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Spontaneously resolving late-onset ocular myasthenia related to COVID-19. A case report

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Myasthenia gravis (MG) is the most common disease of the neuromuscular junction disorders with bimodal distribution of age, which is often under-estimated in the elderly. Some clinical cases show an association between MG and COVID-19, since molecular mimicry between SARS-CoV-2 and AChR proteins could be responsible for the onset of the disease.
We report a 77-year-old woman who developed right eyelid ptosis five days after COVID-19 infection. Positive serum anti-acetylcholine receptor antibodies allowed the diagnosis of myasthenia gravis. It should be noted that there were no significant decremental changes on 3 Hz repetitive motor nerve stimulation study, even for the affected orbicularis oculi muscle. Clinical and pathophysiological data suggest that inflammation during COVID-19 could trigger an overproduction of autoantibodies previously present in the body at a subclinical level. This is the first case of COVID-19 infection complicated by myasthenia gravis, to the best of our knowledge, that resolves spontaneously.

Key words: late-onset myasthenia gravis, COVID-19, SARS-CoV-2

Introduction

Myasthenia gravis (MG) is the most common disease of the neuromuscular junction disorders that is explained by autoantibodies against some components of the postsynaptic muscle terminal plaque. For a correct diagnosis, the presence of eyelid ptosis, diplopia, dysarthria, facial paresis are necessary, as well as the study of slow repetitive nerve stimulation and the dosage of serum antibodies against antiacetylcholine receptors. MG has a variable clinical presentation with a bimodal age distribution: the first peak is between 20 and 40 years and mainly affects women while the second peak above 60 years mainly concerns men [1]. Although MG is found primarily in young women, it is under-recognized in the elderly and is often mistaken for cerebrovascular diseases. For older women, the incidence of MG peaks is around age 70 [2]. Here, we report the case of ocular myasthenia caused by COVID-19 in a 77-year-old woman.

Case report

A 77-year-old woman with known vascular risk factors, including atrial fibrillation, was diagnosed with COVID-19 (positive nasopharyngeal swab for SARS-CoV-2 reverse transcriptase-PCR, RT-PCR) in January 2023. Five days afterwards, she noticed a drooping of right upper eyelid and felt eye fatigue, which presented the main characteristics of myasthenia gravis (MG), with eye movement anomalies at the end of the day which disappeared with rest. No dysphonia or dysarthria and/or facial weakness were observed. The ocular motility study showed no abnormalities. No neurological deficits in the motor or sensory domains were found. The composite MG score[3] was 4 (3 for ptosis and 1 for

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weak eye closure). Physical examination and imaging ruled out the diagnosis of vascular or inflammatory disorder of the central nervous system.

Since the woman had many risks related to vascular factors, a brainstem stroke was suspected. However, the Doppler ultrasound examination of the neck vessels was normal and the brain magnetic resonance imaging (MRI) showed no parenchymal abnormalities. Furthermore, a complete etiological evaluation of the stroke was negative.

Serum anti-acetylcholine receptor (AchR Ab) antibody titers were initially elevated at 16.2 nmol/L (< 0.40: negative) and 14.5 nmol/L 4 months after COVID-19 infection, favoring diagnosis of immune-mediated myasthenia. However, slow, repetitive nerve stimulation at 3 Hz of several nerves including the facial nerve with recording on the orbicularis oculi muscle showed no significant decremental response (> 10% decrease in amplitude between the first and fourth responses) (Tab. I).

Conduction studies of the median, ulnar, radial, and facial nerves were normal. Chest tomography revealed no thymoma or lung disease related to COVID-19 infection. No symptomatic (cholinesterase inhibitors) or immunosuppressive treatment was initiated due to the mild MG phenotype involving only the orbital segment and the spontaneous clinical improvement. Ten days later, the patient's symptoms had disappeared.

Table I. Low rates of repetitive nerve stimulation test of the left and right orbicularis oculi (facial nerve).

Muscles	Time	Decrement	
Right orbicularis oculi		**Amplitude**	**Area**
Run 1	H: 50:49	0.015	-0.28
Run 2	H: 51:15	3.7	1.09
Run 3	H: 52:17	0.55	-0.11
Run 4	H: 53:20	4.2	-0.74
Run 5	H: 54:22	-8.8	-3.9
Left orbicularis oculi			
Run 1	H: 57:26	-4.9	-4.4
Run 2	H: 57:49	-0.7	-3.0
Run 3	H: 58:50	-4.7	-4.5
Run 4	H: 59:52	-4.4	-3.0
Run 5	H1:00:52	-5.4	-

Discussion

Myasthenia gravis (MG) is the most common disorder of neuromuscular transmission with fluctuating fatigability and muscle deficit as a hallmark of disease. MG is caused by autoantibodies directed against the muscle nicotinic acetylcholine receptor (Achr) or muscle-specific tyrosine kinase (Musk), resulting in impaired neuromuscular transmission and muscle weakness. Although MG is found mainly in young women, it is an under-recognized condition in the elderly, often mistaken for cerebrovascular disease. For older women, the incidence of MG peaks around age 70 [2]. This case shows a late-onset MG diagnosis initially mistaken for a transient ischemic attack as MG mimics stroke in elderly patients [3], due to the concomitant motor deficit. Patients with autoimmune MG are more likely to have worse outcomes during the COVID-19 pandemic due to their immunocompromised condition and possible respiratory and bulbar muscle weakness [4].

