Chronic inflammatory demyelinating polyradiculoneuropathy

In a remote northern Ontario hospital

Taryn Taylor MSc MD CCFP DipSportMed

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is an acquired demyelinating syndrome that targets myelin sheaths of the peripheral nervous system. The course might be relapsing or steady, or follow a stepwise progression, with most younger individuals presenting with the relapsing course and older individuals presenting with the progressive course.[1] It is more common in men, and usually presents with symmetric, gradually increasing weakness of the legs and, to a lesser extent, the arms.

Based on pathologic findings and response to immune-modulating therapy, CIDP is believed to have an autoimmune pathogenesis.[2] However, both cellular and humoural immunity have been implicated. It is closely related to Guillain-Barré syndrome; it is considered the chronic counterpart of this acute disease but is rarely preceded by an infection.[3] Chronic inflammatory demyelinating polyradiculoneuropathy is considered the peripheral counterpart of multiple sclerosis because of similarities between the 2 diseases: presence of focal demyelination and coexistent axon damage, immune-mediated pathophysiology, and relapsing or progressive disease course.[4]

The prevalence of CIDP is reported to be from 1 to 7.7 per 100 000 people,[5] but it is often underrecognized owing to its varied presentation and the limitations of clinical, serologic, and electrophysiologic diagnostic criteria. Despite these limitations, awareness and early diagnosis by primary care physicians who can facilitate treatment is important in preventing irreversible axonal loss and improving functional recovery.

Case

During a hospitalist locum placement in a small northern Ontario community, I managed the care of a 70-year-old retired miner with progressive polyneuropathy. In retrospect, he had a history suggestive of nonspecific peripheral neuropathy going back 1 to 2 years, presenting as numbness of the right foot and gradually leading to a painful tingling sensation. Symptoms later appeared in the left foot and spread to both calves, but his mental illness was often the priority in terms of management. He had no relevant medical history and no low back pain or recent infections. Pruritic lesions were identified on the foot, and bloodwork results were positive for antinuclear antibodies. A rheumatologist was consulted, and punch biopsy and nerve tissue biopsy were performed; these showed no evidence of vasculitis.

A few months later he started to experience falls and have difficulty with ambulation. He was admitted to hospital where he could initially walk for 10 to 20 minutes with a walker. Within 1 month he was falling frequently in the hospital and required a wheelchair. Eventually, a more aggressive process led to complete paralysis of his lower limbs, with substantial bilateral upper extremity

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EDITOR'S KEY POINTS

- The diagnosis of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is based on a variety of factors including clinical history and results of comprehensive neurologic examination, electrophysiologic studies, and laboratory and pathology studies, as well as the absence of other causes of neuropathy.
- Treatment of CIDP and other acquired demyelinating polyneuropathies focuses on halting the inflammatory process that causes demyelination and secondary axonal loss. It is important to initiate treatment early to halt the syndrome and prevent axonal loss resulting in irreversible functional decline.
- This case highlights the sheer breadth of family medicine, especially in a small community with limited access to specialists and rapid turnover of hospitalists. It also touches on the difficulties of diagnosis complicated by mental illness.

POINTS DE REPÈRE DU RÉDACTEUR

- Le diagnostic de la polyradiculonévrite inflammatoire démyélinisante chronique (CIDP) se fonde sur divers facteurs, notamment une anamnèse clinique et les résultats d'un examen neurologique complet, d'études électrophysiologiques et d'études de laboratoire et de pathologie, ainsi que sur l'absence d'autres causes de neuropathies.
- Le traitement de la CIDP et des autres polyneuropathies démyélinisantes acquises vise à arrêter le processus inflammatoire qui cause la démyélinisation et la perte axonale secondaire qui engendrent un déclin fonctionnel irréversible.
- Ce cas met en évidence l'étendue de la médecine familiale, surtout dans une petite communauté où l'accès aux spécialistes est limité et où il y a un roulement rapide des hospitalistes. Il démontre aussi les difficultés de ce diagnostic compliqué par une maladie mentale.

weakness. A neurologist was consulted urgently and electrophysiologic studies revealed slowing of motor and sensory nerve conduction velocities and conduction block, which was consistent with demyelination (**Box 1**). A trial of intravenous immunoglobulin (IVIG) was initiated with no benefit, and the patient refused steroid treatment. A lumbar puncture was done, results of which showed a slight elevation in protein levels but no leukocytes. He was eventually unable to move either of his legs and developed increased weakness of the upper extremities, especially the hands, leaving him unable to feed himself.

