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Effects of intravascular photobiomodulation on motor deficits and brain perfusion images in intractable myasthenia gravis: a case report

Chiao-Hsin Lan, Yu-Che Wu, Cheng-Chun Chiang, Shin-Tsu Chang

Abstract**BACKGROUND**

Myasthenia gravis (MG) is an autoimmune disorder caused by neuromuscular junction failure characterized by muscle weakness and fatigability. We herein report a case of MG that received intravascular laser irradiation of blood (ILIB) interventions and regained muscle power and better quality of life. To our knowledge, no previous study has investigated the benefits of ILIB treatment on patients with MG. We also evaluated the changes in brain perfusion scan and the MG Activities of Daily Living (MG-ADL) and Quantitative MG (QMG) scales.

CASE SUMMARY

A 59-year-old man presented to our outpatient hospital experiencing ptosis, diplopia, fibromyalgia, muscle fatigue, and fluctuating weakness in his limbs for 1 year. Based on his history, physical examination, and laboratory investigations, the final diagnosis was a flare-up of MG with poor endurance and muscle fatigue. The patient agreed to receive ILIB. Brain single-photon emission computed tomography (SPECT) was performed both before and after ILIB therapy. After receiving three courses of ILIB, the brain SPECT images showed greatly increased perfusion of the frontal lobe and anterior cingulate gyri. The patient's MG-ADL scale score decreased markedly from 17/24 to 3/24. The QMG scale score also decreased remarkably from 32/39 to 9/39. The

symptoms of MG became barely detectable and the patient was able to perform his activities of daily living and regain muscle power.

CONCLUSION

ILIB might have beneficial effects on MG, and brain SPECT images provided direct evidence of a positive correlation between ILIB and clinical performance.

Key Words: Myasthenia gravis; Intravascular laser irradiation of blood; MG Activities of Daily Living Scale; Quantitative MG Scale; Single-photon emission computed tomography; Case report

Lan CH, Wu YC, Chiang CC, Chang ST. Effects of intravascular photobiomodulation on motor deficits and brain perfusion images in intractable myasthenia gravis: a case report. *World J Clin Cases* 2022; In press

Core Tip: Myasthenia gravis (MG) is an autoimmune disease without effective treatments. We herein report a case of intractable MG administered a novel therapy, intravascular laser irradiation of blood interventions (ILIB), which regained muscle power and improved quality of life. To our knowledge, this is the first study investigating the benefits of ILIB treatment in patients with MG. We also evaluated the changes in brain perfusion scan and MG Activities of Daily Living Scale, and Quantitative MG Scale scores. We report this case to trigger further research and facilitate the recovery of patients with MG.

5 INTRODUCTION

Myasthenia gravis (MG) is an autoimmune disease that occurs due to the failure of neuromuscular transmission resulting from antibodies against the acetylcholine receptor, muscle-specific kinase, lipoprotein-related protein 4, or agrin in the postsynaptic membrane at the neuromuscular junction. [1-4] During the initial lifetime

5 course of MG, patients often present with ocular symptoms of ptosis and diplopia. [5-6] About half of these patients progress to generalized disease within 2 years. [7] The clinical manifestation of this disorder is fluctuation and variable weakness in the ocular, bulbar, limb, and respiratory muscles, which lead to major symptoms such as dysarthria, dysphagia, fatigable chewing, fatigable limb, or axial weakness. Skeletal muscle fatigue manifests as weakened muscle contractile force. [8-10]

8 The conventional treatment of MG usually includes a combination of symptomatic therapy with acetylcholinesterase inhibitors (e.g., pyridostigmine), immunosuppressive drugs, and immunotherapy using either intravenous immunoglobulin (IVIG) or plasma exchange in selected patients thymectomy. [10-14] The common therapeutic goal of these treatments is to help patients return to normal function as soon as possible while minimizing the side effects. However, patients receiving these treatments often experience adverse side effects and have difficulties in recovering. [15]

6 A novel alternative therapy is intravascular photobiomodulation, also known as intravascular laser irradiation of blood (ILIB). ILIB treatment utilizes a helium-neon laser with a wavelength of 632.8 nm (red light). An optic fiber is inserted into a superficial vein to deliver the laser light. [16] ILIB is considered an alternative treatment for diseases such as chronic spinal cord injury, cerebral stroke, traumatic brain injury, rheumatoid arthritis, chronic Sjögren's syndrome, fibromyalgia, and chronic pain conditions, due to its effects in increasing microcirculation and improving oxygen supply. [17-21] Before this case, the usefulness of ILIB in patients with MG had not been reported. This study presents a case diagnosed with MG that was treated with ILIB therapy, which resulted in regained muscle power and improved quality of life.

