspects of fatigue, ultimately promoting independence and social integration. This review highlights that a comprehensive, individualized OT approach is essential for effective fatigue management in patients with NMDs.

Diagnostic Utility of Autoantibody Panels in Neuromuscular Disorders: From Myasthenia Gravis and CIDP to Inflammatory Myopathies

Parna Ghannadikhosh, Alireza Motamedi, Rebecca Kashefimehr, Aylar Mahmoud Alilou, Shakiba Alizadeh, Mohammadmahdi Tehrani Ghadim, Sheida Shaafi

Neuromuscular disorders such as myasthenia gravis (MG), chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), and idiopathic inflammatory myopathies (IIM) are often immune-mediated and associated with specific autoantibodies. The detection of disease-specific autoantibodies has greatly enhanced diagnostic confirmation and subclassification of these conditions in the past decade. However, the overall diagnostic utility of comprehensive autoantibody panels across these disorders remains to be systematically evaluated.

We searched PubMed, Web of Science, and Scopus (2015–2025) for human studies (cohort studies, randomized trials, or case–control studies) evaluating the diagnostic performance or utility of autoantibody panels in MG, CIDP, and IIM. Inclusion criteria were studies reporting on diagnostic sensitivity, specificity, or clinical yield of relevant autoantibodies (e.g. anti-acetylcholine receptor [AChR], anti-MuSK, anti-LRP4 for MG; nodal/paranodal antibodies for CIDP; myositis-specific antibodies for IIM). Data on patient populations, autoantibody test results, and diagnostic outcomes were extracted. Given heterogeneity of outcomes, a narrative synthesis was performed instead of meta-analysis

In total, 7 studies met inclusion criteria, providing insight into the added diagnostic value of multi-antibody testing. We found that incorporating broad autoantibody panels markedly improves diagnostic sensitivity and helps define subgroups. Myasthenia Gravis: Panels including AChR, MuSK, and LRP4 antibodies detected over 90% of MG cases, greatly reducing the seronegative population. AChR antibodies alone are present in ~85% of generalized MG with high specificity. CIDP: Approximately 5–10% of patients meeting CIDP clinical criteria harbor antibodies against nodal/paranodal proteins such as neurofascin-155 or contactin-1. The presence of these antibodies delineates a distinct subset of autoimmune nodopathy. Inflammatory Myopathies: In IIM, expanded myositis-specific autoantibody (MSA) panels yield a positive result in up to 60–70% of patients. Utilizing a panel of MSAs and myositis-associated antibodies allows clinicians to classify patients into more precise myositis subtypes.

Autoantibody panels offer high diagnostic yield across MG, CIDP, and inflammatory myopathies, confirming diagnoses and uncovering clinically distinct subgroups that inform prognosis and treatment. Our review of recent studies underscores that incorporating antibody testing into routine workups (with careful attention to test limitations) can significantly improve diagnostic accuracy and personalized care for patients with neuromuscular autoimmune disorders. The continued discovery of novel autoantibodies and improvements in assay technology are likely to further expand their diagnostic utility in the coming years

Keywords: Autoantibodies, Myasthenia gravis, Serology

Emerging Biologics in Generalized Myasthenia Gravis: Integrating FcRn and Complement Inhibitors into Clinical Practice

Azra Rashidnezhad

Generalized myasthenia gravis (gMG) is a chronic autoimmune disorder characterized by fluctuating muscle weakness. Traditional long-term therapies, including corticosteroids and immunosuppressants, remain the cornerstone of management. However, their slow onset of action, cumulative adverse effects, and limited efficacy in some patients highlight the need for more targeted and rapidly effective maintenance options.

Recently, targeted biologics have transformed the therapeutic landscape. Neonatal Fc receptor (FcRn) inhibitors, such as efgartigimod, rozanolixizumab, accelerate IgG clearance and induce rapid improvement. Complement inhibitors including eculizumab, ravulizumab, and zilucoplan, block terminal complement activation, protecting the neuromuscular junction. Approved between 2017–2023, these therapies shift management from broad immunosuppression to targeted biologics, though questions remain about optimal timing, sequencing, and long-term safety.
We reviewed key phase II–III trials and real-world studies (2017–2025). FcRn inhibitors improved Myasthenia Gravis Activities of Daily Living (MG-ADL) scores within 1–2 weeks, with extension studies confirming benefits across repeated cycles. Efgartigimod (ADAPT trial) and rozanolixizumab (MycarinG trial) both showed superiority over placebo in AChR-Ab positive patients, with good tolerability. Complement inhibitors include eculizumab (REGAIN trial and subsequent real-world and adolescent studies), ravulizumab (CHAMPION MG trial and post-hoc analyses), and the subcutaneous C5 blocker zilucoplan (RAISE trial). These agents demonstrated potential improvements in functional outcomes and reduced exacerbation rates. Their benefits were particularly notable in patients with refractory gMG.

While zilucoplan and ravulizumab showed statistically significant improvements in primary or post-hoc analyses, the primary endpoint in the REGAIN trial for eculizumab was inconclusive. However, subsequent studies provide supportive evidence of its efficacy. C5 inhibitors carry meningococcal infection risk, necessitating vaccination, whereas FcRn inhibitors do not.

These therapies provide fast, targeted immunomodulation, contrasting with traditional agents, and ongoing research explores earlier initiation, sequencing, and maintenance strategies. The cost-effectiveness, access disparities, and long-term immunologic consequences are areas of ongoing investigations. Observing these effects in our practice emphasizes their real-world impact.

- FcRn inhibitors: rapid onset, favorable safety, effective across trials.

