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Single Case – General Neurology

Dose Adjustment of Subcutaneous IgG in Chronic Inflammatory Demyelinating Polyneuropathy

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Keywords
Chronic inflammatory demyelinating polyradiculoneuropathy · Demyelinating polyneuropathy · Subcutaneous Ig · IVIG · Inflammatory polyneuropathy

Abstract
Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is an immune-mediated neuropathy that is characterized by a slowly progressive sensory and motor involvement lasting at least 2 months. We present a CIDP patient on subcutaneous Ig (SCIg). Upon fine-tuning his dose from 24 to 28 g/week, this showed a dramatic improvement in both hand grip (13–25%) and dorsiflexion (73–278%). Follow-up nerve conduction studies also demonstrated significant improvements in latencies, motor amplitudes, and conduction velocities. Ongoing surveillance of CIDP patients receiving SCIg therapy is therefore necessary to ensure therapeutic optimization.

Introduction

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is an immune-mediated neuropathy that is characterized by slowly progressive sensorimotor dysfunction developing over at least 2 months [1]. Diagnosis depends on clinical, laboratory, and electrophysiological criteria [2]. The criteria derived from the European Federation of Neurological

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Societies and Peripheral Nerve Society (EFNS/PNS) are the most widely used criteria, which are based on both clinical and electrodiagnostic abnormalities [2]. Proven treatments for CIDP include immunoglobulins, corticosteroids, and plasmapheresis [3].

In terms of safety profiles of these treatments, IVIg is a preferred long-term treatment. Subcutaneous Ig (SCIg) represents another option for Ig administration, which has been a successful and well-tolerated treatment in immunodeficiency syndromes for more than 25 years [4]. SCIg has been shown to maintain clinical equipoise in stable multifocal motor neuropathy patients who previously received IVIg [5].

Case Report

We present the case of a 44-year-old male followed up in our neuromuscular clinic at the McMaster University Medical Centre, diagnosed with CIDP 4 years ago based on EFNS/PNS criteria. His disease manifested in the form of weakness and numbness in his distal limbs.

Antibodies against the node of Ranvier proteins were found to be negative.

He responded very well to IVIg 1 g/kg every 4 weeks; however, he was complaining of end-of-cycle symptoms manifesting predominantly in reduced grip strength and ankle weakness. Therefore, his treatment was changed to biweekly SCIg at a dose of 24 g/week, which is equivalent to 96 g/month or 1.2 g/kg.

His grip strength was measured using a JAMAR Dynamometer. His right maximum hand grip strength was 41 kg, while his left was 48 kg. Peak isometric dorsiflexion torque (Biodex) measured 18.4 Nm on the right and 9.2 Nm on the left. His nerve conduction studies showed a prolonged right median distal motor latency of 8.4 ms. His compound muscle action potential (CMAP) amplitude revealed a 65% conduction block (i.e., 10.1 mV distally and 3.5 mV proximally). Conduction velocity was slowed well into the demyelinating range at 20.5 m/s, while F-wave latency was prolonged at 52.5 ms. The right common peroneal nerve terminal motor latency (TML) was prolonged at 10.9 ms with a CMAP amplitude that revealed a 54% conduction block (2.8 mV distally and 1.3 mV proximally). Conduction velocity was slowed to 31.5 m/s.

Given his persisting clinical symptoms and abnormal electrophysiology, his SCIg dose was augmented to 28 g/week or 1.4 g/kg/month. He reported improvement in his strength 1 month after adjusting his SCIg dose.

At his next follow-up, 6 months later, he reported a significant improvement in his strength. Objective strength testing confirmed the patient-reported outcomes demonstrating significant improvements in both grip (right, 51 kg; left, 54 kg) (Fig. 1) and dorsiflexion (right, 31.8 Nm; left, 34.8 Nm) (Fig. 2).

