ECRONICON OPEN ACCESS

EC OPHTHALMOLOGY
Case Report

A Case Report: Post-Covid-19 Ocular Myasthenia Gravis and Brief Literature Review

Mualla Şahin Hamurcu[1], Bilge Başçiftçi[1]* and Semra Mungan Öztürk[2]

[1]Department of Ophthalmology, University of Health Sciences, Ankara City Hospital, Ankara, Turkey

[2]Department of Neurology, University of Health Sciences, Ankara City Hospital, Ankara, Turkey

***Corresponding Author:** Bilge Başçiftçi, Department of Ophthalmology, University of Health Sciences, Ankara City Hospital, Ankara, Turkey.

Received: August 12, 2021 ; Published: November 30, 2021

Abstract

Coronavirus disease 2019 (COVID-19) has developed as a pandemic and it has been shown that COVID-19 not only causes symptoms of the respiratory system, but can also cause neuromuscular complications. We report the third case of ocular myasthenia gravis emerging after getting infected by COVID-19 virus, in a 46 years old woman. The patient was admitted to hospital with severe muscle and joint pain along with flu-like symptoms and then she tested positive for SARS-Cov-2 COVID-19 by nasopharyngeal RT-PCR testing. Her ptosis in the right superior eyelid appeared 10 days after her COVID-19 PCR test resulted positive. Single fiber EMG was compatible with motor endplate dysfunction and acetylcholine receptor (AchR) antibody (Ab) was positive with high titer. Oral corticosteroid therapy, the dose of which was gradually increased, was started to the patient and objective improvement was observed in the patient's ptosis and enophthalmos in the first week after the initiation of treatment. COVID-19 is leading to immune-mediated damage by the release of inflammatory cytokines. Myasthenia gravis (MG) displays itself with the destruction of the connection between muscles and the nerves. This eradication of the connections cause weakness of the muscles.

Keywords: *Myasthenia Gravis; Covıd-19; Ptosis*

Introduction

Myasthenia gravis (MG) is a disease affecting the neuro-muscular junction, which results in classical symptoms of variable degree of muscle weakness and fatigability [1]. Weakness of these muscles most of the time involves muscles of the eye with diplopia and ptosis, whereas this aforementioned weakness can be in either generalized or localized form. This issue generally concerns proximal muscles rather than distal muscles [2]. Disease is precipitated by pathogenic autoantibodies towards the skeletal muscle acetylcholine receptor (AChR) in the neuro-muscular junction [3]. The definite origin of the autoimmune response in MG is not known, yet thymic gland abnormalities such as thymic hyperplasia or tyhmus neoplasias essentially play a role in patients with autoantibodies. Meanwhile, genetic predisposition plays a crucial role in patients who develop this disorder [4-6].

Only ocular findings are present in 15% of patients with myasthenia gravis. The main symptoms of ocular myasthenia gravis are ptosis which is isolated or associated with extraocular muscles, unilateral or bilateral, aggravated towards the end of the day; and diplopia with fluctuations during the day. Due to involvement of the levator palpebrae superioris muscle complex, ptosis arises.

There are some clinical tests, that are non-invasive, to help diagnostic testing for ocular myasthenia gravis. Cogan's Lid Twitch test, lid fatigability test and ice test along with rest test can be counted as examples for such non-invasive tests [7]. First of all, in "lid fatigability test", when the patient had prolonged upward embosom, ptosis intensifies [1]. Cogan lid twitch which is another clinical sign of ocular

myasthenia gravis is revealed by having the patient look upwards, followed by downwards direction. As the affected eye saccades up, the upper lid overshoots. Nevertheless, Cogan's lid twitch is not specific to ocular MG [8]. Meanwhile, "Hering's law of equal innervation" emphasizes that each of the reciprocal eye muscles are innervated equally. So, manual lifting of the more ptotic eyelid reduces the muscle strength required to keep the eyelid elevated; and then the contralateral levator palpebrae superioris muscle relaxes and causes incrementation of ptosis [1].

There are a couple diagnostic tests including neostigmine test, edrophonium chloride test, serum acetylcholine receptor antibody (AchR Ab) and some electrophysiological tests. Single fiber electromyography (SFEMG) and repetitive nerve stimulation (RNS) tests are examples of the electrophysiological tests [7]. In healthy individuals, muscle action potential amplitude stays the same in RNS, however more than 10% decline in this amplitude is typically seen in MG patients, especially by the fourth or fifth response [9]. Nevertheless, solely 33% of patients that have pure OMG demonstrate this reduced response [10]. Single-fiber electromyography (SFEMG) is the most sensitive diagnostic tool for determining abnormal neuromuscular transmission as we have seen in OMG. 85 - 100% sensitivity is existent in SFEMG for ocular myasthenia gravis when it is used on the frontalis muscle or orbicularis oculi muscle [11,12].

