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Update in Neuromuscular Disorders

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There has been substantial progress in the understanding of pathophysiology of immune-mediated neuropathies and autoimmune myasthenia gravis (MG). This review focuses the atypical phenotypes of chronic inflammatory
demyelinating polyradiculoneuropathy (CIDP) and the recent therapeutic trials, and addresses the new immunological findings of multifocal motor neuropathy (MMN) and alternative therapeutic options. In addition, recent advances on pathogenesis and treatment of MG will be covered.

CIDP is a heterogeneous disorder with diverse clinical phenotypes. Fatigue, pain and tremor have been recently emphasized as often disabling symptoms in CIDP in addition to motor and sensory deficit. Typical CIDP accounts for more than half of cases. The atypical CIDP phenotypes include pure sensory, pure motor, distal acquired demyelinating symmetric neuropathy (DADS), multifocal acquired demyelinating sensory and motor neuropathy (MADSAM, Lewis–Sumner syndrome) and focal variants. Among these subtypes, sensory CIDP is the most frequent and the most difficult to identify because of lack of demyelinating features on nerve conduction studies. Based on small retrospective case series, atypical CIDP phenotypes may have a different course. In the recent randomized clinical trial comparing intravenous immunoglobulin (IVIg) with intravenous methylprednisolone, IVIg was superior based on discontinuation rate due to inefficacy, adverse events or intolerance. However, improvement after corticosteroids seems to be more sustained than after IVIg indicating superior long-term immunosuppressive and immunomodulating effect of corticosteroids in CIDP. Subcutaneous immunoglobulin (SCIg) treatment can be a potential alternative for stable CIDP, which was recently evaluated in a small double-blind placebo controlled trial. In CIDP patients refractory to first-line therapy, alternative diagnoses should be considered. POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, M component, and skin changes) may strongly resemble CIDP with motor predominance and high cerebrospinal fluid protein content. Accurate and early diagnosis of POEMS syndrome is important because of the different therapeutic treatment and prognosis in both diseases. Recent electrophysiologic studies showed that the neuropathy of POEMS syndrome can be differentiated from CIDP by a more uniform demyelination and more severe axonal loss. Lenalidomide and dexamethasone have been suggested as effective alternatives in the treatment of the neuropathy of POEMS syndrome.

Although MMN may share some characteristics CIDP and its variant, it is recognized as a distinct disease. The Task Force of European Federation of Neurological Societies and Peripheral Nerve Society reviewed clinical and electrophysiological features constituting the main support of the diagnosis in MMN and revised guidelines for its management. IgM anti-GM1 ganglioside antibodies are seropositive in 40-50% of MMN cases. Recently, anti-NS6S (IdoA-GlcNS-6S, a disulfated glucosamine–uronic acid heparin disaccharide) antibodies were detected in MMN patients and reported having the same positivity as that of anti-GM1 antibodies. Concomitant

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tests for both antibodies may raise the seropositivity for MMN patients. The mainstay treatment of MMN is periodic IVIg infusions, but other therapeutic options have been recently assessed. SCIg may be a possible alternative to IVIg. The recent open-label clinical trials evaluated the efficacy of complement inhibitors and anti-CD20 monoclonal antibody for the treatment of MMN.
Seropositive MG is heterogeneous, determined by autoantibodies to AChR, MuSK, Lrp4, or low-affinity AChR. Pathogenesis of MG differs according to epidemiological and genetic factors, thymus pathology, autoantibody isotype, and autoantigenic target. Recently, rituximab and complement-inhibitors for the treatment of MG have been explored. Rituximab seems to be especially effective in MuSK+ MG, although it shows effectiveness in both AChR+ and MuSK+ MG. In MuSK+ MG, response to rituximab is fast and sustained with a striking decrease in antibody titers. A phase II double-blind placebo controlled trial reported that patients with drug-resistant MG improved significantly after 16-week treatment with eculizumab, suggesting that it could be an option in refractory AChR+ MG. Therapeutic strategies should be targeted at each subtype of MG.

Key Words: Chronic inflammatory demyelinating polyradiculoneuropathy, Multifocal motor neuropathy, POEMS syndrome, Autoimmune myasthenia gravis