Dropped Head Syndrome in Myasthenia Gravis After a SARS-CoV-2 Infection: Case Report

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Abstract

Introduction: The current pandemic by the SARS-CoV-2 has affected the world's general population. While the predominant presentation is with respiratory disease, neurological complications are increasingly recognized. Post-infectious immune-mediated disorders such as Guillain Barré syndrome and Myasthenia Gravis (MG) have been described.

Case presentation: We report a case with an unusual presentation of myasthenia gravis after a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection . We also present a retrospective review of the literature of all the reported cases of *de novo* myasthenia gravis associated with SARS-CoV2 infection from march-2020 to april-2021.

Conclusion: Myasthenia gravis could also be the result of an autoimmune reaction triggered by SARS-CoV-2 infection.

Introduction

The dropped head syndrome is an uncommon but extremely disabling condition that results either because of weakness of the neck extensors or increased tone of the flexor muscles [1]. A wide range of neurological conditions can present with head drop including parkinsonism or neuromuscular disorders, the first being primarily seen with a dystonic feature and the second as weakness [2].

The largest series of patients with myasthenia gravis (MG) presenting with head ptosis as the main feature was reported by *Sih et al*. They described 15 patients with dropped head syndrome with the majority being men, above 52 years old, with other muscles involved, positive acetylcholine receptors (AChR) antibodies and a notable response to treatment [3]. Other authors report that dropped head syndrome is more frequent in anti-muscle-specific tyrosine kinase (MuSK) patients compared to anti AChR [4].

Currently, infections have been suggested to be a possible causal factor for immune mediated disorders. This is supported by the molecular mimicry hypothesis, where the microorganism precipitates an immunological reaction against auto antigens through cross-reactivity mediated by T cells, B cells and antibodies [5]. There are few documented cases of MG as a post infectious disease and different theories have been raised but none has been proven. The reported cases of post infectious MG are related to infections, such as: Measles, Epstein-Barr virus, West Nile virus, Varicella Zoster and Leptospira [6,7].

We describe a case of a patient that presented with head drop and positive antibodies against AChR, two months after a SARS-CoV-2 infection.

Case Presentation

A 58–year old man was admitted to the Emergency Department with a chief complaint of weakness in the neck. 11 weeks before this presentation he required hospitalization because of viral pneumonia with a positive test of a nasopharyngeal swab for SARS-CoV-2 RNA. He subsequently developed respiratory insufficiency and sepsis needing mechanical ventilation, prone position, systemic steroids, anticoagulation and vasopressors. He began to respond and after 2 weeks he was extubated successfully. The patient was sent home with intensive physical therapy 4 weeks before the current presentation. On a follow up visit at the outpatient clinic after 8 weeks of the SARS-CoV-2 infection, he complained about having pain and discomfort on the neck with fatigue while walking.

On admission, the patient stated that he had ten days of weakness on his neck specially while standing (*see video*). The patient was still having intensive physical therapy. He denied having diplopia, dysphagia, dysphonia, fasciculations, cramps or weakness in other muscles. The medical history was unremarkable except for a diagnosis of asthma in childhood and the past history of viral pneumonia.

Relevant findings at the neurological evaluation include generalized hypotrophy and localized weakness of neck extensors (3), neck flexors (4), both deltoids (3) and both infraspinatus (3). Fatigability was present after exertion and he noticed weakness worsened in the afternoon. He could count until fifteen with a single maximal inspiration. Bedside measurements of PEF (positive expiratory force) and NIF (Negative inspiratory force) were 73 CmH20 and 59 CmH20 from predetermined values of 111 CmH20 and 208 CmH20 respectively.

He had normal initial laboratory analysis including: hemogram, renal function, electrolytes, thyroid function and creatine phosphokinase (CPK). No radicular enhancements, signs of myelopathy or soft tissue collection on cervical MRI were found. No abnormalities were seen in the nerve conduction study and electromyography (EMG).

Complementary studies with repetitive nerve stimulation (RNS) and single-fiber EMG (SFEMG) were performed. *Trapezius* and *Nasalis* RNS, showed a reduction >10% of the muscular action potential with the repetition of the stimulus (Fig. 1, panel A). SFEMG in the orbicularis oculi muscle revealed a mean consecutive difference of 64 µs, with 15 pairs (41%) having an outlier range jitter (Fig. 1, panel B). Thoracic and abdominal CT scans showed no evidence of thymoma or other space occupying lesions.