It has been shown that some infectious agents such as viruses or bacteria can provoke a myasthenic crisis in pre-diagnosed myasthenia gravis patients. However, there is no certain evidence on infectious agents that cause MG in normal individuals yet.

With the epidemic of the novel COVID-19; it is found that the coronovirus infection immensely and extremely affects patients with neuromuscular diseases. It is possible that associated neuromuscular disorders (NMDs) have occurred previously but have been overshadowed by systemic manifestations. In cases with COVID-19 infection, it has been revealed that neurological findings are also seen in addition to atypical pneumonia or respiratory distress.

This is the third case of ocular myasthenia gravis triggered by coronavirus SARS-CoV-2 infection and we tried to define the clinical course, pathophysiological mechanisms and briefly review the current literature on COVID-19 in myasthenia gravis patients.

Case Report

A 46 years old woman was presented with ptosis on her right superior eyelid. She had no chronic diseases and no regular drug administration. She had a smoking history of 15 pack years and there is no record of alcohol consumption. Her medical history was considerable for coronavirus infection. In January 2021, she was admitted to hospital with severe muscle and joint pain along with flu-like symptoms. She had no symptoms of shortness of breath, difficulty in swallowing, fatigue in chewing or proximal muscle weakness. Then she tested positive for SARS-Cov-2 COVID-19 by nasopharyngeal RT-PCR testing. After the diagnosis, Favipiravir-200 mg 2 x 8 pills for the first day and then 2 x 3 pills for the following 4 days were used. Patient's complaint appeared 10 days after her COVID-19 PCR test resulted positive. Her eyelid ptosis towards the evening was increasing.

On our examination, she had right eye ptosis that was fatigable. Her eye movements were bilateral free in all directions, there was no diplopia or pain with movements. Autorefraction was (+3,00), (-3,50)@150 in the right eye and (-0,25) in the left eye. Vision was 5/10 in the right eye, which was amblyopic, and 10/10 in the left eye. Her eye pressure was normal for both of the eyes. Bilateral direct and indirect light reflexes were normal and there was no reactive afferent pupil defect existent. Pupils were isocoric. She had enophthalmos accompanying ptosis in right eye.

In biomicroscopy, bilateral anterior and posterior segment examination was normal. She pointed out generalized fatigue, muscle and joint pain. Nonetheless, she reported no focal weakness on neurological examination. She had normal muscle strength and normal tendon reflexes.

In neurology consultation, according to MRI-Angiography there was no evidence of venous thrombus in the superior sagittal sinus, inferior sagittal sinus, sinus rectus and both transverse and sigmoid sinuses. EMG was performed and there was no finding suggestive of

neuromuscular junction disease on repetitive nerve stimulation test. Single fiber EMG was performed and it was compatible with motor endplate dysfunction with the method examined. Existence of acetylcholine receptor antibody (AchR Ab) was confirmed with high level 5.58 nmol/L (normal < 0.25 nmol/l). No monoclonal antibody was detected in immunofixation electrophoresis. At the pulmonological consultation, there was no pathology detected based on thorax and pulmonary CT-Angiography.

Based on the combination of findings from patient's history, laboratory tests and electrodiagnostic testing; the patient was diagnosed with post-covid infection ocular myasthenia gravis with positivity of AchR Ab. 7.5 mg prednisolone per oral was started for 5 days, then this administration was increased to 10 mg for 5 days; following up with 12.5 mg for 1 month and then with 15 mg for 1 month**.** Objective improvement was observed in the patient's ptosis and enophthalmos in the first week after the initiation of treatment. No side effects of corticosteroids were observed during the follow-up of the patient.

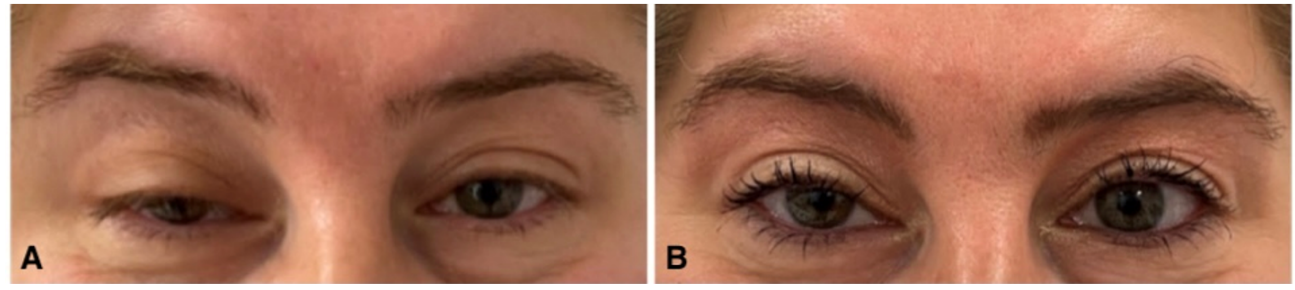

Figure 1: *Photography of the patient: Right upper eyelid ptosis and enophthalmos at presentation (A). 7 days after corticosteroid treatment, significant improvement was observed in the patient's ptosis and enophthalmos (B).*