Numerous post-COVID case reports are available in the medical literature indicating that MG may occur in the context of COVID-19 and may have an etiological relationship [5]. In a study of three patients diagnosed with MG after the onset of COVID-19), a significant decrease was observed through repetitive facial nerve stimulation such as elevated serum AChR antibody levels. All patients had classical treatment for MG, including plasmapheresis in one more severe case [6]. On the contrary, our patient presented only mild eyelid ptosis especially in the evening with minimal impact on vision, which improved spontaneously after 10 days. The signs of COVID-19 infection were not serious and did not require specific antiviral treatment.

The first description [6] of ocular MG involved a 65-year-old woman with cough, fever, and diarrhea who was admitted to hospital two weeks after the onset of symptoms. Electrodiagnostic testing showed a decremental response of more than 10% on the repetitive nerve stimulation test of the orbicularis oculi, and antibodies against the acetylcholine receptor were positive [6]. In our case, clinical signs suggestive of MG, as in a previous study [5], appeared within a week of the onset of fever.

The link between COVID-19 and autoimmune disorders is plausible, as COVID-19 can alter the regulation of the immune system and, consequently, favor the onset of autoimmune phenomena [7]. A study of 40 adult Italian patients with no known autoimmune disease and COVID-19 revealed increased levels of inflammatory markers, including antinuclear antibodies [8]. Increased production of pre-existing low-level AchR antibodies, likely caused by molecular mimicry between SARS-CoV-2 proteins and AChR, may be responsible for the development of this phenotype. There is evidence that low-level autoantibodies can be frequently detected in the general population; however there are no prognostic factors able of determining whether these individuals will develop an autoimmune disease, as they were not clinically diagnosed at the time of sample collection [9].

In contrast to the results of some studies showing that patients with a de novo autoimmune response had a worse prognosis, our patient had a spontaneous remission of her blepharoptosis, suggesting that the inflammatory response depends on the initial level of inflammatory/autoimmune markers [10]. There is no correlation between the anti-AChR antibody titer of the antigenic repertoire and the severity of the disease, but the lowest levels of anti-AChR antibodies are observed in elderly patients with thymic atrophy[11]. In fact, the level of anti-AChR Ab checked four months later was slightly lower than the acute phase of COVID-19 infection, as an argument in favor of an autoimmune reaction. Some sub-AChR units could be targeted with COVID-19 specific proteins [5], which would unmask previously asymptomatic MG.

This report presents a rare case of a patient who developed ocular myasthenia (MG) a few days after COVID-19 infection with spontaneous improvement without treatment. This sequential appearance

of COVID-19 and mild MG appears unique. Although the temporal association between COVID-19 infection and MG does not necessarily imply a causal link, the data suggest that COVID-19 infection could trigger the clinical expression of MG by involving molecular mimicry as an essential etiological factor. Furthermore, it highlights the importance of a comprehensive neurological assessment in elderly patients with stroke-like symptoms.

Conflict of interest statement

The author declared no potential conflicts of interest with respect to the research, authorship, and publication of this article.

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Data availability

The datasets used during the current study are available from the corresponding author, upon reasonable request.

Author contributions

The author conceived the study, examined the patient, analyzed the data, and wrote the manuscript.

Ethical consideration

The subject gave her written informed consent to participate and publish this study which

complies with the Declaration of Helsinki. The data were gathered without patient identification.

The author confirms that the approval of an institutional review board was not required for this work.

References

1 Carr AS, Cardwell CR, McCarron PO, et al. A systematic review of population based epidemiological studies in Myasthenia Gravis. BMC Neurol 2010;10:46. https://doi.org/10.1186/1471-2377-10-46

2 Aarli JA. Myasthenia gravis in the elderly: is it different? Ann N Y Acad Sci 2008;1132:238-243. https://doi.org/10.1196/annals.1405.040.

3 Burns TM, Conaway MR, Cutter GR, et al. Less is more, or almost as much: a 15-item quality-of-life instrument for myasthenia gravis. Muscle Nerve 2008;38:957-963. https://doi.org/10.1002/mus.21053

4 4 Muppidi S, Guptill JT, Jacob S, et al. COVID-19-associated risks and effects in myasthenia gravis (CARE-MG). Lancet Neurol 2020;19:970-971. https://doi.org/10.1016/S1474-4422(20)30413-0

5 Restivo DA, Centonze D, Alesina A, et al. Myasthenia gravis associated with SARS-CoV-2 infection. Ann Intern Med 2020;173:1027-1028. https://doi.org/10.7326/L20-0845

6 Sriwastava S, Tandon M, Kataria S, et al. New onset of ocular myasthenia gravis in a patient with COVID-19: a novel case report and literature review. J Neurol 2021;268:2690-2696. https://doi.org/10.1007/s00415-020-10263-1

7 Gracia-Ramos AE, Martin-Nares E, Hernández-Molina G. New onset of autoimmune diseases following COVID-19 diagnosis. Cells 2021;10:3592. https://doi.org/10.3390/cells10123592

8 Sacchi MC, Tamiazzo S, Stobbione P, et al. SARS-CoV-2 infection as a trigger of autoimmune response. Clin Transl Sci 2021;14:898-907. https://doi.org/10.1111/cts.12953

9 Deshpande P, Lucas M, Brunt S, et al. Low level autoantibodies can be frequently detected in the general Australian population. Pathology 2016;48:483-490. https://doi.org/10.1016/j.pathol.2016.03.014

10 Schett G, Manger B, Simon D, et al. COVID-19 revisiting inflammatory pathways of arthritis. Nat Rev Rheumatol 2020;16:465-470. https://doi.org/10.1038/s41584-020-0451-z

11 Eymard B. Anticorps dans la myasthénie [Antibodies in myasthenia gravis]. Rev Neurol (Paris). 2009;165:137-143. French. https://doi.org/10.1016/j.neurol.2008.11.020