CASE PRESENTATION

Chief complaints

A 59-year-old man experienced ptosis, diplopia, fibromyalgia, muscle fatigue, and fluctuating limb weakness for 1 year. Worsening weakness in bilateral lower limbs

caused walking disability. The patient then came to our outpatient hospital in hopes of regaining muscle power and better walking ability.

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History of present illness

The patient's symptoms had started 1 year ago with recurrent episodes of weakness in four limbs. His eyelid dropped soon after he woke up and double vision appeared spontaneously. He also required a ventilator to maintain his daily sleeping.

History of past illness

The patient was initially diagnosed with MG on August 5, 2018, accompanied by severe ptosis, diplopia, and fibromyalgia. He visited a neurologist in a local medical center, who prescribed acetylcholinesterase inhibitor, pyridostigmine (oral: 60 mg/tab, 2 tabs three times daily), for 1 year. Later, the patient was treated with immunosuppressive drugs; namely, rituximab (intravenously: 375 mg/m², once weekly for 4 wk), and received six courses of IVIG to improve his conditions. However, the severe ptosis, diplopia, and fibromyalgia persisted without any sign of recovery. The patient reported no improvements in the weaknesses of his bilateral lower limbs, which caused walking disability and muscle fatigue, which severely affected his daily life.

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Personal and family history

The patient had no significant personal or family history.

Physical examination

During his visit, the MG Activities of Daily Living Scale (MG-ADL scale) [22] total score was 20/24 (Figure 1; Table 1), while that for the Quantitative MG Scale (QMG scale) [23] was 32/39 (Figure 2; Table 2). The patient's vital signs were within the normal ranges. Repetitive stimulation test at 3 Hz revealed decremental responses (11.8%) in both orbicularis oculi muscles but not in the right abductor pollicis brevis muscle, which suggested the need to consider post-synaptic neuromuscular junctional disorder.

Laboratory examinations

Laboratory evaluation revealed positivity for acetylcholine receptor antibody (5.97 nmol/L). The blood biochemistry examinations revealed mildly decreased complement C3 (74.8 mg/dL) levels compared to normal values (79–152 mg/dL). The urine analysis showed normal values.

Imaging examinations

No abnormalities were noted on electrocardiograms and chest X-rays. Regional cerebral perfusion (rCBF) scans by brain single-photon emission computed tomography (SPECT) were performed 30 mins after the intravenous injection of 30.8 mCi Tc-99m ECD. eZIS (Easy Z-score Imaging System) was used for statistical analysis. The first brain SPECT showed decreased rCBF in the frontal regions and anterior cingulate gyri (**Figures 3 and 4**). Magnetic resonance imaging of the chest showed no evidence of a thymic mass.

FURTHER DIAGNOSTIC WORK-UP

The results of the antinuclear autoantibodies (ANA) test were negative. The levels of RA factor (serum) were within normal limits (<20 IU/mL). The levels in anti-cyclic citrullinated peptide (anti-CCP) screening were also normal (0.6 U/mL). The patient was negative for HLA-B27. Finally, the result of the myositis 16-specific Ag panel was unremarkable.

FINAL DIAGNOSIS

Based on the patient's history, physical examinations, and laboratory investigations, the final diagnosis of the presented case was a flare-up of MG with poor endurance and muscle fatigue.

TREATMENT

The patient was advised to undergo ILIB and agreed. He received three courses of ILIB (60 minutes each session for 10 consecutive days per course, with a rest interval of 1–2 wk). A helium-neon (He-Ne) laser illuminator (YJ-ILIB-5, Bio-ILIB Human Energy Ltd, Taiwan) was applied with a wavelength of 632.8 nm, energy of 12.6 to 14.4 J, energy density of 6428.57 J/cm², power output of 2.5–3.5w/cm², power intensity of 1.79–2.04 w/cm², and irradiation time of 3600 s/session [20]. The laser power was adjusted depending on the patient's responses.