Discussion

A few case reports of SARS-Cov-2 COVID-19 infections in patients with pre-diagnosed MG have been reported [13-15]. As far as we know, lately there is just one published case series of myasthenia gravis which has developed as a complication of COVID-19 infection; whereas the 3 patients in this case series were that of generalized myasthenia gravis [16]. We report a case of ocular myasthenia gravis coming up shortly after SARS-Cov-2 COVID-19 infection who responded well to corticosteroid treatment.

In our brief literature review, we have inspected two patients who have ocular MG that emerged just after COVID-19 infection [17,18]. The first patient suffered from ptosis, the most common and initial symptom of ocular MG, after positivity for SARS-Cov-2 COVID-19 by nasopharyngeal RT-PCR testing, as in our case.

Also, no focal weakness on neurological examination was reported and acetylcholine receptor (AchR) antibody (Ab) was positive with high titer, in parallel with our case. The patient's EMG test was consistent with a neuromuscular transmission defect, with a reduced response on RNS test of left orbicularis oculi muscle more than 10%, whereas our patients' EMG had no finding suggestive of neuromuscular junction disease on RNS test. However, the single fiber EMG of our patient was compatible with motor endplate dysfunction; so we made a diagnosis of post-COVID-19 ocular MG in our patient. In our case; the patient displayed significant improvement at her ptosis with the corticosteroid treatment, though it should be noted that pyridostigmine was used and improvement was observed in the patient that in the literature we reviewed [17]. The second patient in the literature we inspected suffered from diploia and ptosis as well as about 1 month earlier she had sypmtoms of mild respiratory symptoms, muscle and join pain, headache, anosmia, ageusia but she had no fever. Also, no focal weakness on neurological examination was reported, acetylcholine receptor (AchR) antibody (Ab) was positive with high titer and a positive test with edrophonium chloride was reported. A nasopharyngeal RT-PCR test taken about one month after onset of

respiratory symptoms was resulted negative, that indicates no acute COVID-19 infection, so antibodies (IgA/IgG) against SARS-CoV-2 were performed and were found positive in serum. The patient that in the literature we reviewed, responded well to intravenous immunoglobulins and oral anticholinesterase-pyridostigmine [18].

In our case report, the patient possessed ocular symptoms of MG after getting infected by SARS-Cov-2 COVID-19infection. At the same time, she had a good response to corticosteroid therapy which is an immunosuppressant. In the course of the outbreak of the novel coronavirus SARS-CoV-2, it has been established that neurological complications in the form of autoimmune reactions such as Lambert-Eaton syndrome, Guillain-Barré syndrome (GBS) and Myasthenia Gravis (MG) can be exacerbated.

Yet, the pathophysiological mechanism underlying the disease has not been fully determined and requires more research. Notwithstanding, it is evident that inflammatory response and autoimmune mediated mechanisms play an influential role in the pathogenesis of the MG. In postsynaptic neuromuscular junction, acetylcholine receptors are destructed by the antibodies and the inflammatory cytokines that resulted in decrement of the muscle action potential [19].

It has been shown that, COVID-19 virus can enter the cells using the angiotensin converting enzyme 2 (ACE2) receptor. COVID-19 has affinity to angiotensin converting enzyme 2 receptors which are expressed in several organs such as lungs, liver, kidneys; where it directly causes the produciton of autoantibodies and leads to an inflammatory pathway [20,21]. Furthermore, chronic inflammatory autoimmune diseases owe their causes to inflammatory T-helper 17 (Th-17) cells and Treg cells. These diseases are either organ specific or systemic, as a result of the imbalance between forenamed cells [22].

There are also few reports about myasthenia gravis that has developed weeks after contracting Varicella zoster virus, West Nile virus, and Zika virus [23,24]. In our brief literature review, after COVID-19 infection, neuromuscular findings appeared after generally 1 to 3 weeks [25,26]. Our case had neuromuscular manifestations, that is ptosis, after 10 days of positivity for SARS-Cov-2 COVID-19 by nasopharyngeal RT-PCR testing. It could be considered that myasthenia gravis may be a complication of the COVID-19 infection or a post-infectious rise of MG.

Conclusion

In literature, this is the third case of ocular myasthenia gravis emerging in a patient after getting infected by SARS-Cov-2 COVID-19 virus. It has been shown that COVID-19 not only causes symptoms of the upper and lower respiratory system, but can also cause neuromuscular complications. As an outcome of this case report, myasthenia gravis should be regarded as a neuromuscular complication of COVID-19 infection that can present itself with fatigable ptosis.

