

## LETTER

## Management of patients with generalised myasthenia gravis and COVID-19: four case reports

### INTRODUCTION

Myasthenia gravis (MG) is an autoimmune disease characterised by fluctuating muscle weakness with potentially life-threatening symptoms due to insufficiency of respiratory muscles. Treatment usually includes immunosuppressive drugs and cholinesterase inhibitors. COVID-19 is an infection caused by the newly discovered severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), defined as a pandemic by the World Health Organisation (WHO).

Although guidelines for the management of patients with MG during the COVID-19 pandemic have been published,<sup>1</sup> these recommendations are based on theoretical considerations only, as no clinical data are available.

We describe four patients with generalised MG affected by COVID-19 (around 10% of patients in our cohort). Clinical data are summarised in [table 1](#).

### Case 1

A 36-year-old female patient, class IIa according to the Myasthenia Gravis Foundation of America (MGFA) score (166 cm, 67 kg), presented to Geneva University Hospital on 15 March 2020 with myalgia, coughing and fever >38°C on the same day. She was taking azathioprine (AZA)

50 mg, reintroduced at the end of January 2020, and pyridostigmine 60 mg five to six times per day. The last deterioration of MG had occurred in January 2020 requiring intravenous immunoglobulin (IVIG) treatment (Myasthenia Muscle Score 65/100). COVID-19 real-time PCR (RT-PCR) revealed a positive result. Chest X-ray showed no pulmonary infiltration and peak flow was at 400 mL (82%). The Myasthenia Muscle Score<sup>2</sup> was at 71/100 (bulbar and trunk involvement, leg weakness). As the immunosuppressive therapy was supposedly not effective here (small dosage and short treatment period), it was interrupted to avoid aggravation of the viral infection. On 17 March, the patient developed acute hypophonia and her Myasthenia Muscle Score dropped to 58/100. Suspecting myasthenic deterioration with bulbar involvement, she was treated with IVIG over 5 days. Hypophonia resolved rapidly and her score increased to 79/100. She was discharged home on day 10 after onset. Four weeks after onset, the main complaints consisted of anosmia and ageusia, related to COVID-19.<sup>3</sup> Her Myasthenia Muscle Score was at 90/100 and AZA was reinitiated.

### Case 2

A 36-year-old female patient, MGFA class IIIb (100 kg, 165 cm), developed fever, headache, coughing and difficulty breathing on 16 March 2020. MG had been unstable prior, with deteriorations generally linked to worsening of her Behçet's disease. The last deterioration had occurred in December 2019 (Myasthenia Muscle Score 65/100). She was taking pyridostigmine 60 mg four to five

times per day, prednisone 25 mg/day and subcutaneous immunoglobulins 12 g every 4 days. She had also been under AZA 150 mg/day, but had stopped this medication by herself 2 weeks prior to admission. COVID-19 RT-PCR revealed a positive result on 17 March. She presented to the emergency room (ER) on 17, 20 and 27 March for follow-up. Chest X-ray did not show pulmonary infiltration and peak flow remained stable (250–300 mL/min). The Myasthenia Muscle Score (on 20 March) was at 68/100, without bulbar involvement. Serology testing (on 11 April) revealed positive SARS-CoV-2 antibody indices for IgA (7.8) and IgG (6.0). The patient suffered from fluctuating symptoms, namely breathing difficulty, headaches and chest pain until May 2020. A reinfection was excluded by two additional negative RT-PCR.

### Case 3

A male patient, MGFA class IIa (55 years, 99 kg, 183 cm), presented with fever, coughing, shivering, odynophagia and fatigue since 12 March 2020, and was admitted on 19 March and tested positive for COVID-19. Chest X-ray showed no pulmonary infiltrate. He was taking pyridostigmine 3×30 mg/day and metoprolol succinate 25 mg/day (introduced by his general practitioner). Neurological examination revealed double vision and unilateral ptosis on Simpson test and no bulbar involvement (Myasthenia Muscle Score 90/100). His neurological status remained stable and he was discharged home without having received any MG-specific treatment on day 13 after