Fig. 1. Electro-diagnosis including RNS and SFEMF

Panel A. Slow RNS at 2-3 Hz with five stimuli at the trapezius muscle. Maximal Decrement is shown between the first and fourth compound muscle action potential (CMAP).

Panel B. SFEMF of the orbicularis oculi muscle. Recording shows variation of the triggering (signalled in green) and the slave potential (signalled in yellow) between fiber pairs indicating an increased Jitter.

A postsynaptic myasthenic syndrome was suspected and a trial of pyridostigmine was administered with clinical improvement. Binding antibodies against AChR in serum were elevated (56 pmol/l with a normal value <0.5 pmol/l) while MuSK antibodies were negative.

Discussion And Conclusions

Neurologic manifestations of patients infected with SARS-CoV-2 have been increasingly recognized. However, the pathophysiological mechanism is not yet known. Some authors propose that it might be a combination of the direct viral infection of nerve cells and the associated inflammatory response which can be parainfectious or post infectious [8]. MG is an autoimmune disease where antibodies bind to AChR or to other postsynaptic proteins at the neuromuscular junction. Similar to what happened with Guillain-Barré syndrome, MG could also be the result of the autoimmune reaction triggered by SARS-CoV-2 infection [9].

So far nine cases with SARS-CoV-2 infection who subsequently develop MG have been described, all with typical features including ptosis and diplopia (see Table 1). six exhibited a generalized phenotype which predominantly involved bulbar muscles and three had restricted ocular symptoms [10, 11, 12, 13, 14, 15, 16]. Two individuals with a generalized subtype had antibodies against MuSK, the others being positive for anti AChR. The majority were between 64 and 77 years of age. None of the patients had a past history of immune mediated disorders and none had thymic hyperplasia of thymoma. The time range between the SARS-CoV-2 symptoms and the onset of weakness varied from five days to eight weeks. All of the individuals had clinical improvement with treatment. Interestingly our patient presented with head ptosis as the predominant feature and time since SARS-CoV-2 symptoms to neurologic manifestations lasted 11 weeks, more than the cases reported in the literature. The patient outcome was of clinical improvement and as the majority, anti AChR were positive.

Further studies are required to investigate more about the relationship and the possible mechanisms that might cause MG after a SARS-CoV-2 infection. The unanswered question is whether we are facing a post-SARS-CoV-2 myasthenic syndrome or a manifestation of an unmasked MG being triggered by the infection.

Table 1
Review of published cases of COVID-19 associated with the development of Myasthenia gravis.

Author/Country	Patient age/sex	Medical History	Time from SARS-CoV-2 symptoms to neurological symptom onset	Clinical Presentation	MG type with antibody profile	Management	Clinical Outcome
Sriwastava et al/USA	65y/F	No	11 days	Fatigable left eyelid ptosis and diplopia.	Ocular MG AChR	Pyridostigmine	Improvement
Restivo et al/Italy	64y/M	No	5 days	Diplopia and muscular fatigability.	Generalized MG AChR	Pyridostigmine Prednisolone	Improvement
Restivo et al/Italy	68y/M	No	7 days	General muscular fatigability, diplopia, and dysphagia.	Generalized MG AChR	Immunoglobulin	Improvement
Restivo et al/Italy	71y/F	No	5 days	Bilateral ocular ptosis, diplopia, and hypophonia.	Generalized MG AChR	Plasmapheresis	Improvement
Huber et al/Germany	21y/F	No	2 weeks	Diplopia and right-sided ptosis	Ocular MG AChR	Immunoglobulin Pyridostigmine	Improvement
Pérez-Álvarez et al/Spain	48/M	Schizophrenia psoriasis and Positive ANA	15 days	Diplopia	Ocular MG AChR	None	Improvement
Muralidhar-Reddy et al/India	65y/M	Diabetes and hypertension	6 weeks	Dysphagia and dysphonia	Generalized MG AChR	Immunoglobulin Pyridostigmine, prednisolone and Azathioprine	Improvement
Muhammed et al/United Kingdom	24y/F	No	4 weeks	Diplopia, ptosis, slurred speech, dysphagia, and global limb weakness.	Generalized MG Anti-MuSK	Immunoglobulin Pyridostigmine Prednisolone	Improvement
Assini et al/Italy	77y/M	No	8 weeks	Chewing difficulty, dysphonia, diplopia, and ptosis, worsened by muscular activity	Generalized MG Anti-MuSK	Pyridostigmine Azathioprine	Improvement

Declarations

i. Ethics Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

ii. Funding (information that explains whether and by whom the research was supported)

This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

iii. Conflicts of interest/Competing interests (include appropriate disclosures) A statement specifying whether or not the authors have a conflict of interest should be included. Further details on Disclosure of Potential Conflicts of Interest can be found below.