- C5 inhibitors: potent efficacy in refractory gMG, durable responses, but meningococcal infection risk.

- Real-world data align with trial findings, though cost and infrastructure limit access.

- Both classes represent the most significant therapeutic advance in gMG treatment in decades.

- Seeing these outcomes in daily practice reinforces the potential of targeted biologics.

FcRn and C5 inhibitors are reshaping the management of gMG, offering rapid, targeted, and effective treatment beyond traditional therapies. Integrating these biologics into clinical algorithms requires careful patient selection, sequencing, cost consideration, and safety monitoring. Early use may prevent disability and improve long-term outcomes, though further studies are needed. These biologics mark the beginning of a precision medicine era in MG.

Keywords: MyastheniaGravis, FcRn, Complement

A Revelation in ALS monitoring & care

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Abstract

Background

Amyotrophic lateral sclerosis (ALS) is a rare and progressive disease of the nervous system that occurs due to the destruction of motor neurons in the brain and spinal cord, which ultimately leads to disability and death of patients, and there is no definitive treatment for it; Kermanshah Province lacks integrated epidemiological data on ALS patients.

Objectives:

Launching a web-based ALS registration system in Kermanshah

Obtaining standard demographic, clinical, and risk factor data

Implementing a regular follow-up program to monitor disease progression

Supporting health planning and increasing specialized and public awareness

Studying methods to improve patients' quality of life and the effectiveness of therapeutic interventions and providing research programs accordingly

Establishing a multidisciplinary clinic for ALS patient care; Consisting of neurologists, occupational therapists, speech therapists, physiotherapists, nutritionists, pulmonologists, gastroenterologists, psychologists and social workers in the next steps.

Method:

Statistical population: All ALS patients in the provincial health centers

Sampling: Referrals to neurology clinics + social media solicitation

Data collection tool: Online questionnaire by a trained neurologist or nurse

Key variables:

-Demographic information (age, sex, place of residence, occupation)

- Clinical findings (initial symptoms, date of diagnosis, ALSFRS-R score)

- Treatments and response to them

- Risk factors

- History of previous diseases and medications

- Laboratory findings and genetic tests

Patient follow-up:

- Monthly for advanced or rapidly progressing cases

- Quarterly for early cases

- In person, by phone or online

Expected impact:

Creation ALS Epidemiological Database in Western Iran

Identify risk factors for developing prevention strategies

Improve clinical management and policy-makers' decision-making

Create a research platform for future interdisciplinary studies

Ethics and data ownership:

Obtain informed consent; data coding and encryption

Limited access based on personnel role; data ownership with Kermanshah University of Medical Sciences (KUMS)

Release of aggregated data as open access; individual data only with written consent

Evaluation of carotid Intima-Media Thickness (IMT) in amyotrophic lateral sclerosis disease using ultrasonography

Maryam Rezaee Semnani, Bahram Haghi Ashtiani

Amyotrophic lateral sclerosis (ALS), a progressive fatal disease, is recognized by the degeneration of upper and lower motor neurons, which causes motor and non-motor symptom .Multiple pathological signaling pathways have been proposed to be responsible for ALS, including endoplasmic reticulum stress,

oxidative stress, mitochondrial dysfunction, (TDP-43), (SOD1) aggregation...ALS disease is highlighted by two categories of inflammation: systemic inflammation &neuroinflammation. about systemic inflammation, hyperlipidemia is involved in heightening the risk of atherosclerosis .A common index that evaluates the risk of atherosclerosis is carotid artery intima-media thickness (IMT), which could be used as an indicator of systemic inflammation or dyslipidemia. This study aims to evaluate the carotid IMT in the ALS group to compare it with the normal group and different disease severity.

There was a single-center study that consecutive recruited ALS patients from Firoozgar Hospital from March 2021 to August 2023. A total number of 106 ALS patients were diagnosed by a neuromuscular expert

considering Gold Coast and revised El Escorial criteria through complete clinical and serological examination along with the findings of EMG, NCS, and MRI Patients with high blood pressure, suffering from diabetes or dyslipidemia, previous history of stroke or metabolite disorders, and consumption of alcoholic drinks or smoking were excluded from this study. In addition, during the ultrasonography, participants who detected a plaque with more than 2 mm in diameter in the CCA,ICA,ECA were excluded from the study.

All patients received Riluzole , while some proportion of them received Sertraline and Edaravone. In contrast, the control group did not consume any drugs. Eventually, a total number of 42 ALS patients were enrolled, in addition to 53 age and BMI-matched normal participants .All patients were included in the study after receiving informed consent representing sufficient information. This project was approved by the ethical committee of the Iran University of Medical Sciences .he IMT of the common carotid artery in ALS patients was obtained using a SonoSite M-Turbo ultrasound machine.

The baseline data were analyzed through a t-test and Wilcoxon Test .Turkey post hoc tests were applied to analyze the subgroups in the one way ANOVA. The correlation between the factors measured in the current study was evaluated through Pearson in the case of normal distribution, otherwise, Spearman was utilized.

A total number of 42 patients with ALS and 53 normal age and BMI matched participants enrolled in this study At the baseline, there was no significant difference between the age and BMI of the ALS and normal groups, while there was a remarkable difference in right and left IMT. There was a significant correlation between mean IMT values and age in both ALS and normal groups, while no remarkable correlation was defined between mean IMT and BMI.BMI was negatively correlated with the prognosis of ALS. The risk of ALS disease increased in the participants with increased IMT and increasing age was highly associated with increasing the risk of ALS. The results revealed a significant difference in the prognosis of the disease by increasing the disease severity. The results highlighted that the IMT OR increased with the severity of the ALS disease ,Likewise, the OR of the age was increased with higher intensity, in contrast to the BMI value.