Bibliography

1. Nair AG., *et al*. "Ocular myasthenia gravis: a review". *Indian Journal of Ophthalmology* 62.10 (2014): 985-991.

2. Gilhus NE. "Myasthenia Gravis". *The New England Journal of Medicine* 375.26 (2016): 2570-2581.

3. Patrick J and Lindstrom J. "Autoimmune response to acetylcholine receptor". *Science* 180.4088 (1973): 871-872.

4. Berrih S., *et al*. "Anti-AChR antibodies, thymic histology, and T cell subsets in myasthenia gravis". *Neurology* 34.1 (1984): 66-71.

5. Roxanis I., *et al*. "True epithelial hyperplasia in the thymus of early-onset myasthenia gravis patients: implications for immunopathogenesis". *Journal of Neuroimmunology* 112.1-2 (2001): 163-173.

6. Giraud M., *et al*. "Linkage of HLA to myasthenia gravis and genetic heterogeneity depending on anti-titin antibodies". *Neurology* 57.9 (2001): 1555-1560.

7. Apinyawasisuk S., *et al*. "Validity of Forced Eyelid Closure Test: A Novel Clinical Screening Test for Ocular Myasthenia Gravis". *Journal of Neuro-Ophthalmology* 37.3 (2017): 253-257.

8. Keane JR. "Vertical diplopia". *Seminars in Neurology* 6.2 (1986): 147-154.

9. Ozdemir C and Young RR. "The results to be expected from electrical testing in the diagnosis of myasthenia gravis". *Annals of the New York Academy of Sciences* 274 (1976): 203-222.

10. Costa J., *et al*. "Repetitive nerve stimulation in myasthenia gravis--relative sensitivity of different muscles". *Clinical Neurophysiology* 115.12 (2004): 2776-2782.

11. Padua L., *et al*. "SFEMG in ocular myasthenia gravis diagnosis". *Clinical Neurophysiology* 111.7 (2000): 1203-1207.

12. Howard JF Jr. "Electrodiagnosis of disorders of neuromuscular transmission". *Physical Medicine and Rehabilitation Clinics of North America* 24.1 (2013): 169-192.

13. Anand P., *et al*. "COVID-19 in patients with myasthenia gravis". *Muscle and Nerve* 62.2 (2020): 254-258.

14. Delly F., *et al*. "Myasthenic crisis in COVID-19". *Journal of the Neurological Sciences* 414 (2020): 116888.

15. Rein N., *et al*. "Description of 3 patients with myasthenia gravis and COVID-19". *Journal of the Neurological Sciences* 417 (2020): 117053.

16. Restivo DA., *et al*. "Myasthenia Gravis Associated With SARS-CoV-2 Infection". *Annals of Internal Medicine* 173.12 (2020): 1027-1028.

17. Sriwastava S., *et al*. "New onset of ocular myasthenia gravis in a patient with COVID-19: a novel case report and literature review". *Journal of Neurology* 12 (2020): 1-7.

18. Huber M., *et al*. "Postinfectious Onset of Myasthenia Gravis in a COVID-19 Patient". *Frontiers in Neurology* 11 (2020): 576153.

19. Koneczny I and Herbst R. "Myasthenia Gravis: Pathogenic Effects of Autoantibodies on Neuromuscular Architecture". *Cells* 8.7 (2019): 671.

20. Baig AM., *et al*. "Evidence of the COVID-19 Virus Targeting the CNS: Tissue Distribution, Host-Virus Interaction, and Proposed Neurotropic Mechanisms". *ACS Chemical Neuroscience* 11.7 (2020): 995-998.

21. Ni W., *et al*. "Role of angiotensin-converting enzyme 2 (ACE2) in COVID-19". *Critical Care* 24.1 (2020): 422.

22. Galassi G and Marchioni A. "Myasthenia gravis at the crossroad of COVID-19: focus on immunological and respiratory interplay". *Acta Neurologica Belgica* 121.3 (2021): 633-642.

23. Saha A., *et al*. "Post-varicella myasthenia gravis". *Singapore Medical Journal* 48.6 (2007): e177-180.

24. Felice KJ., *et al*. "Postinfectious myasthenia gravis: report of two children". *Journal of Child Neurology* 20.5 (2005): 441-444.

25. Tsai LK., *et al*. "Neuromuscular disorders in severe acute respiratory syndrome". *Archives of Neurology* 61.11 (2004): 1669-1673.

26. Ellul MA., *et al*. "Neurological associations of COVID-19". *The Lancet Neurology* 19.9 (2020): 767-783.

Volume 12 Issue 12 December 2021