

HOW I TREAT CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY

Chronic inflammatory demyelinating polyradiculoneuropathy (also known as chronic inflammatory demyelinating polyneuropathy, CIDP) is a heterogeneous disorder with a broad spectrum of clinical phenotypes.¹ CIDP is a treatable condition and early diagnosis and treatment is important to avoid worsening disability.² However, CIDP symptoms are non-specific and shared across many immune-mediated conditions, and misdiagnosis is common.³

Review the following three hypothetical scenarios in which patients present with clinical features of peripheral neuropathy. For each scenario, consider how you would best manage the patient and reflect on the questions provided.

Case study 1: Sarah

Presentation

Sarah is a 73-year-old woman presenting with a 1-year history of back pain and right L5 radicular pain associated with difficulty walking.

Examination

Physical examination reveals wasting of the intrinsic hand muscles, bilateral foot drop, absent lower limb reflexes, symmetrical sensory loss below the mid shins, and foot deformity.

Spinal imaging shows moderate L3/4 canal stenosis and right L5 foraminal narrowing. Nerve conduction studies show absent sensory nerve action potentials, upper limb motor conduction velocities of 16–17 m/s without temporal dispersion, and absent peroneal and tibial compound muscle action potentials.

A sural nerve biopsy shows ubiquitous onion bulb formation with variable myelin thinning and no significant inflammatory infiltrates.

Diagnosis and initial treatment

Sarah's presentation is consistent with a right L5 radiculopathy. However, she has signs and investigation results consistent with a chronic demyelinating neuropathy with secondary axonal degeneration. The neurologist decides to commence intravenous immunoglobulin (IVIg). At 4 month review, objective outcome scales demonstrated no response. Oral prednisolone 25mg daily was commenced; no response was documented at 3 month review.

? WHAT ARE THE NEXT STEPS?

- ▶ Given the lack of response to IVIg and prednisone, the provisional diagnosis of possible CIDP should be re-evaluated and Sarah should be referred for a neuromuscular specialist opinion and possible further investigation.

Review

Further history at her neuromuscular consultation reveals that Sarah's gait has been abnormal for decades, and her son has 'funny feet' with lower limb areflexia, pes cavus, and bilateral foot drop. A multiplex ligation-dependent probe amplification (MLPA) genetic test for Charcot-Marie-Tooth disease (CMT) type 1A (CMT1A) returns positive.

? WHAT ARE THE NEXT STEPS?

- ▶ All immunotherapies should be withdrawn. Alternative treatments, such as physiotherapy, should be trialled.

Practice points

- ▶ CMT, especially CMT1A is commonly misdiagnosed as CIDP. A careful family history and examination of relatives should be considered in all cases.⁴
- ▶ Motor conduction velocities that demonstrate uniform demyelination without temporal dispersion favour an inherited neuropathy.⁵ Uniform velocities of 15–20 m/s are typical of CMT1A. In this case, **correct interpretation of the neurophysiology in the context of the clinical presentation could have avoided an unnecessary trial of IVIg and steroids. Failure to respond to immunotherapies should prompt a review of the diagnosis before continuing treatment or increasing dosage.**

Case study 2: Ian

Presentation

Ian is a 77-year-old man presenting with a 15-month history of gait deterioration. His symptoms began when his left leg became numb, followed 9 months later by right leg numbness and bilateral finger paraesthesia. He complains of progressive gait unsteadiness.

Examination

Physical examination reveals a wide-based, unsteady gait and positive Romberg's test. Ian is unable to stand on his toes or heels, has global areflexia, reduced pinprick sensation to both knees, and reduced joint position sensation to his ankles.

Serum protein electrophoresis/immunofixation reveals no paraprotein. Anti-MAG antibodies are negative. His estimated glomerular filtration rate (eGFR) is 28 (reference rate: ≥ 60 mL/min/1.73 m²) and his serum creatinine clearance is 192 μ mol/L (reference range: 60–110).

His Medical Research Council sum score (MRC-SS) is 60; his overall neuropathy limitations scale (ONLS) is 4; and his score on the Inflammatory Rasch-Built Overall Disability Scale (iRODS) is 41.

Cerebrospinal fluid examination was not performed as the patient was anticoagulated on warfarin as a result of prior embolic stroke.

Diagnosis and initial treatment

CIDP commonly presents in older males and rarely has a sensory predominant phenotype. Nerve conduction studies demonstrate a sensorimotor demyelinating neuropathy fulfilling the European Academy of Neurology/Peripheral Nerve Society (EAN/PNS) criteria for CIDP.⁶



WHAT SHOULD IAN'S INITIAL TREATMENT BE?

- ▶ Ian should be started on intravenous methylprednisolone (IVMP) 1 g monthly for 6 months.⁷

Review

On detailed follow-up at 6 months, Ian's ONLS has decreased to 2 and his iRODS has increased to 45.

Practice points

- ▶ Corticosteroids were preferred to IVIg in this case because of an indolent sensory presentation, prior embolic stroke, and pre-existing renal impairment, all of which are relative contraindications to IVIg. In addition, a rapid onset of action was not considered imperative due to the absence of motor weakness.
- ▶ Oral prednisolone could be used as an alternative to IVMP, commencing at 1 mg/kg/d and tapering to zero over 8 months.⁸

Case study 3: Joanne

Presentation

Joanne is a 42-year-old woman presenting with a 2-week history of perioral and tongue paraesthesias, followed by distal upper and lower limb paraesthesias, ascending numbness and weakness. She reports having a non-specific viral illness with flu-like symptoms and a mild headache several weeks prior to presentation. She has no respiratory, autonomic, or bulbar symptoms.