Measuring carotid IMT value using ultrasonography is suggested as a non-invasive method to monitor the possible systemic inflammatory responses in ALS disease. Based on the result of the study which revealed

the increased IMT is independent of the BMI of the patients and less affected by the patient medication consumption, by measuring the IMT the severity of the disease could be evaluated.

Keywords: ALS -IMT- Inflammation -Ultrasonography- Biomarker

Neutral lipid storage disease with myopathy presenting as Bilateral asymmetrical wrist drop and foot drop

Fateme Qabel, Fariba Zemorshidi, Yalda Nilipour

Neutral Lipid Storage Disease with Myopathy (NLSD-M) is a rare autosomal recessive disorder characterized by progressive adult-onset myopathy, systemic lipid accumulation, and variable cardiac, hepatic, and multi-organ involvement. Distal weakness usually appears late in the disease course.

We describe a 32-year-old man with progressive limb weakness over 2–3 years, initially presenting with bilateral asymmetric wrist drop and foot drop. Neurological examination showed diffuse proximal and distal weakness with scapular winging, while sensory findings were normal. Family history revealed one sister with similar symptoms and another who died of cardiac failure. Laboratory studies revealed markedly elevated creatine phosphokinase and liver transaminases. Electromyography demonstrated an irritable myopathy. The patient underwent muscle biopsy and genetic testing for suspected hereditary myopathy.

Muscle biopsy showed lipid accumulation with Jordan's anomaly. Genetic analysis identified a homozygous likely pathogenic variant in PNPLA2 confirming NLSD-M, and a heterozygous pathogenic variant in MYO3A, consistent with sensorineural hearing loss.

Pulmonary function testing indicated moderately severe restrictive impairment, likely due to respiratory muscle involvement. Cardiac evaluation revealed mild dysfunction; Holter monitoring and electrophysiological studies were advised.

This case illustrates an atypical presentation of NLSD-M with early distal weakness manifesting as bilateral asymmetric wrist drop. It highlights the phenotypic variability of NLSD-M and emphasizes the need to consider genetic myopathies in patients with unusual patterns of weakness.

Keywords: Neutral Lipid Storage Disease Myopathy

Cluster of Six Cases of Guillain-Barre Syndrome (GBS) Variants Presenting with Miller Fisher–Like Symptoms Within a Short Interval at a Local Hospital: A Case Series

Mozaffar Hosseininezhad , Maryam Mohammadkhani, Maral Pornazar

Miller Fisher syndrome (MFS) is an uncommon clinical variant of Guillain–Barré syndrome (GBS), characterized by the triad of ophthalmoplegia, ataxia, and areflexia. It accounts for approximately 5–10% of GBS cases in the United States and Europe, and up to 20% in Asia. The condition is usually self-limiting, although intravenous immunoglobulin (IVIG) and plasma exchange are considered effective treatment modalities.

• Reports of multiple MFS cases presenting in a single hospital within a short time interval are rare and may suggest environmental, infectious, or epidemiological factors.

• Here, we report a cluster of six patients with Miller Fisher–like symptoms admitted to Poursina Hospital, Rasht, over an unusually short period of three months. We highlight their clinical features, management, and outcomes.

Case 1:

A 48-year-old man presented with ataxia, ophthalmoplegia, unresponsive dilated pupils, areflexia, and nasal speech. Neurological evaluation, including brain MRI, was unremarkable. He received five days of IVIG and was discharged in good condition with partial improvement. At follow-up, no significant sequelae were noted.

Case 2:

A 19-year-old man with a recent upper respiratory infection presented with acute ophthalmoplegia, unreactive dilated pupils, ataxia, and areflexia. Brain MRI, laboratory studies, and electroneurodiagnostic tests were normal. He was diagnosed with MFS and treated with a five-day course of IVIG, resulting in complete recovery at discharge.

Case 3:

A 38-year-old man with a recent upper respiratory infection presented with limb paresthesia, acute ophthalmoplegia, ataxia, and areflexia. Brain MRI, electroneurodiagnostic studies, and laboratory tests were unremarkable. He was diagnosed with MFS and treated with IVIG for five days, achieving partial improvement before discharge.

Case 4:

A 40-year-old man with a history of gout presented with acute dysarthria and ophthalmoplegia. upper limb paresthesia and ataxia. An abnormal plantar reflex was noted on one side, and brain MRI was unremarkable. He received five days of IVIG, with significant improvement in ataxia, ophthalmoplegia, and sensory symptoms.

Case 5:

A 56-year-old woman presented with severe vertigo and ataxia for three weeks before admission. Neurological examination revealed diplopia and areflexia. Brain MRI and cerebrospinal fluid (CSF) analysis were normal. She received five days of IVIG and was discharged with mild improvement. At follow-up, CASPR2 antibody positivity was detected.

Case 6:

A 65-year-old man with a recent upper respiratory infection presented with severe bilateral facial palsy and ataxia. Laboratory tests and brain MRI were unremarkable. He was diagnosed with atypical GBS and treated with IVIG, with good clinical response.

Miller Fisher syndrome is a rare variant of GBS, typically characterized by ophthalmoplegia, ataxia, and areflexia. It accounts for 5–10% of GBS cases globally, and the occurrence of multiple cases within a short interval is unusual.

