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COVID-19

A mild course of COVID-19 infection in a generalized Myasthenia gravis patient under eculizumab treatment

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Dear Editor-in-Chief,

Myasthenia gravis (MG) is an autoimmune disease, in which about 10–15% of patients are treatment-refractory despite all current therapies [1]. Eculizumab is a monoclonal antibody that inhibits the activation of the complement system by inhibiting the enzymatic cleavage of C5 into C5a and C5b. It was approved for treating treatment-refractory generalized MG (gMG) in 2017 [2]. Although eculizumab and placebo recipients were not found to be significantly different regarding primary endpoints, eculizumab recipients had improvements in activities of daily living, health-related quality of life parameters, and muscle strength in the REGAIN study [1]. These improvements continued in the long-term open-label extension of REGAIN study [3]. Eculizumab was also suggested to be effective in Coronavirus disease 2019 (COVID-19) infection [4]. Herein, we present a treatment-refractory anti-AChR-positive gMG patient, whose symptoms almost entirely improved following treatment with eculizumab and had a mild course of COVID-19 infection under eculizumab treatment.

A 24-year-old female patient diagnosed with anti-AChR positive gMG in 2013. The first complaints were double vision, ptosis, and hoarseness. She was treated with a combination of pyridostigmine and oral methylprednisolone and operated for thymic hyperplasia in the same year. Since her complaints progressed including extremity weakness, ptosis, and bulbar signs, 5 days of intravenous immunoglobulin (IVIg) (0.4 gr/kg) were given and followed by monthly doses. Then Azathioprine was tried with partial recovery. Rituximab, which is an anti-CD20 monoclonal antibody (375 mg/m2 every 6 months), was started when dysphagia and lower extremity weakness progressed in 2019 and Azathioprine was stopped. Though extremity weakness improved slightly with rituximab, bulbar signs and ptosis stayed the same. She had myasthenic crisis under the treatment of oral methylprednisolone, monthly IVIg, and rituximab. She was started to feed by a nasogastric tube. She was admitted to our clinic in August 2020. She was under methylprednisolone 64 mg/day, pyridostigmine 480 mg/day, monthly IVIg (0.4 gr/kg), and rituximab. There was bilateral ptosis, lateral and vertical gaze palsy, diplopia, extremity, and bulbar muscle weakness on neurological examination. Her muscle strength was 3/5 in the upper extremities and 2/5 in the lower extremities, and she was mobilizing with a wheelchair. She used a nasogastric tube for the last 6 months due to dysphagia; she could count to eight in one breath, and her speech was hoarse. Seven sessions of plasmapheresis were performed as rescue therapy. Although dysphagia and lower extremity weakness improved slightly, ptosis and diplopia did not change. Then, ineffective rituximab treatment was discontinued, and mycophenolate mofetil was started, in addition to oral methylprednisolone and monthly IVIg. Screening for a thymic remnant, antibody to muscle-specific kinase, and other autoimmune diseases were negative. The patient continued to worsen under mycophenolate mofetil. She had IV methylprednisolone treatment (1 gr/day) for 7 days without any improvement. Three months later, mycophenolate mofetil was stopped, and eculizumab was started.

Prior to the eculizumab treatment, the symptom severity was in Class IVb according to the Myasthenia Gravis Foundation of America (MGFA), her MG-Activity of daily living (MG-ADL) score was 21 and her quantitative MG

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(QMG) score was 39. She was using methylprednisolone (64 mg/day) and pyridostigmine 60 mg (eight times/day). The first dose of eculizumab was administered following vaccination against Neisseria meningitidis in March 2021. Her dysphagia improved, and the nasogastric tube was removed 5 days after the first dose. In a week, muscle strength was improved almost completely, and she started walking and climbing stairs with unilateral support. Although the gaze palsy and diplopia remarkably ameliorated, fluctuating partial ptosis continued on the left. Her MG-ADL and QMG scores were reduced to 8 and 11 in the first week after Eculizumab administration, respectively. As a result, the doses of oral methylprednisolone and pyridostigmine were tapered to 8 mg/day and 240 mg/day, respectively, and monthly IVIg was ceased. She did not experience any critical side effects, except temporary mild myalgia. Though the patient significantly benefited from the Eculizumab treatment administered every 2 weeks, the symptoms gradually worsened towards the end of each 2-week treatment cycle. Thus, we could not stop Eculizumab treatment for COVID-19 vaccination. Approximately 9 months after starting eculizumab, she had COVID-19 infection with mild symptoms and without pneumonia. She did not receive any treatment for COVID-19 and not hospitalized. However, her myasthenic symptoms (bulbar signs and extremity weakness) worsened following COVID-19, her MG-ADL score increased to 16, and her QMG score were increased to 28. She received 5 days IVIg (0.4 gr/kg/day) with a good response. The patient is still under eculizumab treatment (1200 mg every 2 weeks). There are no bulbar signs except fatigue when eating solid foods rarely and mild shortness of breath after a strong effort. She can walk and climb stairs unassisted. She is in MGFA Class-IIB, her MG-ADL score is 6, and her QMG score is currently 5.

Although our patient was refractory to other immunosuppressants, she responded to eculizumab in 1 week, and the responsiveness continued for 10 months. The remarkable improvement of the symptoms in a week following the first eculizumab dose was relatively rapid compared to REGAIN study. The mean period to obtain a significant improvement in this study was considered 4 weeks [2]. Our case suggests eculizumab has a significant superiority over other immunosuppressants, which require more time to be effective. She did not experience any severe side effects related to eculizumab, and other immunosuppressive treatments could be ceased except oral methylprednisolone. Besides, there was no need for any precautions before its administration except vaccination against Neisseria meningitides, and routine blood tests are not necessary in follow-up [2]. Recently, Zilucoplan which is another complement C5 inhibitor was found to be effective to treat gMG, emphasizing the importance of the complement system in the pathophysiology of MG [5].

Patients with MG have more severe COVID-19 disease course and higher mortality rate compared to the normal population [6, 7]. Although it was shown that COVID-19 could cause myasthenic crisis in 40% or death in 24% of myasthenic patients [6], our patient had mild symptoms probably due to concurrent Eculizumab therapy. There is little evidence of the COVID-19 outcome in myasthenic patients using eculizumab could be milder [8]. Our case supports that these patients may have a milder COVID-19 infection and eculizumab may be continued safely during COVID-19 infection. However, it should keep in mind that myasthenic symptoms might be worsened due to baseline bulbar weakness, respiratory dysfunction and immunosuppressive treatments [6].

In conclusion, eculizumab was well tolerated in the presented case, provided an early response and she also experienced a relatively mild course during COVID-19 disease.

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Declarations

Ethics approval We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

Conflict of interest The authors declare no competing interests.

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