History, Diagnosis, and Management of Chronic Inflammatory Demyelinating Polyradiculoneuropathy

P. James B. Dyck, MD, and Jennifer A. Tracy, MD

From the Department of Neurology, Mayo Clinic, Rochester, MN.

CME Activity

Target Audience: The target audience for *Mayo Clinic Proceedings* is primarily internal medicine physicians and other clinicians who wish to advance their current knowledge of clinical medicine and who wish to stay abreast of advances in medical research.

Statement of Need: General internists and primary care physicians must maintain an extensive knowledge base on a wide variety of topics covering all body systems as well as common and uncommon disorders. *Mayo Clinic Proceedings* aims to leverage the expertise of its authors to help physicians understand best practices in diagnosis and management of conditions encountered in the clinical setting.

Accreditation: In support of improving patient care, Mayo Clinic College of Medicine and Science is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC) to provide continuing education for the health care team.

Credit Statement: Mayo Clinic College of Medicine and Science designates this journal-based CME activity for a maximum of 1.0 AMA PRA Category 1 Credit(s).™ Physicians should claim only the credit commensurate with the extent of their participation in the activity.

MOC Credit Statement: Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 1 MOC point in the American Board of Internal Medicine's (ABIM) Maintenance of Certification (MOC) program. Participants will earn MOC points equivalent to the amount of CME credits claimed for the activity. It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

Learning Objectives: On completion of this article, you should be able to (1) understand common clinical and electrophysiological features of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) and pitfalls in its diagnosis, (2) describe typical pathological findings of the nerve in CIDP, and (3) describe typical first-line treatments of CIDP and options for long-term treatment (including corticosteroid-sparing agents).

Disclosures: As a provider accredited by ACCME, Mayo Clinic College of Medicine and Science (Mayo School of Continuous Professional Development) must ensure balance, independence, objectivity, and scientific rigor in its educational activities. Course Director(s), Planning Committee members, Faculty, and all others who are in a position to control the content of this educational activity are required to disclose all relevant financial relationships with any commercial interest related to the subject matter of the educational activity. Safeguards against commercial bias have been put in place. Faculty also will disclose any off-label and/or investigational use of pharmaceuticals or instruments discussed in their presentation. Disclosure of this information will be published in course materials so that those participants in the activity may formulate their own judgments regarding the presentation. In their editorial and administrative roles, Karl A. Nath, MBChB, Terry L. Jopke, Kimberly D. Sankey, and Jenna M. Pederson, have control of the content of this program but have no relevant financial relationship(s) with industry.

The authors report no competing interests.

Method of Participation: In order to claim credit, participants must complete the following:

1. Read the activity.
2. Complete the online CME Test and Evaluation. Participants must achieve a score of 80% on the CME Test. One retake is allowed.

Visit www.mayoclinicproceedings.org, select CME, and then select CME articles to locate this article online to access the online process. On successful completion of the online test and evaluation, you can instantly download and print your certificate of credit.

Estimated Time: The estimated time to complete each article is approximately 1 hour.

Hardware/Software: PC or MAC with Internet access.

Date of Release: 6/1/2018

Expiration Date: 5/31/2020 (Credit can no longer be offered after it has passed the expiration date.)

Privacy Policy: http://www.mayoclinic.org/global/privacy.html

Questions? Contact dletcsupport@mayo.edu.

Abstract

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is probably the best recognized progressive immune-mediated peripheral neuropathy. It is characterized by a symmetrical, motor-predominant peripheral neuropathy that produces both distal and proximal weakness. Large-fiber abnormalities (weakness and ataxia) predominate, whereas small-fiber abnormalities (autonomic and pain) are less common. The pathophysiology of CIDP is inflammatory demyelination that manifests as slowed conduction velocities, temporal dispersion, and conduction block on nerve conduction studies and as segmental demyelination, onion-bulb formation, and endoneurial inflammatory infiltrates on nerve biopsies. Although spinal fluid protein levels are generally elevated, this finding is not specific for the diagnosis of ClDP. Other neuropathies can resemble CIDP, and it is important to identify these to ensure correct treatment of these various conditions. Consequently, metastatic bone surveys (for osteosclerotic myeloma), serum electrophoresis with immunofixation (for monoclonal gammopathies), and human immunodeficiency virus testing should be considered for testing in patients with suspected CIDP. Chronic inflammatory demyelinating polyradiculoneuropathy can present as various subtypes, the most common being the classical symmetrical polyradiculoneuropathy and the next most common being a localized