In this series, six patients with MFS or MFS-like presentations were admitted within a three-month period, representing an atypical epidemiological pattern. All patients were treated with IVIG, with varying degrees of improvement, and no mortality occurred. Notably, one patient was later found to have CASPR2 antibody positivity, emphasizing the importance of considering differential diagnoses, including autoimmune encephalitis.

This unusual cluster raises the possibility of shared environmental or infectious triggers and underscores the importance of vigilance in diagnostic evaluation. The favorable outcomes across all cases reinforce the generally good prognosis of MFS when promptly treated.

We describe six cases of Miller Fisher syndrome or MFS-like presentations occurring within a short time frame at a single hospital. Although rare, such clustering highlights the need for careful epidemiological monitoring and consideration of overlapping autoimmune or post-infectious mechanisms.

Keywords: GBS- miller fisher syndrome- epidemiology

Effectiveness of Occupational Therapy Interventions on Motor Function and Quality of Life in Patients with Progressive Myopathies: A Systematic Review of Evidence from 2021–2025

Seyed Parsa Fallah Abbasi MSc

Progressive myopathies are a group of neuromuscular disorders characterized by gradual muscle weakness, fatigue, and functional limitations. Given the chronic and incurable nature of these disorders, rehabilitation primarily focuses on preserving function, preventing deformities, and improving quality of life. Occupational therapy (OT) is a cornerstone of rehabilitation, aiming to maximize independence in activities of daily living (ADL).

Objective:
This study systematically reviewed recent evidence (2021–2025) on the effectiveness of occupational therapy interventions in patients with progressive myopathies.

Methods:
A systematic search was conducted in PubMed, Scopus, and Web of Science. Articles published between 2021 and 2025 that investigated occupational therapy interventions in patients with muscular dystrophies and other progressive myopathies were included. Primary outcomes were motor function, independence in ADL, and quality of life.

Twelve eligible studies demonstrated that occupational therapy interventions—including functional training, ADL retraining, assistive device prescription, and family education—significantly improved functional independence, reduced caregiver dependence, and enhanced quality of life. Evidence also highlighted the importance of early initiation and long-term continuation of OT programs.

Occupational therapy plays a crucial and effective role in the rehabilitation of patients with progressive myopathies. Integrating OT interventions into multidisciplinary rehabilitation protocols can meaningfully improve patients' quality of life.

Keywords: OccupationalTherapy, Myopathies, MuscularDystrophy, QualityOfLife, ActivitiesOfDailyLiving

A Case of Progressive Flaccid Quadriparesis in a Young Woman: Diagnostic Pitfalls and the Role of Backward Reasoning

Ali Shoeibi, Fariba Zemorshidi, Morteza Saeidi, Parvaneh Layegh, Sepideh Zolfaghari

Acute flaccid weakness with sensory symptoms in young patients often raises clinical suspicion for Guillain-Barré syndrome (GBS), particularly in the context of recent infection. However, multiple other neurologic and metabolic disorders can present with similar features, making accurate diagnosis challenging.

A careful and structured clinical reasoning process is critical when typical findings do not fully align with the initial diagnosis. Electrodiagnostic studies, laboratory workup, and imaging can reveal important clues to alternative etiologies that may be easily overlooked.

We present a case that illustrates this diagnostic complexity and emphasizes the importance of reassessing initial assumptions through backward reasoning when clinical and paraclinical data diverge.

A 19-year-old female presented with progressive weakness in all four limbs and inability to ambulate, preceded by upper respiratory symptoms. Neurological examination revealed flaccid quadriparesis, areflexia, and impaired proprioception. Initial suspicion was Guillain-Barré syndrome (GBS), but electrodiagnostic studies showed preserved motor conduction and absent superficial peroneal sensory response, consistent with distal sensory polyneuropathy. (shown in table 1-4)

MRI revealed posterior column T2 hyperintensities from C1-T3 (figure 1). Hematologic workup showed macrocytic anemia and severe vitamin B12 deficiency. Treatment with cobalamin led to significant recovery over three months.

The patient was fully informed of the purpose and scope of this publication and provided written consent for the disclosure of her clinical information in accordance with journal and ethical guidelines.

The patient presented with quadriparesis, recent respiratory infection, and areflexia, initially suggesting Guillain-Barré syndrome (GBS). However, electrodiagnostic studies showed no motor involvement and a pure sensory neuropathy, leading to reconsideration. Further evaluation revealed macrocytic anemia and vitamin B12 deficiency, which can cause sensory symptoms, ataxia, and posterior column changes. Recent nitrous oxide exposure likely worsened the condition. Differentiating GBS from B12 deficiency is crucial: GBS may require immunotherapy and respiratory monitoring, while B12 deficiency is reversible with supplementation. This case highlights the need for broad differentials, reevaluation of data, and considering B12 deficiency in atypical neuropathies.

This case highlights the diagnostic overlap between Guillain-Barré syndrome and vitamin B12 deficiency—two conditions with markedly different management pathways. In patients presenting with acute sensory symptoms and weakness, especially when electrodiagnostic findings are atypical for GBS, clinicians should consider alternative diagnoses, including reversible metabolic causes. The use of structured clinical reasoning, particularly backward reasoning, can be instrumental in avoiding misdiagnosis and ensuring timely treatment.