The patient was transferred to a larger centre, and repeat nerve conduction studies and electromyography revealed worsening of motor and sensory nerve conduction velocities, which favoured the diagnosis of CIDP. A full-body computed tomography scan was performed to rule out malignancy or indicators of paraneoplastic syndrome. Pulmonary function tests were done to rule out involvement of the nerves innervating the diaphragm. The patient was given high-dose prednisone (80 mg/d) and, once his condition stabilized, was transferred back to the rural hospital where physiotherapy was initiated.

Approximately 1 year following the diagnosis of

Box 1. Differential diagnosis

Acute
- Guillain-Barré syndrome

Chronic
- Multifocal motor neuropathy
- Multifocal sensory neuropathy
- Multiple sclerosis
- Distal acquired demyelinating symmetric neuropathy
- Multifocal acquired demyelinating sensory and motor neuropathy (also known as Lewis-Sumner syndrome)
- Anti–myelin-associated glycoprotein syndrome
- GALOP (gait ataxia, late-onset polyneuropathy) syndrome
- Anti–sulfatide antibody syndrome (with serum M-protein)
- Anti–GM2 antibody syndrome
- POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes) syndrome
- Perineuritis
- Immunoglobulin M anti–GD1b antibody syndrome (occasionally)
- Drug- or toxin-related demyelinating polyneuropathy
- Creutzfeldt-Jakob disease
- Diphtheria
- HIV-associated CIDP
- Lepromatous, mixed axonal-demyelinating, and colonized Schwann cell neuropathies

CIDP—chronic inflammatory demyelinating polyradiculoneuropathy.

CIDP, the patient is still in a chronic care hospital and is starting to walk with assistance. He remains on daily prednisone and has been given intermittent IVIG treatments. He has developed diabetes and is now dependent on insulin. One of the side effects of long-term prednisone use is acute psychosis, which is a serious complication in the medical management of a patient who already has schizoaffective disorder and active delusions. A psychiatrist was consulted to assist with ongoing care of the patient and risperidone was initiated. The patient's improvement has been slow but substantial, and the hope is that he will eventually regain the ability to live independently.

Discussion

The diagnosis of CIDP is based on a variety of factors including clinical history, comprehensive neurologic examination, electrophysiologic studies, laboratory and pathologic studies, and the absence of other causes of neuropathy. The diagnosis is often difficult to make because of the clinical heterogeneity of the syndrome, its multifocality and partiality for proximal nerve segments, and the limitations of electrophysiologic and pathologic techniques in distinguishing between primary demyelinating and axonal processes.[6]

Classically, CIDP is characterized by symmetrical weakness involving distal and proximal muscles and large-fibre sensory dysfunction persisting for at least 2 months.[7,8] Deep tendon reflexes are globally reduced or absent in CIDP. The patient might present with cranial nerve, peripheral nerve, or autonomic dysfunction. Key identifying electrophysiologic features of CIDP include nerve conduction block and slowed conduction velocity, suggestive of demyelination.[2,7] The diagnosis of CIDP requires both pathology and laboratory studies, and a full description of diagnostic criteria can be found in the 2010 revised European Federation of Neurological Societies–Peripheral Nerve Society guidelines (**Box 2**).[7]

First-line treatment for CIDP includes corticosteroids, plasmapheresis, and IVIG, which can be prescribed alone or in combination with an immunosuppressant drug. Intravenous immunoglobulin and plasmapheresis have been proven to be beneficial in randomized, double-blind, placebo-controlled trials.[9-11] Despite less definitive published evidence of efficacy, corticosteroids are considered standard therapy because of their long history of use and cost–effectiveness. Two-thirds of patients will respond to one of these therapies and it is, therefore, beneficial to change therapies if one is not working. A number of chemotherapeutic and immunosuppressive agents have also been shown to be effective in treating CIDP, but strong evidence of benefit is lacking. Therefore, these agents are primarily used in conjunction with proven modalities.

