# Remission of myasthenia gravis following cervical adjustment

**Eric Chun Pu Chu, David Bellin**

New York Chiropractic and Physiotherapy Centre, New York Medical Group, Hong Kong, China

*Correspondence to:* Eric Chun Pu Chu, BSc, MHA, DC, PhD (Hon). New York Chiropractic and Physiotherapy Centre, 41/F Langham Place Office Tower, 8 Argyle Street, Hong Kong, China. Email: eric@nymg.com.hk.

**Abstract:** Myasthenia gravis (MG) is an autoimmune disorder, caused by circulating antibodies against the acetylcholine receptor (AChR) and associated proteins. Anticholinesterase medications and immunomodulating therapies are the mainstays of current treatment. Presented here is a case of a 51-year-old female who had been diagnosed with MG based on symptoms and continued elevation of antibody to AChR (anti-AChR) by her family physician. The patient's anticholinesterase medication was halted due to significant side effects affecting bowel function. She only received acupuncture treatment in the past 4 months prior to this presentation. Myasthenic symptoms deteriorated and the anti-AChR titer kept elevating after stopping medication. She originally came to us due to neck and back pain rather than myasthenic complaints. This case is interesting that her back pain and myasthenic symptoms went into complete remission within 1 month of initiating chiropractic adjustment. The concomitant recession of the myasthenic symptoms raises considerable interest for the mystery of MG, including the causal link between stress and autoimmune disease, the role of ACh in immune regulation, and the possible mechanisms of disease amelioration. Further studies would shed more light on the efficacy of various modalities in treating MG.

**Keywords:** Acetylcholine receptor antibody (anti-AChR); autoimmune disease; chiropractic manipulation; myasthenia gravis (MG)

Received: 31 January 2019; Accepted: 12 April 2019; Published: 22 April 2019.

doi: 10.21037/acr.2019.04.04

**View this article at:** http://dx.doi.org/10.21037/acr.2019.04.04

## Introduction

Acetylcholine (ACh) is a potent regulator of neuronal activity throughout the peripheral and central nervous system. Upon nerve stimulation, ACh is released into the nerve terminal and binds to the post-synaptic ACh receptor (AChR), initiating the muscle endplate potential. In myasthenia gravis (MG), circulating antibodies block the AChRs, and prevent the transmission of nerve impulses to the muscles (1). AChR antibodies are detected in 80–85% of MG patients. MG patients who do not have detectable antibodies against AChRs are termed as seronegative MG (2). The hallmark of MG is fatigability of skeletal muscles. Patients present with fluctuating and fatigable weakness of specific muscle groups. Symptoms of weakness worsen during periods of activity and improve after periods of rest (3). The mainstays of medication are acetylcholinesterase inhibitors to directly block the breakdown of ACh (4), and immunosuppressants to reduce the autoimmune process. Thymectomy may improve symptoms in certain cases.

## Case presentation

A 51-year-old Asian woman had been having drooping of the left eye for 6 months. She subsequently developed diplopia and weakness in both arms and legs. At that time, brain MRI and contrast-enhanced chest CT did not show any pathology. The results of pulmonary function test excluded respiratory weakness and of motor nerve conduction revealed no significant changes. Her AChR antibody was elevated at 18 nmol/L (reference range, <0.30 nmol/L). ESR was raised at 40 mm/h (reference range, 0–20 mm/h), other inflammatory markers (included WBC, CRP, and RA factor) were normal. She was diagnosed as having MG, and had been started on oral

pyridostigmine bromide (an anticholinesterase). The drug was halted after only 4 weeks, because of the digestive side effects (nausea and abdominal cramping). She was unwilling to take immunosuppressant drugs worrying the likelihood of weakening body defenses. The patient only received acupuncture in attempt to enhance muscle strength over the past 4 months. However, her symptoms progressively deteriorated with difficulties climbing stairs, and managing household chores. A further rise in AChR antibody titer was noted from 18 to 25 nmol/L.

The patient also complained of chronic neck and low back pain, for which she sought for chiropractic service. On presentation, she manifested classical significant myasthenic weakness in her ocular, proximal arm and leg muscles. Muscle strength was 3/5 in the upper and lower extremities bilaterally. Sensation was intact throughout. Deep tendon reflex and skin sensation were intact in bilateral upper and lower limbs. Orthopedic examination showed restricted neck extension and lumbar flexion, and pain was exacerbated by activity. Magnetic resonance imaging of the spine demonstrated multilevel discovertebral degenerative disease, with intervertebral foraminal narrowing at right C3/4, right C4/5, left C5/6, left C6/7 and bilateral L5/S1, and L4/5 spondylolisthesis.