Keywords: VitaminB12deficiency Guillain-Barrésyndrome backwardreasoning sensoryneuropathy clinicalreasoning

Quantitative muscle MRI in neuromuscular disorders: fat fraction, T2 mapping, diffusion metrics and AI based segmentation; a systematic review

Rebecca Kashefimehr, Aylar Mahmoudalilou, Shakiba Alizadeh , Mohammadmahdi Tehrani Ghadim, Parna Ghannadikhosh, Sheida Shaafi

Quantitative muscle MRI is emerging as a powerful biomarker in neuromuscular disorders (NMDs), enabling objective assessment of fat replacement, inflammation, and microstructural integrity. Proton density fat fraction (PDFF), water T2 mapping, and diffusion tensor/kurtosis imaging provide complementary insights into disease burden and progression. Recently, AI-based segmentation has accelerated image analysis and enhanced reproducibility. However, variability in acquisition, analysis, and reporting limits cross-study comparability and clinical translation. We systematically reviewed original studies using PDFF, T2, diffusion metrics, and AI segmentation across NMDs, aiming to summarize quantitative values, disease associations, responsiveness, and methodological quality.

We performed a systematic review following PRISMA 2020 guidelines. PubMed, Embase, and Scopus were searched without year limits for English-language original studies evaluating quantitative muscle MRI in neuromuscular disorders. Eligible studies included those reporting proton density fat fraction (PDFF), T2 mapping, diffusion metrics (DTI/DKI/IVIM), or AI-based segmentation. Case reports, reviews, and non-human studies were excluded. Two reviewers independently screened titles, abstracts, and full texts, resolving discrepancies by consensus. Data extraction captured study design, patient population, MRI acquisition parameters, quantitative outcomes, clinical correlations, and, where applicable, AI model architecture and performance metrics. Risk of bias was assessed using, QUADAS-2, and TRIPOD-AI depending on study type. Due to heterogeneity, results were synthesized narratively.

Initial search retrieved 4,422 records. After removal of duplicates, 3,150 unique articles were retained for title and abstract screening. Following this, 164 articles underwent full-text review based on predefined eligibility criteria. Ultimately, 34 studies met all inclusion criteria and were included in the systematic review. Quantitative muscle MRI demonstrates distinct cross-sectional and longitudinal patterns in neuromuscular disorders. Proton density fat fraction (PDFF) mapping reveals characteristic fatty replacement in affected muscles and significantly elevated PDFF compared to controls. Cross-sectionally, higher muscle fat fractions correlate strongly with worse muscle strength and functional scores. T2 mapping complements PDFF by detecting edema/inflammation: T2 values are elevated in involved muscles, indicating early pathological changes before overt fat replacement. Similarly, diffusion tensor imaging (DTI) metrics capture microstructural deficits.

Advances in AI-based segmentation further enhance the utility of quantitative MRI. Deep learning methods now achieve high accuracy in automatically delineating muscle and fat on MR images (Dice similarity coefficients often >0.90). This enables reliable, operator-independent quantification of PDFF and other metrics across multiple muscles and timepoints, improving reproducibility and throughput. While severe fatty infiltration can still challenge segmentation algorithms, ongoing improvements and training on disease-specific data are closing this gap. Overall, quantitative muscle MRI, from PDFF and T2 mapping to DTI, provides objective biomarkers that mirror clinical severity and progression. These techniques show promise for noninvasive disease monitoring, aiding in tracking neuromuscular disease progression and evaluating therapeutic responses, and they are poised for broader adoption as sensitive outcome measures in both research trials and clinical practice.

Key words: PDFF; T2 mapping; Biomarkers

Effectiveness of Occupational Therapy Interventions in Duchenne Muscular Dystrophy

Fatemeh Motaharinezhad

Duchenne muscular dystrophy (DMD) is a severe, progressive neuromuscular disorder characterized by early-onset muscle weakness, functional decline, and loss of independence. Although pharmacological approaches such as corticosteroid therapy may delay disease progression, they are insufficient to address the broad spectrum of functional and psychosocial challenges faced by patients. This systematic review aimed to investigate the role and effectiveness of occupational therapy interventions in managing symptoms and enhancing quality of life in individuals with DMD.

A systematic search was conducted in PubMed, Scopus, Web of Science, and SID databases for articles published between 2000 and 2025. The keywords included Duchenne muscular dystrophy, occupational therapy, rehabilitation, and functional outcomes. After screening and applying inclusion and exclusion criteria, eligible studies were critically appraised for methodological quality.

From the identified literature, 13 studies met the inclusion criteria. Evidence indicated that occupational therapy interventions provided benefits in four main domains: (1) promoting independence in activities of daily living, (2) supporting energy conservation and adaptive strategies to manage fatigue, (3) preventing contractures and maintaining upper limb function through structured exercises and assistive devices, and (4) enhancing psychosocial well-being and participation via patient- and family-centered education. The findings also emphasized the importance of early and continuous occupational therapy within a multidisciplinary care framework for optimal outcomes.

This systematic review underscores the crucial role of occupational therapy in the comprehensive management of DMD. Occupational therapy interventions can significantly improve functional performance, delay secondary complications, and enhance psychosocial adaptation. Future high-quality randomized controlled trials with long-term follow-up are needed to strengthen the evidence base and guide best-practice recommendations for occupational therapy in DMD care.

Keywords: Duchenne, Occupational therapy, Rehabilitation.

Antiseizure Medication-Induced Polymyopathy — Emerging Insights and Clinical Implications

Mohammad Reza Najafi, Mohammad Amin Najafi

Antiseizure medications (ASMs) are indispensable in epilepsy management but may induce polymyopathy—a rare neuromuscular complication marked by diffuse muscle weakness, elevated creatine kinase, and myopathic changes on biopsy.

To summarize recent developments in understanding ASM-induced polymyopathy, including mechanisms, risk factors, and clinical management.