asymmetrical form, multifocal CIDP. There are 3 well-established, first-line treatments of CIDP—corticosteroids, plasma exchange, and intravenous immunoglobulin—with most experts using intravenous immunoglobulin as first-line therapy. Newer immune-modulating drugs can be used in refractory cases. Treatment response in CIDP should be judged by objective measures (improvement in the neurological or electrophysiological examination), and treatment needs to be individualized to each patient.

 ■ Mayo Clin Proc. 2018;93(6):777-793

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is an acquired peripheral neuropathy due to an autoimmune attack of peripheral nerve myelin. Because myelin is the main target of the condition, nerve fibers with the most myelin (largest fibers) are the most involved and patients present with weakness, numbness, and sensory ataxia (symptoms of large myelinated fiber dysfunction). The course of CIDP can be varied, and presentations include relapsing-remitting, stepwise progressive, or gradually progressive. The clinical pattern of CIDP is unlike typical peripheral neuropathies that are length-dependent (meaning that the most distal segments are most involved). By contrast, CIDP usually presents as a polyradiculoneuropathy with weakness in both proximal and distal segments (patients have both foot drop and difficulty getting out of chairs). Unlike another immune-mediated demyelinating neuropathy that presents as a monophasic illness with spontaneous recovery, acute inflammatory demyelinating polyradiculoneuropathy (AIDP; also known as Guillain-Barré syndrome), CIDP is a progressive neuropathy that worsens over time. Chronic inflammatory demyelinating polyradiculoneuropathy is responsive to immune-modulating therapy, and controlled trials have shown that corticosteroids, plasmapheresis, and intravenous immunoglobulin (IVIG) are all effective treatments. Chronic inflammatory demyelinating polyradiculoneuropathy usually presents in the "classical" form as a symmetrical disorder with proximal and distal weakness but also can manifest as a variety of other subtypes that can be multifocal or selectively involve sensory or motor nerve fibers. Chronic inflammatory demyelinating polyradiculoneuropathy should be separated from other forms of demyelinating neuropathy: AIDP; monoclonal gammopathy of undetermined significance (MGUS)—associated neuropathies; human immunodeficiency virus—associated neuropathy; some forms of diabetic neuropathy; uremic neuropathy; inherited peripheral neuropathies (most especially type 1 Charcot-Marie-Tooth disease); and POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, M-protein, skin changes), a paraneoplastic neuropathy associated with osteosclerotic myeloma or Castleman disease, which is often misdiagnosed as CIDP.

HISTORY OF CIDP

Acquired hypertrophic neuropathies have been recognized for many years, and Austin[1] described cases of probable CIDP in 1958 by recognizing a fluctuating motor-predominant neuropathy that produced severe weakness that would either improve spontaneously or in response to corticosteroids. He noted that some of the cases presented with weakness without muscle atrophy and hypothesized that focal areas of segmental demyelination rather than axonal degeneration were likely the pathological cause because of the lack of atrophy. In a 1975 historical study of 53 personally evaluated patients, Dyck et al[2] introduced the name chronic inflammatory polyradiculoneuropathy (to which the term *demyelinating* was subsequently added) and thus defined CIDP as a separate disease entity. In this article, the authors described the cardinal clinical, laboratory, electrophysiological, and pathological features of CIDP that are still recognized today. They found that it was a motor-predominant polyradiculoneuropathy that produced proximal and distal weakness and ataxic gait. They also found that there were elevated cerebrospinal fluid (CSF) protein levels and nonuniform slowing of conduction in proximal nerve segments with motor conduction blocks on electrophysiological testing. Pathologically, they found areas of segmental demyelination, onion-bulb formation (stacks of Schwann cell cytoplasmic processes), and mononuclear cell infiltrates, often perivascularly in the