The authors declare that they have no competing interests.

iv. Data Availability

The data that support the fndings of this study are available from the corresponding author upon reasonable request

v. Consent to participate/fort publication

There is informed consent from the patient informed consent was obtained from the patient for publication of this case report and accompanying images or videos.

vi. Authors' contributions A statement specifying the contributions of every author should be added in the text. Further details on the Criteria for Authorship can be found below.

Habib Georges Moutran Barroso: writing, editing and design.

Hellen Kreinter Rosembaun: writing, editing and design.

Carlos Martínez Rubio: editing and design.

César Forero Botero: editing and design.

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Figures

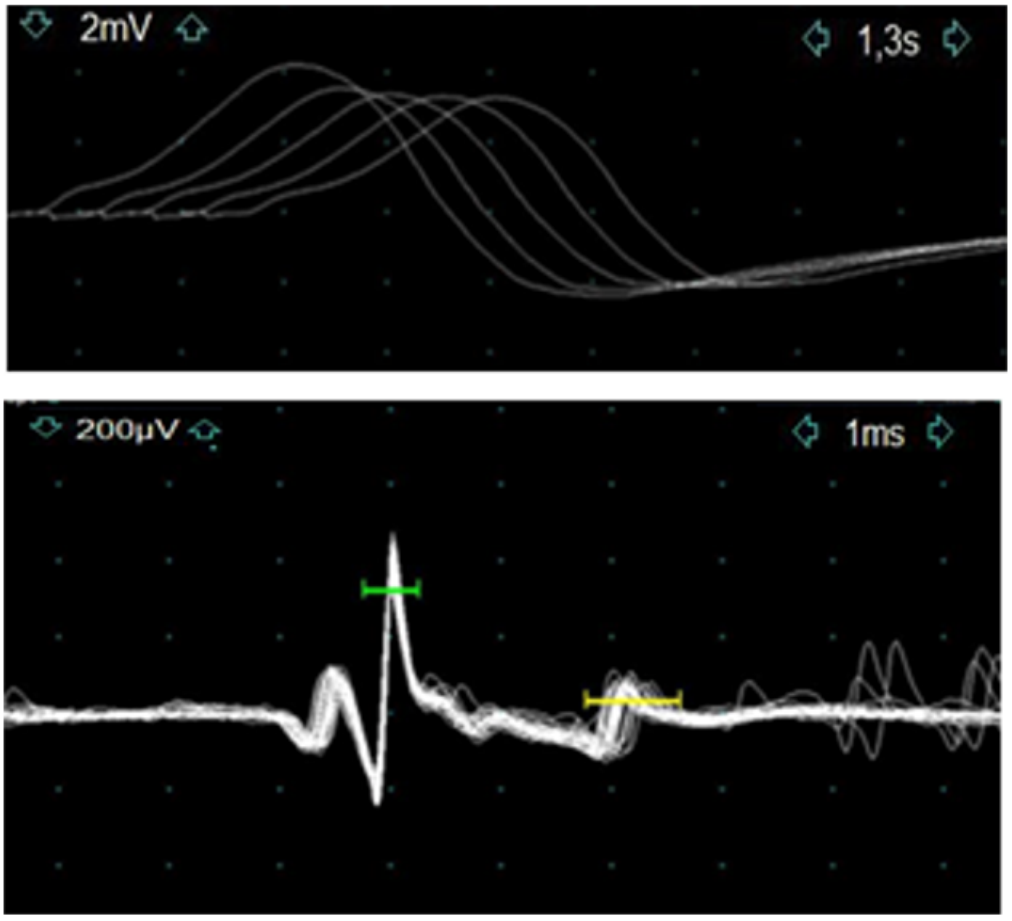

Figure 1

Electro-diagnosis including RNS and SFEMF