Enzyme-inducing ASMs such as phenytoin, carbamazepine, and valproic acid have been linked to mitochondrial dysfunction, calcium dysregulation, and immune-mediated muscle injury. Genetic variants affecting drug metabolism and immune response may increase susceptibility. Chronic ASM use may contribute to systemic effects—bone demineralization, hormonal imbalance—that exacerbate neuromuscular symptoms. Diagnosis is often delayed due to symptom overlap with other myopathies and lack of routine muscle monitoring.

ASM-induced polymyopathy is underrecognized and potentially reversible. Early identification through clinical vigilance and personalized pharmacogenomic profiling is essential. Routine neuromuscular assessment and interdisciplinary management may improve outcomes in affected patients.

Keywords: antiseizure medications, polymyopathy, drug-induced myopathy

Integrated Electrodiagnosis and Imaging Protocols in Neuromuscular Disease: Systematic Review of Combined Nerve Conduction, Ultrasound, MRI and AI Analytics

Parna Ghannadikhosh, Alireza Motamedi, Sheida Shaafi

Neuromuscular diseases frequently require a multimodal diagnostic approach. Electrodiagnostic (EDX) tests (such as needle EMG and nerve conduction studies) and imaging modalities (ultrasound and MRI) provide complementary information on nerve and muscle pathology. However, interpreting the large volume of data from these studies can be challenging. Artificial intelligence (AI) techniques are emerging as powerful tools to integrate and analyze complex neuromuscular data, enabling improved disease classification and more precise diagnoses. We systematically reviewed the literature on integrated EDX, imaging, and AI approaches in neuromuscular disease diagnosis.

We conducted a systematic review in PubMed, Scopus and Embase databases for peer-reviewed original studies in humans using keywords related to EDX (EMG or nerve conduction), imaging (neuromuscular ultrasound or muscle MRI), and AI or machine learning analysis up to August 2025. Two reviewers independently screened titles, abstracts, and full texts. Conflicts were resolved by agreement. Data were extracted on the modalities used, conditions studied, and the role of AI (classification, segmentation, or severity grading). Quality assessment of the included studies was performed using JBI's critical appraisal tools.

A total of 1398 articles were found in initial search, out of those, 1365 were remained after removing duplicates. 54 articles were assessed in full text screening. Finally, nine studies met the inclusion criteria, together examining over 1,750 participants with sample sizes ranging from 38 to1,034 patients. Using multiple modalities generally improved diagnostic accuracy. AI applications in these studies fell into three categories. Classification models distinguished healthy vs diseased cases or different neuromuscular disorders, often with high accuracy (≥90%). Segmentation automatically delineated nerves or muscles on images to quantify structural changes. Grading assessed disease severity or functional status. Conditions covered included carpal tunnel syndrome, ALS, and various myopathies including Duchenne and facioscapulohumeral muscular dystrophies, and inflammatory myositis.

This review demonstrates that AI enhanced electrodiagnostic and imaging methods consistently outperform traditional analysis and provide quantitative metrics that could standardize neuromuscular diagnosis. In ultrasound, machine learning and deep learning models improved classification of neuromuscular disorders, CTS detection and Heckmatt grading beyond conventional echo intensity ratios. MRI-based AI segmentation achieved near-manual accuracy in large cohorts and provided a foundation for automated quantitative MR neurography. These findings suggest that integrated approaches like combining ultrasound, MRI and NCS data with AI analytics could produce objective biomarkers and reduce reliance on invasive electrodiagnostic testing. However, there are limitations like lacking cross modal integration, small sample sizes. Future research may focus on multimodal datasets that combine electrodiagnostic measurements with imaging and clinical parameters, allowing more accurate AI models.

Keywords: Electrodiagnosis, Neuromuscular disorders , Electromyography

A survey on mutation spectrum in Iranian patients with limb-girdle muscular dystrophies

Sheyda Khalilian, Mohadeseh Fathi, Dr Mohammad Miryounesi, Soudeh Ghafouri-Fard

Limb–girdle muscular dystrophies (LGMD) is a term to designate diverse types of muscular dystrophies that predominantly affect proximal skeletal muscles (1). They are inherited as autosomal disorders, either dominant or recessive. They are extremely heterogeneous in terms of underlying genetic causes. The advent of whole exome sequencing (WES) method has facilitated identification of genetic causes of LGMDs with more than 30 autosomal loci identified for this type of disorders (1). Most of cases are inherited in an autosomal recessive manner and designated as different types of LGMD2. Studies in different populations have shown that 10-33% of LGMD2 cases are due to mutations in the CAPN3 gene that encodes an intracellular nonlysosomal cysteine protease modulated by calcium ions (2). Besides, 5-30% of cases exhibit mutations in the DYSF gene that encodes a ubiquitous transmembrane protein contributing to the calcium-mediated sarcolemma resealing (2).
This study was performed on 49 Iranian cases of LGMD. Cases were referred to the Comprehensive Genomic Center, Tehran, Iran during 2018-2024 for molecular diagnosis and counseling. All methods were carried out in accordance with relevant guidelines and regulations. All experimental protocols were approved by ethical committee of Shahid Beheshti University of Medical Sciences. Informed consent forms were signed by patients or their legal representatives. Clinical signs and symptoms, biochemical tests and EMG were compatible with the diagnosis of LGMD in most cases. Thus, patients were investigated by WES technique.
Tables 1 to 7 show a summary of clinical and molecular data. Patients had variable degrees of muscle weakness and elevated CPK levels. Ten patients had pathogenic/likely pathogenic variants in the CAPN3 gene and were categorized as Calpainopathy (LGMD 2A/R1) (Table 1). Another 13 patients were categorized as Dystroglycanopathy (LGMD type C, 9) (Table 2). In addition, four patients were classified as Sarcoglycanopathy (LGMD 2C-2F/R3-R6) (Table 3).

