Neuromuscular Disease—Dynamic Progress at Work

With 7 new treatments in 5 years, including some of the first approved gene therapies, the field of neuromuscular disorders is making rapid dynamic progress.

By Aziz Shaibani, MD, FACP, FAAN, FANA

Neuromuscular disease (NMD) is among the most dynamic neurology subspecialties. The incidence of NMDs (160/100,000) is comparable to that of Parkinson's disease and is increasing because of improved diagnosis and management. The NMDs carry high mortality, morbidity, and economic burden.

Symptoms of NMDs, including muscle cramps, pain, muscle weakness, numbness, and fatigue comprise almost half of all presenting symptoms for a general neurology practice. Over the last 5 years, at least 7 new agents were approved by the Food and Drug Administration (FDA) to treat various NMDs (eg, Duchenne's muscular dystrophy, spinal muscular atrophy, amyloidosis, amyotrophic lateral sclerosis, Lambart Eaton syndrome, and myasthenia gravis). We are in a decade of biologic and genetic advances with monoclonal antibodies, gene interference, and gene replacement among these new treatments. There has been an explosion of genetic diagnosis for NMDs that accounts for many of these advances and allows ever more people with these diseases to access treatment and hope for their futures.

I am honored to be guest editor of this issue of *Practical Neurology* and invited experts from different fields to give updates on diagnosis and management across the spectrum of NMDs. We begin with diagnosis, for which genetics continues to evolve with Sanger gene sequencing, genetic panels, and whole-exome and whole-genome sequencing having become much more affordable; Drs. Orengo and Murdock give us a practical update on how this effects NMDs. The degree to which elevated creatine kinase (CK) levels should be investigated has been controversial, and Drs. Silvestri and Wolfe share a redefined diagnostic approach in light of emerging genetic testing and outcomes studies. Skin biopsy for epidermal nerve fiber density estimation to diagnose small fiber neuropathy has become popular; Dr. Saperstein elucidates the value and limitations of this diagnostic procedure.

Moving on to treatment, new therapies, albeit modest, are emerging for ALS. Drs. Brent and Ajroud-Driss share the present and future of ALS management. Monoclonal antibodies have changed the therapeutic landscape for refractory myasthenia gravis, which Drs. Nguyen and Phan comprehensively address. Seeing children with SMA type 1, who were not expected to live beyond the first year of their life, crawling and walking was not even conceivable 10 years ago. New gene-interference and gene-replacement treatments have made that possible, and Drs. Rai and Elsheikh cover these exciting developments, including information on care of both children and adults with SMA. Congenital myasthenic syndromes comprise rare heterogenous diseases of the neuromuscular junction; Dr. Iyadurai provides a thorough overview of advances in this field brought by genetic testing and also covers current treatment. Myositis and myopathies are ably covered by Drs. Varon and Machado for inclusion body myositis; Drs. Hussein, Pokala, and Kuo for noninflammatory dystrophic and metabolic myopathies, and Dr. Felice for distal myopathies.

Muscle cramps are common, and quantitative and objective measurements to guide treatment and clinical trials are needed. Drs. Katzberg and Sadeghian give an expert update on these issues in an online-only article.

Throughout the issue, we use a similar style and emphasize illustrations and algorithms to enhance readability and learning. I would like to thank the authors for their contributions and Anne M. Sydor, PhD the editor in chief for proposing this topic and for her diligence in collecting and editing the articles in a timely manner.

More articles on muscle than nerve disease may reflect my own prejudices as well the limitation of space. We hope that other important topics such as inflammatory neuropathies and myopathies, hereditary neuropathies, neuropathic pain, and dystrophinopathies will be covered in future issues.

I hope you will be satisfied and happy with this issue. ■

Aziz Shaibani, MD, FACP, FAAN, FANA
Director, Nerve and Muscle Center of Texas.
Clinical Professor of Medicine/ Baylor College of Medicine
Houston, TX