pISSN 1738-6586 / eISSN 2005-5013 / J Clin Neurol 2018;14(1):98-99 / https://doi.org/10.3988/jcn.2018.14.1.98

Subcutaneous Immunoglobulins Are a Valuable Treatment Option in Myasthenia Gravis

Martina Garnero
Sabrina Fabbri
Chiara Gemelli
Luana Benedetti
Giovanni Luigi Mancardi
Angelo Schenone
Marina Grandis

Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, and Maternal and Child Health, University of Genova, Genova, Italy

Dear Editor,

Subcutaneous immunoglobulins (SCIg) were initially applied in primary immunodeficiencies,[1] and are now known to offer significant advantages over intravenous Ig (IVIg), including simpler administration and stable Ig serum levels.[2] These features reduce both the risk of adverse events related to rapid peaks of Ig in serum, such as headache, and the need for repeated venipuncture. Furthermore, SCIg are therapeutically equivalent to intravenous preparations while supporting patient autonomy due to self-administration.[2] This treatment has recently been extended to inflammatory neuromuscular disorders such as chronic inflammatory demyelinating polyneuropathy, multifocal motor neuropathy, and inclusion-body myositis.[3]

Few patients with myasthenia gravis (MG) receive SCIg.[3] Bourque and colleagues recently reported on a retrospective cohort study that included nine patients refractory to conventional therapies who changed to or started using de novo SCIg.[4]

We report the case of a woman who in 1994 presented with diplopia, mild dysphagia, hypophonia, and proximal weakness with muscle fatigue at an age of 41 years. She was diagnosed as myasthenia [Osserman-Jenkins class IIb, Myasthenia Gravis Foundation of America (MGFA) clinical classification class IIIb, Myasthenia Gravis Composite Scale (MGCS) score=12, and Quantitative Myasthenia Gravis (QMG) test score=8] based on the detection of antibodies against acetylcholine receptors and decreased responses in repetitive nerve stimulation. The patient's clinical course improved with prednisone (1 mg/kg) and pyridostigmine.

In 1999 she underwent a thymectomy via a partial upper sternum-splitting incision for thymic follicular hyperplasia, which did not produce any clinical benefit. Immunosuppression therapy with cyclophosphamide (150 mg daily) was introduced 1 year later, but after 7 months the patient experienced an acute myasthenic crisis with respiratory failure (Osserman-Jenkins class III, MGFA clinical classification class IVb, MGCS score=29, QMG test score=24), which responded to five sessions of plasmapheresis. She was subsequently started on IVIg (2 g/kg, 120 g over five consecutive days) every 3 months, which resulted in clinical improvement. In February 2002, when the patient had reached the maximum allowable cumulative dose, the cyclophosphamide was discontinued and mycophenolate mofetil (1,500 mg daily) was started. However, this was interrupted after a few months due to persisting gastric pain.

Clinical stability as characterized by the persistence of mild diplopia and proximal weakness with muscle fatigue (MGFA clinical classification class IIb, MGCS score=6, and QMG test score=6) was obtained with pyridostigmine, azathioprine (150 mg), and IVIg infusion every 3 months, which was maintained for almost 3 years. Azathioprine was discontinued in 2008 due to severe pancytopenia, while IVIg were administered monthly via an implanted port, which was inserted due to difficulties in obtaining peripheral venous access.

In 2015, after a period of clinical stability, the patient was admitted to hospital for a Staphylococcus aureus catheter-related bloodstream infection (CRBSI). Consequently, the port was

Received May 23, 2017
Revised June 12, 2017
Accepted June 16, 2017

Correspondence
Martina Garnero, MD
Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, and Maternal and Child Health, University of Genova, Largo P. Daneo 3, Genova 16132, Italy
Tel +39 010 3537075
Fax +39 010 35338751
E-mail martina.garnero@hotmail.it

removed, and antibiotic treatment with vancomycin (2 g daily) was administered for 10 days, which produced clinical remission.

In February 2016, after obtaining informed consent for off-label treatment, we started SCIg treatment at two infusion sites at the same monthly dose of IVIg (120 g) three times weekly. The patient had no adverse reactions to SCIg administration, and at 15 months from the beginning of therapy she exhibited sustained clinical stability without relapses.

The treatment of MG generally includes IVIg only for acute exacerbations. However, in a few cases in which immunosuppressive drugs are ineffective or poorly tolerated, Ig may become a chronic therapy. In our patient, SCIg were tried when the implanted port was removed due to a CRBSI, and this produced an immediate good clinical response. Furthermore, SCIg induced a persistent clinical stability that had not been obtained with previous treatments, and improved the patient's autonomy.

This case suggests that SCIg is a valid and effective therapy and should be considered in selected cases as a therapeutic option for MG as well as for other inflammatory neuromuscular diseases.

Conflicts of Interest

The authors have no financial conflicts of interest.

Acknowledgements

The research grant from Csl Behring is gratefully acknowledged.

REFERENCES

1. Berger M, Cupps TR, Fauci AS. Immunoglobulin replacement therapy by slow subcutaneous infusion. *Ann Intern Med* 1980;93:55-56.
2. Berger M. Subcutaneous immunoglobulin replacement in primary immunodeficiencies. *Clin Immunol* 2004;112:1-7.
3. Yoon MS, Gold R, Kerasnoudis A. Subcutaneous immunoglobulin in treating inflammatory neuromuscular disorders. *Ther Adv Neurol Disord* 2015;8:153-159.
4. Bourque PR, Pringle CE, Cameron W, Cowan J, Chardon JW. Subcutaneous immunoglobulin therapy in the chronic management of myasthenia gravis: a retrospective cohort study. *PLoS One* 2016;11:e0159993.