White matter change in the brain MRI was reported in case 35 who was further demonstrated to have a homozygote pathogenic variant in the LAMA2 gene (c.283+1G>A).

In the current study, we summarized the results of molecular genetics investigations in patients with different variants in the LGMD-related genes. As expected, the majority of patients were born to consanguineous parents and the mode of inheritance was supposed to be autosomal recessive. Among 49 patients, five patients were compound heterozygote for variants in the LGMD-related genes. While the majority of variants were located in the exonic regions, two intronic variants, namely c.2861+1G>A and c.355-3T>G were identified in the DYSF and POMGNT1 genes, respectively. CAPN3 and LAMA2 genes were the genes encompassing the highest frequencies of pathogenic or likely pathogenic variants in this cohort.

Our study has some limitations. First, the disease onset was not clear in some cases, complicating the identification of the genotype-phenotype correlations. Second, some of the clinical findings were not compatible with a pure diagnosis of LGMD.

Keywords: muscular dystrophy genetics

Expanding the Phenotypic Spectrum of GFER Variants: Myopathy, Neuropathy, and Congenital Cataracts in an Iranian Family

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Introduction

Mitochondrial disorders encompass a wide range of syndromes caused by mutations in mitochondrial or nuclear genes. They often manifest with neuromuscular, ocular, auditory, and systemic dysfunction. Among nuclear genes, Growth Factor ERV1-like (GFER), also known as Augmenter of Liver Regeneration (ALR), encodes a key sulfhydryl oxidase that regulates oxidative protein folding and mitochondrial homeostasis. Pathogenic GFER mutations have been associated with autosomal recessive conditions characterized by muscular hypotonia, congenital cataracts, and developmental delay. Previous reports have described patients with severe neonatal phenotypes, including lactic acidosis, encephalopathy, and multisystemic involvement. However, milder forms with later-onset muscle weakness have also been observed. Here, we present two Iranian siblings with congenital cataracts, proximal myopathy, and pure motor demyelinating polyneuropathy due to a homozygous GFER variant, highlighting novel clinical aspects.

Case Presentation

The proband, a 35-year-old man, presented with instability and recurrent falls since adolescence. He had congenital bilateral cataracts requiring surgery at 18 months; vision was lost in the right eye despite intervention. He reported paresthesia, progressive proximal weakness, myalgia, and fatigue. Weakness mainly affected hip and shoulder girdle muscles, with difficulty rising from the floor and climbing stairs.
Neurological exam revealed mild facial paresis, ophthalmoparesis, proximal limb weakness (MRC 3–4), and positive Gowers' sign, without sensory or cerebellar deficits. Serum CK and liver enzymes were elevated. Electrophysiology revealed chronic pure motor demyelinating polyneuropathy with conduction block. Muscle biopsy showed mitochondrial pathology with ragged-red fibers, COX-deficient fibers, and re-innervation features. Brain MRI was normal.
His brother, aged 32, had cataract surgery at 12 months and preserved vision. He reported mild proximal lower limb weakness but no sensory or systemic complaints.
Neurological exam revealed subtle proximal weakness with Gowers' sign. CK levels were elevated; EMG demonstrated mild non-irritable myopathy. Neither sibling exhibited developmental delay or cognitive impairment. Family history revealed consanguinity (first cousins). Genetic testing identified a homozygous GFER variant (c.581G>A, p.Arg194His), confirmed by Sanger sequencing. Parents were heterozygous carriers, and segregation was consistent with autosomal recessive inheritance.

Results

The clinical evaluation showed that both affected siblings shared congenital cataracts and proximal myopathy but exhibited different severities. The proband had progressive weakness, mitochondrial myopathy on biopsy, and electrophysiological evidence of motor demyelinating neuropathy. His brother displayed milder myopathy without neuropathic involvement. Laboratory data revealed elevated CK and liver enzymes in both. Genetic analysis confirmed a homozygous missense mutation in GFER (p.Arg194His), previously implicated in mitochondrial disease. In silico modeling suggested that

substitution of Arg194 with histidine disrupts enzymatic activity, destabilizes protein structure, and impairs mitochondrial oxidative folding.
These findings provide the first report of pure motor demyelinating neuropathy linked to GFER, suggesting a role in peripheral nerve myelination.

Conclusion
This study expands the clinical spectrum of GFER-related mitochondrial disorders. Unlike previous reports describing severe neonatal encephalopathy with multisystemic dysfunction, our cases demonstrate a milder phenotype limited to cataracts, proximal myopathy, and motor demyelinating neuropathy. The proband's muscle biopsy confirmed mitochondrial pathology, while electrophysiology highlighted a unique pure motor neuropathy, not previously associated with GFER variants. These observations underscore the variability of disease expression, even within the same family. The findings emphasize the importance of considering GFER mutations in patients with combined myopathy, neuropathy, and congenital cataracts, particularly in consanguineous populations. Further studies are warranted to clarify the mechanistic role of GFER in myelin biology and to explore potential therapeutic strategies targeting mitochondrial dysfunction in these patients.