The chiropractic treatment focused on correcting the spinal dysfunction and releasing the nerve interference from degenerative spondylosis. Contact specific, high-velocity, low-amplitude adjustment, namely, Diversified Chiropractic Technique, was applied to the dysfunctional sites of the lower cervical and lower lumbar spine three sessions a week. The neck and back pain relieved in a few treatment sessions, and abated within one month. Cervical and lumbar range of motion also restored with treatment. It is noteworthy that the patient unexpectedly experienced improvement of double vision and of the other myasthenic symptoms as early as one week after treatment initiation. Her myasthenia went into remission within 1 month of treatment initiation. She continued the treatment and monitoring on a monthly basis for the next 3 months. The patient has now been followed for longer than 8 months over the phone and still remains symptom-free and medication-free.

## Discussion

ACh is "a neurotransmitter" that is prevalent in the central and peripheral nervous systems. MG is caused by antibodies attacking the ACh receptor (AChR), which produce a compromise in the end-plate potential, and impair the synaptic transmission mediated by ACh (1). However, the traditional view of ACh acting solely as a neurotransmitter has to be revised (5). Overwhelming evidence indicates that cells outside the cholinergic neuronal network synthesize, contain and release ACh (5). ACh is not only a neurotransmitter but is a molecule that can be released by and acted on non-neuronal cell of the integumentary, respiratory, cardiovascular, digestive, reproductive, immune and musculoskeletal systems (6). The discovery of ACh derived from non-neuronal cells hinted at the role of ACh in the immune regulation.

Autoimmune MG is a rare disease particularly attacking the neuromuscular junctions. Estimated incidence in the total population is 5 to 30 cases per million person-years (7). MG is arguably the best understood autoimmune disease. Nevertheless, the implication of chemical messengers, other than ACh, in MG remained unexplored to date (8). For instance, autoimmune MG can be precipitated in individuals with no pre-existing myasthenic symptoms after traffic collisions (9,10), cardiac surgery (11,12) and medication (13). For most cases reviewed, it seems more than a coincidence that such a rare disease starts shortly after certain traumatic insults and petered out fairly quickly afterwards. Conceptually, antibodies to the AChR (anti-AChR) must be presented in the circulation prior to the development of neurophysiological manifestations in subclinical patients (14). A surge in circulating glucocorticoid levels in response to acute stress may exert a direct inhibitory action on the AChR, and therefore can precipitate myasthenic symptoms (15). Glucocorticoids may exert contradictory effects on immune system depending on their concentration. Such an eventuality (pharmacological muscle denervation) is occasionally observed in myasthenic patients at the initiation of steroid therapy (16).

The immune system does not function autonomously, but rather its output is coordinated by physiological units of reflex action (17,18). Animal studies have provided evidence for a tight inter-relationship between ACh and inflammatory reactions (17,19). Investigators had also observed that ACh-producing T cells in the spleen of mice were integral to the inflammatory reflex (17,19). According to the cholinergic anti-inflammatory pathway proposed, tonic stimulation of the vagus nerve promotes the release of ACh. ACh acts on macrophages and prevents the overproduction of proinflammatory cytokines (such as tumor necrosis factor, interleukin-1β, interleukin-6 and high-mobility group box 1 protein) (17,20). Through this mechanism, tonic parasympathetic nervous activity

prevents the overproduction of cytokines and protects the body from the harmful effects of excessive inflammation (17,19). Experimentally, direct vagus nerve stimulation by implanting an electronic device may lead to therapeutic effect in autoimmune and inflammatory disorders (21,22). Another noteworthy aspect that chiropractic manipulation appears to boost the immune system by influencing T and B lymphocyte counts, NK (natural killer) cell numbers, antibody levels, phagocytic activity and plasma β-endorphin levels (23).

The 2016 international consensus guidance is a major contribution to the treatment and management of MG (4). Anticholinesterase medications and immunomodulating therapies are the mainstays of current treatment. In MG, patients tend to experience fluctuations in disease activity with periods of exacerbation, improvement and remission (3). Control of symptoms with medicines is satisfactory only in a proportion (39%) of MG patients, and drug-free remissions are very few (6%) (3). A recent article by Al-Hashel and colleagues mentioned that spontaneous MG remissions occur in 11 to 21% of patients and mostly occur in the early period, but they rarely last longer than some months (24). Published reports regarding noticeable amelioration of myasthenic symptoms yielding by chiropractic correction of cervical subluxation complex have been described (9,25,26). The remission of MG following spinal manipulations in those subjects reported, and in our case after stopping medication, may be coincidental. However, with respect to the clear time-order relationship in these patients, it is difficult to escape the assumption that spinal manipulation might have played a promising role in ameliorating the symptoms. The carotid sinus contains numerous baroreceptors and is located in the lateral neck. We speculate that chiropractic manipulations unintendedly trigger the baroreceptors, namely, manipulations could bridge the interaction between vagus nerve stimulation and cholinergic anti-inflammatory reaction. The present study is limited by the lack of convincing evidence for the efficacy of chiropractic manipulation. These viewpoints warrant further investigation to find better regimens for alleviating patient burden.

## Acknowledgements

None.

## Footnote

*Conflicts of interest:* The authors have no conflicts of interest to declare.