Repeat nerve conduction studies were stable to improved. For example, while the right median TML was unchanged at 8.5 ms, the distal CMAP amplitude increased to 12.6 mV with a dramatic diminution of the conduction block (12%) and hastening of conduction velocity at 27.5 m/s (34%). The F-wave latency also improved measuring 41.1 ms (22%). The right common peroneal TML shortened to 8.5 ms (21%) despite a stable distal CMAP amplitude of 2.3 mV.

Whereas the peroneal conduction velocity improved by only 10% measuring 34 m/s, the F-wave latency improved dramatically from 85.6 to 41.1 ms (52%).

Discussion

This case highlights the critical therapeutic threshold phenomena that beset our CIDP patients and reflects the urgent need to make responsive dosing adjustments when patient-reported outcomes suggest undertreatment. SCIg therapy is ideal in this regard as minor dosing changes can be adjudicated without the complex scheduling challenges of hospital-based periodic infusions. We have collected objective strength data to support the dramatic improvements in both hand grip (13–25%) and dorsiflexion (73–278%). Follow-up nerve conduction studies also demonstrated significant improvements in latencies, motor amplitudes, and conduction velocities.

Increased dosing of SCIg compared to IVIg is generally considered to be secondary to lymphatic transport and premature exposure to the antibodies to the reticuloendothelial system – the major source of catabolism. Early predictions suggested a 1:1.5 conversion rate but 1:1 has also been shown to be effective [4, 6]. Independent of which conversion is initially adopted, future dosing may need to be adjusted to maximize the clinical dose-response relationship.

In conclusion, ongoing surveillance of CIDP patients receiving SCIg therapy is therefore necessary to ensure therapeutic optimization. Furthermore, predictive modelling of IgG dosing in neurologic indications, such as CIDP, fails to recognize the distinct pathophysiologic variability in these patients. Perfunctory IgG dosing then should be replaced with patient-responsive dosing, which is particularly well-suited to home-based SC therapy.

Statement of Ethics

A written informed consent was obtained from the patient to publish this case report.

Disclosure Statement

The authors have no conflicts of interest to disclose.

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Author Contributions

Steven Baker, MD, McMaster University, Hamilton, ON, Canada: author, design and conceptualization of the study; performed data collection and analysis; drafted, revised and edited the manuscript.

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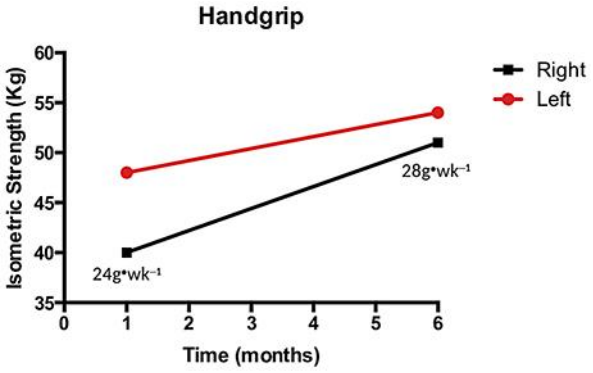

Fig. 1. Hand grip strength improvement after 6 months of fine-tuning SCIg dose from 24 g/week to 28 g/week.

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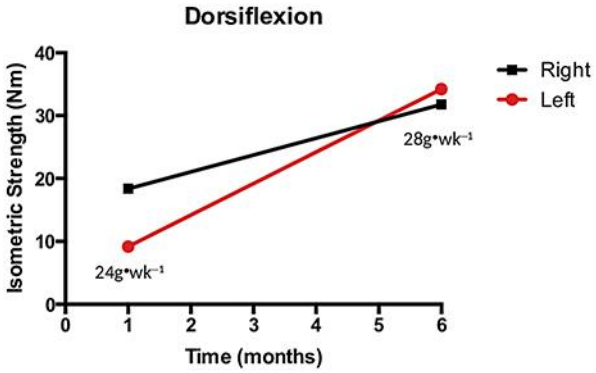

Fig. 2. Dorsiflexion strength improvement after 6 months of fine-tuning SCIg dose from 24 g/week to 28 g/week.