Unveiling Demyelinating Features in an Iranian Patient with *MTRFR* Mutation

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Introduction

Hereditary spastic paraplegia (HSP) is a genetic disorder characterized by progressive lower limb spasticity and weakness, leading to gait disturbances. HSP results from neurodegeneration within corticospinal tracts and is categorized into pure forms, which present with spastic paraparesis and hyperreflexia, and complex forms, which exhibit additional neurological features. More than 85 genes, inherited through various genetic patterns, are associated with HSP. Commonly observed mutations, particularly in SPG4, SPG3A, SPG11, and SPG7, disrupt mitochondrial and protein functions, leading to axonal degeneration. This case report presents an Iranian patient with a known *MTRFR* mutation, emphasizing novel findings of demyelinating features revealed by nerve conduction studies, which have not been previously documented in relation to this mutation.

Case Presentation

A 37-year-old Iranian man from Kurdistan was referred to our neuromuscular clinic with a history of progressive gait disturbances. He was born at term through an uncomplicated delivery, but his parents reported visual impairment early on, particularly night blindness. Developmentally, he was normal until age seven, when he began experiencing spastic weakness in his lower limbs, leading to frequent falls. Over time, weakness in his upper limbs progressed, with reported episodes of nocturnal myoclonus. However, he had no issues with swallowing, sensory perception, sphincter control, or hearing. The patient's medical history included paroxysmal supraventricular tachycardia treated with two ablation procedures. His parents were consanguineous, and he has three siblings, none of whom exhibited similar symptoms.

Upon examination, the patient's visual acuity was limited to finger counting at 10 cm, with bilateral optic atrophy noted during ophthalmoscopy. Motor assessment indicated significant weakness in the distal limbs (upper limb strength 4/5; foot dorsiflexion 0/5; plantar flexion 1/5) alongside marked distal atrophy. Deep tendon reflexes were brisk with non-sustained clonus, and gait analysis revealed spasticity with foot drop. Notably, Hoffmann's sign was positive.

Nerve conduction studies demonstrated chronic demyelinating motor neuropathy with conduction blocks, which were confirmed through optical coherence tomography showcasing bilateral optic atrophy. Routine laboratory tests for common neuropathy causes returned unremarkable results. Genetic testing identified a homozygous *MTRFR* variant (c.394C>T, p.Arg132Ter), consistent with an autosomal recessive inheritance pattern.

Results

Our assessments confirmed that the patient has experienced reduced visual acuity since childhood, along with spastic weakness in his lower limbs appearing around age seven, later progressing to upper limb weakness. His medical history revealed incidents of supraventricular tachycardia requiring ablation.

Electrodiagnostic studies demonstrated chronic demyelinating motor neuropathy with conduction blocks primarily affecting the right median and both ulnar nerves. Confirmation of optic nerve atrophy was accomplished through optical coherence tomography. Genetic analysis revealed a previously documented homozygous mutation in *MTRFR*, aligning with findings in prior studies. This case expands the understanding of *MTRFR* related disorders, revealing the presence of demyelinating features in contrast to the axonal forms reported earlier.

Conclusion

This study emphasizes the diverse clinical manifestations associated with *MTRFR* mutations, expanding beyond previously recognized symptoms such as intellectual disabilities, ataxia, and mitochondrial dysfunction. Our findings reveal that the patient presents with spastic paraplegia, optic atrophy, and neuropathic involvement without evidence of cognitive impairment or ataxia. Unique to this case, nerve conduction studies identified chronic demyelinating motor neuropathy with conduction blocks, contrasting with prior reports which predominantly identified axonal neuropathy in similar patients. This highlights the potential for variation in neuropathological features among patients with *MTRFR* mutations, demonstrating the need for comprehensive clinical evaluations to aid in accurate diagnosis and management.

Clinical and Genetic Characterization of five Iranian families affected to triple A syndrome or Allgrove syndrome with neurological dysfunction

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Introduction: Triple A syndrome (TAS) or Allgrove syndrome is a rare autosomal recessive (AR) disorder primarily defined by achalasia, alacrima, and adrenal insufficiency. It is also often accompanied with neurological features that may affect the central, peripheral, or autonomic nervous systems. TAS shows a wide range of clinical heterogeneity in terms of the age at onset (AAO), symptoms, and their severity. This disorder is caused by variants in the AAAS gene located on chromosome 12q13, which encodes the nuclear pore complex protein known as ALADIN (Alacrima, Achalasia, Adrenal Insufficiency, and Neurologic disorder). ALADIN is important for the transport of certain proteins between the nucleus and cytoplasm. AAAS variants disrupt proper localization, production or function of ALADIN which can be ultimately accompanied by the onset of disease symptoms.

Materials and Methods: In this study, after clinical and paraclinical assessments of six patients from five families, genetic variants in probands were detected using whole-exome sequencing (WES) and validated through Sanger sequencing.

Results: Our patients exhibited variability in AAO and clinical manifestations, which can occur even among family members sharing the same variant. Additionally, a probable correlation between neurological symptoms and variants in exon 6 was evident. Genetically, we identified five variants in the AAAS gene, including three novel, c.470_471delTT;p.Phe157Cysfs*16, c.626T>C;p.Leu209Ser, and c.1222G>C;p.Gly408Arg, and two known variants, c.463C>T;p.Arg155Cys, and c.1066_1067del;p.Leu356Valfs*8. All patients were homozygote, except for one patient, who was a compound heterozygote.

Conclusion :This study, by introducing three novel variants, expanded the mutation spectrum of the AAAS gene and emphasized the high clinical heterogeneity of TAS. Such clinical variability can sometimes lead to misdiagnosis. For instance, in one patient, three classic features of the disease were not observed, which initially led to a diagnosis of neuropathy. Our findings emphasize that WES can be one of the effective methodologies for the diagnosis of TAS.

Keywords :Triple A syndrome, Allgrove syndrome, AAAS gene, Whole exome sequencing