*Informed Consent:* Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

## References

1. Hughes BW, Moro De Casillas ML, et al. Pathophysiology of myasthenia gravis. Semin Neurol 2004;24:21-30.
2. Meriggioli MN, Sanders DB. Muscle autoantibodies in myasthenia gravis: beyond diagnosis? Expert Rev Clin Immunol 2012;8:427-38.
3. Khadilkar SV, Chaudhari CR, Patil TR, et al. Once myasthenic, always myasthenic? Observations on the behavior and prognosis of myasthenia gravis in a cohort of 100 patients. Neurol India 2014;62:492-7.
4. Sanders DB, Wolfe GI, Benatar M, et al. International consensus guidance for management of myasthenia gravis: executive summary. Neurology 2016;87:419-25.
5. Wessler I, Kirkpatrick CJ. Acetylcholine beyond neurons: the non-neuronal cholinergic system in humans. Br J Pharmacol 2008;154:1558-71.
6. Beckmann J, Lips KS. The non-neuronal cholinergic system in health and disease. Pharmacology 2013;92:286-302.
7. Hehir MK, Silvestri NJ. Generalized myasthenia gravis: Classification, clinical presentation, natural history, and epidemiology. Neurol Clin 2018;36:253-60.
8. Han B, Zhang C, Liu S, et al. Non-neuronal cholinergic activity is potentiated in myasthenia gravis. BMC Neurology 2017;17:28.
9. Alcantara J, Plaugher G, Araghi HJ. Chiropractic care of a pediatric patient with myasthenia gravis. J Manipulative Physiol Ther 2003;26:390-4.
10. Petersen JA, Jung HH, Weller M, et al. Autoimmune myasthenia gravis after sternal fracture. Case Rep Neurol 2012;4:20-2.
11. Scoppetta C, Onorati P, Eusebi F, et al. Autoimmune myasthenia gravis after cardiac surgery. J Neurol Neurosurg Psychiatry 2003;74:392-3.
12. Resatoglu AG, Tok M, Yemisci M, et al. Autoimmune myasthenia gravis after coronary artery bypass surgery. Ann Thorac Surg 2006;81:725-6.
13. Dressler D. Subclinical myasthenia gravis causing increased sensitivity to botulinum toxin therapy. J Neural Transm (Vienna) 2010;117:1293-4.
14. Lane R, Wade J, McGonagle D. Myasthenia gravis

 

precipitated by trauma: latent myasthenia and the concept of 'threshold'. Neuromuscul Disord 2009;19:773-5.
15. Dworakowska B, Nurowska E, Dolowy K. Hydrocortisone inhibition of wild-type and αD200Q nicotinic acetylcholine receptors. Chem Biol Drug Des 2018;92:1610-7.
16. Dengler R, Rüdel R, Warelas J, et al. Corticosteroids and neuromuscular transmission: electrophysiological investigation of the effects of prednisolone on normal and anticholinesterase-treated neuromuscular junction. Pflugers Arch 1979;380:145-51.
17. Tracey KJ. The inflammatory reflex. Nature 2002;420:853-9.
18. Rosas-Ballina M, Olofsson PS, Ochani M, et al. Acetylcholine-synthesizing T cells relay neural signals in a vagus nerve circuit. Science 2011;334:98-101.
19. Tracey KJ. Reflex control of immunity. Nat Rev Immunol 2009;9:418-28.
20. de Jonge WJ, Ulloa L. The alpha-7 nicotinic acetylcholine receptor as a pharmacological target for inflammation. Br J Pharmacol 2007;151:915-29.
21. Pavlov VA, Tracey KJ. The vagus nerve and the inflammatory reflex-linking immunity and metabolism. Nat Rev Endocrinol 2012;8:743-54.
22. Koopman FA, Chavan SS, Miljko S, et al. Vagus nerve stimulation inhibits cytokine production and attenuates disease severity in rheumatoid arthritis. Proc Natl Acad Sci USA 2016;113:8284-9.
23. Allen JM. The effects of chiropractic on the immune system: a review of the literature. Chiropr J Aust 1993;23:132-5.
24. Al-Hashel J, Rashad HM, Rousseff RT. An adult patient with ocular myasthenia and unusually long spontaneous remission. Case Rep Neurol Med 2014;2014:372769.
25. Alcantara J, Steiner DM, Plaugher G, Alcantara J. Chiropractic management of a patient with myasthenia gravis and vertebral subluxations. J Manipulative Physiol Ther 1999;22:333-40.
26. Schalow PR. Resolution of myasthenia gravis symptoms following upper cervical chiropractic: a case report. Proceedings of the 11th International Research and Philosophy Symposium, Spartanburg, SC October 16-19, 2014:88. Available online: http://ucmonograph.org/wp-content/uploads/2015/10/2014-IRAPS-SCHALOW-Resolution-of-Myasthenia-Gravis.pdf. Accessed Jan 31, 2019.

doi: 10.21037/acr.2019.04.04
**Cite this article as:** Chu EC, Bellin D. Remission of myasthenia gravis following cervical adjustment. AME Case Rep 2019;3:9.

 