OUTCOME AND FOLLOW-UP

After completing three courses of ILIB, the patient's double vision and eyelid-dropping were remarkably improved, with his MG-ADL scale total score decreasing from 17/24 to 3/24. The weaknesses in both upper and lower limbs changed as anticipated. In the QMG scale, the time for both arms outstretched (90° standing) increased from 0–10 s to 90–240 s, while that for both legs' outstretched (45° supine) increased from 0–10 s to 90–240 s. The patient's breathing also improved. The algisia of both arms caused by fibromyalgia was also alleviated. Notably, the second total score of the QMG Scale decreased from 32/39 to 9/39. The second brain SPECT showed increased activities in the frontal regions and anterior cingulate gyri. (Figures 3 and 4). The patient is content with the efficacy of ILIB treatment.

DISCUSSION

After several years of conventional treatments, including acetylcholinesterase inhibitors and immunosuppressive drugs without subjective improvement, the relatively rapid improvement in motor and respiratory function during ILIB treatment in our case suggests that the patient benefited significantly from ILIB therapy. This patient also made great clinical progress, according to his MG ADL and QMG scale scores. This is the first case report on the novel treatment of MG with ILIB. This is also the first study to describe the benefit of ILIB as a treatment for impaired motor function and analgesia by SPECT imaging of a patient with MG.

We used regional perfusion ¹ brain SPECT images to assess brain function before and after the ILIB intervention. We observed two intriguing findings in this study of a patient with MG.

First, we observed remarkably increased perfusion in the motor areas of the frontal lobe (Figure 3), which indicated a strong relationship between motor function and frontal lobe activity. Recent studies showed that ILIB therapy improved regional cerebral blood flow and provided faster repair of the affected nervous system through increased ATP production. ³ [24-25] The motor cortex comprises three different areas of the frontal lobe, immediately anterior to the central sulcus. These areas are the primary motor cortex (Brodmann's area 4), the premotor cortex (PMC), and the supplementary motor area (SMA). [26] Our SPECT images showed significantly increased perfusion in both the SMA and PMC after ILIB therapy, suggesting that blood flow might re-perfuse, contributing to the improvement in muscle weakness and fatigue.

Second, the SPECT images also showed higher activity in the anterior cingulate cortex (ACC) after ILIB therapy (Figure 4), which indicated a correlation between pain relief and the ACC. Davis *et al* reported that the signal intensity changes within the ACC were correlated with pain intensity [27], sensory, cognitive processes, and motor function including voluntary movement. [28] Hence, higher activities in the ACC, considered a complicated integrative center, showed a re-distribution of blood flow in the brain, which resulted in pain relief in both arms and regained power in the skeletal muscles.

Furthermore, ILIB is considered a treatment that facilitates circulation in the frontal area of the cortex, especially in this case. ILIB may enhance muscular strength and relieve fluctuating and variable fatigue. [29-30] ILIB also plays a role as an immunomodulator through direct or indirect effects on ¹ the immune system [21], which was unbalanced in our case with MG. ¹ The post-treatment imaging study revealed that ILIB effectively facilitated ¹ circulation around the frontal area of the cortex, which improved the clinical symptoms of this patient with MG.

However, the role of the peripheral mechanism in contributing to the recovery of muscle power cannot be ignored. ² To sustain muscle contraction, ATP needs to be

regenerated at a rate complementary to ATP demand. Three major ways are used to replenish ATP in muscle. These systems—phosphagen, glycolytic, and mitochondrial respiration—differ in the substrates used, products, maximal rate of ATP regeneration, capacity of ATP regeneration, and associated contributions to fatigue. [31-32] In addition, ILIB therapy has been reported to promote total cellular ATP synthesis, and antioxidant activity, which contributes to the alleviation of chronic conditions, such as chronic spinal cord injury and fibromyalgia. [17, 20] Therefore, we believe that ILIB therapy might enhance muscle power by increasing ATP synthesis in the peripheral mechanism.

CONCLUSION

MG is an autoimmune disease that previously lacked effective treatments and detailed brain perfusion images. Our case showed the feasible management of this condition with ILIB treatment. The brain perfusion scan demonstrated increased activity in the prior deficit of the brain lesion. ILIB might have beneficial effects on MG and SPECT images could be a good monitor for any deficits in the brain.

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