Treatment of CIDP and other acquired demyelinating polyneuropathies focuses on halting the inflammatory process that causes demyelination and secondary axonal loss. Therefore, therapy must be initiated early in the course of the syndrome to prevent permanent disability. Regardless of the treatment, the generally accepted strategy is to continue therapy until maximum clinical improvement is achieved or until improvement plateaus, followed by maintenance therapy to prevent relapse or progression.[3]

Many individuals are left with residual numbness, weakness, tremors, fatigue, and other symptoms that can lead to long-term morbidity and diminished quality of life. Because of the variability in severity and progression, each case of CIDP is different, and relapses might bring new symptoms and problems. Long-term management is important because less than one-third of patients with CIDP remain in remission without continued therapy.[9]

Box 2. Abbreviated EFNS-PNS supportive criteria for diagnosis of CIDP

CIDP is chronically progressive, stepwise, or recurrent symmetric proximal and distal weakness and sensory dysfunction of all extremities, developing over at least 2 months. Cranial nerves might be affected; and tendon reflexes might be absent or reduced in all extremities

Criteria for diagnosis

- Elevated cerebrospinal fluid protein with leukocyte count < 10/mm^3 (level A recommendation*)
- Magnetic resonance imaging showing gadolinium enhancement or hypertrophy of the cauda equina, lumbosacral, or cervical nerve roots, or the brachial or lumbosacral plexuses (level C recommendation†)
- Abnormal sensory electrophysiology in at least 1 nerve (consensus recommendation):
  - Normal sural with abnormal median (excluding median neuropathy at the wrist from carpal tunnel syndrome) or radial SNAP amplitudes;
  - Conduction velocity < 80% of lower limit of normal (< 70% if SNAP amplitude is < 80% of lower limit of normal); or
  - Delayed somatosensory evoked potentials without central nervous system disease
- Objective clinical improvement following immunomodulatory treatment (level A recommendation*)
- Nerve biopsy showing unequivocal evidence of demyelination or remyelination by electron microscopy or teased fibre analysis (consensus recommendation)

CIDP—chronic inflammatory demyelinating polyradiculoneuropathy, EFNS—European Federation of Neurological Societies, PNS—Peripheral Nerve Society, SNAP—sensory nerve action potential.
*Level A recommendations are supported by good evidence.
†Level C recommendations are supported by fair evidence.
Adapted from Van den Bergh et al.[7]

Conclusion

This case highlights the sheer breadth of family medicine, especially in a small community with limited access to specialists and rapid turnover of hospitalists. It also

touches on the difficulties of diagnosis complicated by mental illness. A number of attempts have been made to define criteria for the diagnosis of CIDP, but it continues to present both diagnostic and treatment challenges to the physician. It is important to initiate treatment early to halt the syndrome and prevent axonal loss resulting in irreversible functional decline.

There are many unanswered questions in the treatment of CIDP, including the appropriate dose of proven therapies, long-term management, and the benefit of emerging therapies. Further studies are needed to answer these questions and direct treatment, with the hope that new treatments that are successful in clinical trials will benefit a broader patient population.

Dr Taylor is a primary care sport medicine physician at the Carleton Sports Medicine Clinic in Ottawa, Ont.

Competing interests
None declared

Correspondence
Dr Taryn Taylor, Carleton Sports Medicine Clinic, 1125 Colonel By Dr, Ottawa, ON K1S 5B6; telephone 613 520-3510; fax 613 520-3974; e-mail **taryntaylor13@yahoo.com**

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