DRASKO SIMOVIC, M.D.

Autoimmune Neuropathies

The exact prevalence of neuropathies in the general population is unknown. The Neuropathy Association, New York, USA, estimates that in the United States alone, up to 20 million patients suffer from peripheral neuropathies. Polyneuropathies have a variety of causes including a subset mediated by immune mechanisms

Guillain-Barré syndrome and variants
Guillain-Barré syndrome (GBS) has an annual incidence of 1 – 2 cases per 100,000 in the general population. Its variants include two subgroups. The first, consisting of syndromes with predominant weakness, includes acute inflammatory demyelinating polyradiculoneuropathy (AIDP), acute motor axonal neuropathy (AMAN) and acute motor sensory axonal neuropathy (AMSAN). The second subgroup, where weakness is not predominant, includes Miller Fisher syndrome, acute panautonomic neuropathy and pure sensory neuropathy.

In GBS syndromes with predominant weakness, the clinical syndrome usually follows a viral illness (60-70%) or Campylobacter jejuni enteritis (30-40%). Clinical presentation usually begins with paresthesias and lower back pain. Ascending muscle weakness follows. The disease can progress for days up to four weeks. Autonomic manifestation, partial or complete ophthalmoplegia and facial weakness may be seen. Ventilator support may be needed in a third of patients. In addition to muscle weakness, physical examination shows distal sensory loss, except in AMAN form, and absent or depressed muscle stretch reflexes. Patients may develop ataxia, tremor, and dysautonomia. Examination of cerebrospinal fluid (CSF) shows elevated protein without leukocytosis in 90 percent of patients.

Electrophysiologic features are characterized by prolonged distal and F-wave latencies, demyelinating ranges of conduction velocities, and partial motor conduction blocks. Although sensory studies are normal in AMAN, in both AMSAN and AMAN a marked reduction of compound muscle action potential amplitude is prominent.

Chronic inflammatory demyelinating polyneuropathy

Chronic inflammatory demyelinating polyneuropathy (CIDP) is an acquired immune mediated neuropathy with a peak incidence in the 40 – 60 year age group. The prevalence is estimated from 1 – 7.7 per 100,000 population and rises with age. It is clinically characterized by a slowly progressive symmetric weakness and a panmodal sensory loss. Weakness usually affects the legs first and is not associated with atrophy or fasciculations. A large fiber sensory loss is present with absent or depressed stretch reflexes. By definition, symptoms develop over at least two months. Elevated CSF proteins are seen in 95 percent of CIDP patients.

The electrophysiologic features include reduction in conduction velocity in two or more nerves, partial conduction block , prolonged distal latencies in two or more motor nerves and absent F-waves or prolonged minimum F-wave latencies. Several variants of CIDP have been described. The main variant with asymmetric findings is referred to as a multifocal acquired demyelinating sensory and motor (MADSAM) neuropathy. It often begins in one limb followed by a spread to other limbs in an asymmetric fashion. Further variants include distal acquired demyelinating sensory (DADS) neuropathy and multifocal acquired sensory and motor (MASAM).

Multifocal motor neuropathy

Multifocal motor neuropathy (MMN) is a rare disorder with a prevalence of 1 – 2 per 100,000. This unique neuropathy is characterized by a progressive, asymmetric, distal weakness that frequently presents as a wrist drop, a bicep weakness or a foot drop with minimal or absent sensory symptoms. Weakness progresses insidiously or in a stepwise manner. Muscle cramps and fasciculations are frequently seen coupled with asymmetric stretch reflexes. Electrophysiologic findings show a persistent, focal, motor conduction block outside the common compression sites. Prolonged F-wave latencies and reduced motor conduction velocities are also seen, with normal sensory responses. Laboratory investigations may be helpful in establishing diagnosis as

antibodies to GM-1 are elevated in 40-50% of patients. Antibodies to other glycolipids, including asialo-GM1, GD1a and GM2, may be seen in a small percentage of patients. Examination of CSF in patients with MMN is usually normal.

Monoclonal gammopathy of undetermined significance and neuropathy

Paraprotein associated neuropathies are a clinically heterogeneous group, depending on the type of a monoclonal paraprotein. Most of the affected patients do not have an underlying plasma cell disorder, thus the term monoclonal gammopathy of undetermined significance (MGUS) was coined. Commonly, patients are over the age of 50, with men being more affected than women. The course is slowly progressive for most of the patients, although rapid progression may be seen in a small number of cases. Approximately 55 percent of MGUS neuropathy patients have IgM monoclonal proteins, while 35 percent have IgG and 10 percent have IgA. In a subset of patients with IgM gammopathy and neuropathy, approximately 50% have antibodies to a myelin associated glycoprotein (MAG). The initial presentation of patients with anti-MAG antibodies is characterized by a mild, distal, lower extremity sensory disturbance. While approximately one-third of these patients have only sensory symptoms, most patients have some degree of distal weakness and in 20% the weakness is severe. Electrophysiologic studies of patients with an anti-MAG neuropathy are characterized by predominantly demyelinating features. Examination of CSF in patients with MGUS neuropathy may show normal or elevated proteins.

Treatment with IVIg

IVIg is a solution of a highly purified immunoglobulin, derived from a large pool of human plasma. The commercially available IVIg contains more then 95% of IgG and less then 2.5% of IgA.

The therapeutic dose of IVIg is 400 mg/kg/day, repeated over five days, for a total of 2gr/kg. The recommended rate of infusion should not exceed 200 ml/hr. Tolerability of IVIg is very good and adverse reactions are usually minor. The most common side effects are headache, nausea, chills, flushing, myalgia, hypotension, hypertension, chest discomfort, and fatigue. Infrequent adverse reactions include thromboembolic evens, skin reactions, aseptic meningitis, renal tubular necrosis, and severe anaphylactic reaction.

Highlights:

The therapeutic dose of IVIg, a highly purified immunoglobulin derived from human plasma, is 400mg/kg/day repeated over 5 days. Tolerability of IVIg is very good and adverse reactions are usually minor.

The benefits of IVIg therapy have been recognized through controlled studies for Guillain-Barré syndrome (GBS), chronic inflammatory demyelinating polyneuropathy (CIDP) and multifocal motor neuropathy (MMN). In monoclonal gammopathy of undetermined significance (MGUS) and neuropathy, the effectiveness of IVIg is variable.

Further controlled trials are needed to clarify the open questions in the treatment of autoimmune neuropathies, including the efficacy of a second IVIg infusion in non responders in GBS, maintenance IVIg dose and frequency in CIDP and MMN, efficacy of IVIg in diabetes associated CIDP and the benefit of combination therapy with other immunomodulating medications.

CAPE COD
6 Main Street
Hyannis, MA 02601
Tel: 508-775-2600

DRASKO SIMOVIC, M.D.
Board Certified in: Neurology, Clinical Neurophysiology, Electrodiagnostic Medicine, Disability Analysis

LAWRENCE
50 Prospect Street #404
Lawrence, MA 01841
Tel: 978-687-2586