Examination

Examination reveals a wide-based unsteady gait, positive Romberg's test, mild proximal and distal weakness, diffuse areflexia and reduced lower limb distal pinprick sensation. Her Guillain-Barré syndrome disability score (GBSDS) is 2 and her MRC-SS is 56.

Nerve conduction studies reveal normal sensory responses, prolonged tibial and peroneal distal motor latencies, absent tibial and peroneal F-responses, and prolonged distal compound muscle action potential durations in both upper and lower limbs. Her cerebrospinal fluid protein is 0.65 g/dL (normal range: < 0.45).

Diagnosis and initial treatment

Joanne's presentation and findings are consistent with a diagnosis of acute inflammatory demyelinating polyneuropathy (AIDP), the most common form of Guillain-Barré syndrome (GBS).⁹

Joanne is given 2 g/kg IVIg in divided doses over 3 consecutive days and improves markedly. She is discharged on Day 6. However, by 2 weeks post-discharge she experiences slowly progressive recurrent weakness, and by 4 weeks, she is unable to mobilise without assistance.

Joanne is readmitted 10 weeks post-onset with diffuse weakness, global areflexia and sensory ataxia. Nerve conduction studies reveal reduced/absent sensory responses and progression of sensorimotor demyelinating abnormalities. Her ONLS is 4, her MRC-SS is 50, and her iRODS is 25.



WHAT CHANGES WOULD YOU MAKE TO JOANNE'S DIAGNOSIS OR TREATMENT?

- ▶ GBS is a monophasic illness and motor progression after 4 weeks (in contrast to incomplete recovery) suggests acute onset CIDP (A-CIDP). Joanne should receive a second induction dose of 2 g/kg IVIg followed by 1 g/kg 3 weekly IVIg.

Review

At 12-month review, Joanne displays complete resolution of her symptoms, with an MRC-SS score of 59 and resolution of her fatigue. Joanne's quality of life has improved and she is back to her normal activities.



AT THIS POINT, WHAT WOULD BE THE APPROPRIATE ACTION REGARDING HER TREATMENT?

- ▶ Given that Joanne has been stable for 12 months, a trial of cessation of immunoglobulin (Ig) should be considered to determine if she is in remission.

During this discussion, Joanne expresses hesitation with the plan as she is concerned about relapse. She is particularly concerned about her ability to look after her family if her symptoms return.



HOW WOULD YOU ADDRESS JOANNE'S CONCERNS?

- ▶ Use a conversation tool to guide your discussion around weaning off Ig – see the NPS tool [Immunoglobulin dose adjustment, weaning and cessation: a conversation guide for health professionals](#).
- ▶ Reassure Joanne that she can be restarted on Ig at any point if relapse does occur.

After a long discussion, Joanne agrees to trial a dose reduction toward cessation. Her weaning plan involves a 20% reduction in Ig dose each month and frequent reviews with documentation of MRCSS and ONLS. After 6 months, Joanne is reviewed and her condition remains in remission.

Practice points

- ▶ Advising patients about dose adjustment, weaning and cessation and the likelihood of treatment being successful before starting Ig treatment can set the stage for conversations around stopping Ig treatment or reducing the dose.
- ▶ IVIg was the preferred treatment for Joanne because she had previously responded quickly and had prominent motor disability where a prompt response is desirable.
- ▶ Many patients with CIDP do not require long-term treatment.⁵ Around 15% of patients with CIDP have a monophasic illness and require only one or two courses of Ig therapy to achieve a sustained improvement.^{10,11}
- ▶ Clinicians should routinely evaluate the need for continued therapy based on the patient's clinical status, and continuation of Ig therapy should depend on evidence of clinical benefit.¹²

Access to Ig in Australia

In Australia, the National Blood Authority (NBA) provides the framework for access to Ig products currently funded under the National Blood Agreement (the Agreement). The NBA manages contracts with suppliers to ensure a safe, secure, adequate and affordable supply of blood and blood product derivatives such as Ig sourced from domestic and imported plasma. The NBA has contracted the Australian Red Cross LifeBlood to assess, authorise and provide clinical advice on established or emerging therapeutic medical conditions identified in the Criteria for the clinical use of immunoglobulin in Australia (the Criteria).¹² The Criteria also define the conditions for which Ig can be used in exceptional circumstances.

To access Ig under the Agreement, a medical officer must submit an application through the National online system BloodSTAR. The system manages the authorisation request and review process and ensures that access to Ig products is consistent with the Criteria. Ig products are funded by the government and provided to eligible patients at no direct cost.

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VALUE IN PRESCRIBING PROGRAM - IMMUNOGLOBULIN PRODUCTS

Increasing the awareness and understanding amongst health professionals of access to immunoglobulin products in Australia, and improving health outcomes for patients through access to better health information to manage their health conditions. Funded by the Australian Government Department of Health through the Value in Prescribing Program: Immunoglobulins Products Grant.