**Table 1** Clinical data of four patients with generalised gravis and SARS-CoV-2

Patient	1	2	3	4
Disease duration	6 years	4 years	2 years	3 years
MGFA classification	IIa	IIIb	IIa	V
Thymectomy	Yes	Yes	No	Yes
AB status	Anti-ACh-Rab	Anti-ACh-Rab	Negative	Anti-ACh-Rab
Main symptoms prior to admission	Ocular, bulbar, lower limb weakness.	Respiratory muscles, limb weakness.	Unilateral ptosis, double vision.	Ocular (double vision).
Comorbidities	M Basedow (resolved in 2015).	Behçet's disease, chronic migraine, hypogonadotrope hypogonadism, hypothyroidism, obesity, thymoma.	Arterial hypertension.	Obesity, left phrenic nerve damage, sleep apnoea.
MG baseline treatment	AZA 50 mg/day, pyridostigmine 60 mg 5–6×/day.	Pyridostigmine 60 mg 4–5×/day, prednisone 25 mg/day, subcutaneous immunoglobulins 12 g every 4 days.	Pyridostigmine 3×30 mg/day.	Pyridostigmine 60 mg 3×/day, rituximab 1 g every 6 months.
MG treatment change	AZA stopped during COVID-19; IVIG 5 days.	None.	None.	Pyridostigmine increased to 360 mg/day.
COVID-19 disease course	Anosmia after 4 weeks.	Fluctuating headaches and respiratory symptoms over 6 weeks.	Fully recovered after around 3 weeks.	Mechanical ventilation >14 days, tracheostoma for 9 weeks.

AZA, azathioprine; IVIG, intravenous immunoglobulin; MG, myasthenia gravis; MGFA, Myasthenia Gravis Foundation of America; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

onset. He fully recovered around 3 weeks after disease onset.

#### Case 4

A 25-year-old, obese, male patient (175 cm, 160 kg, body mass index >50) known for recidivating thymoma resected in 2017, entailing left phrenic nerve damage, was admitted to the ER on 6 April with shivering, headache, coughing and shortness of breath. He tested positive for SARS-CoV-2, but was dismissed without neurological evaluation, and returned on 9 April with fever (38.6°C), tachycardia and difficulty breathing necessitating intubation (MGFA class V). Chest X-ray showed bilateral pulmonary infiltrates, and antibiotic therapy was initiated (azithromycin, tazobactam/piperacilline). Pyridostigmine 60 mg three times a day was continued. The patient had been stable under rituximab 1 g two times per year (last dosage in December 2019; CD19 lymphocytes B count 0%, 4/ $\mu$ L absolute). Follow-up chest X-ray on 15 April showed clear regression of infiltrates. However, he presented a prolonged intubation period (>14 days) requiring high values of positive end-expiratory pressure, due to obesity<sup>4</sup> and phrenic nerve damage. The patient developed weakness of pharyngeal muscles, and after increasing the dosage of pyridostigmine (360 mg/day) tracheostoma could be removed 9 weeks after intubation.

#### DISCUSSION

Patients suffering from MG may be at high risk of developing severe symptoms when affected with COVID-19. Guidelines have been published without clinical data being available.

The evolution observed in these four patients was very variable and seemed to only partly depend on MG disease activity prior to infection, but also on other comorbidities, such as severe obesity

or additional autoimmune diseases. One possible explanation for prolonged disease duration might be an inappropriate response of the immune system in patients suffering from several autoimmune diseases.

Decisions on management of patients with generalised MG with SARS-CoV-2 infection should be taken after careful consideration of patients' individual medical history and under thorough neurological surveillance. IVIG (eg, 2 g/kg) treatment may be introduced in case of worsening of respiratory or neurological symptoms, taking also into account a potential benefit on the course of the SARS-CoV-2 infection itself.<sup>5</sup>

In our view, ongoing immunosuppressive therapy should not be stopped if it is considered to have a stabilising effect on the individual patient with MG. It may even be discussed that patients requiring immunosuppressive therapy show a prolonged but favourable outcome.

Our patients showed slight but no relevant worsening of MG symptoms during active infection, which may suggest that COVID-19 has poor impact on MG disease course. Further data would be necessary to substantiate this hypothesis.

**Annemarie Hübers** <sup>1</sup>, **Agustina M Lascano**,<sup>2</sup> **Patrice H Lalive**<sup>3</sup>

<sup>1</sup>Department of Clinical Neurosciences, University Hospitals Geneva, Geneva, Switzerland

<sup>2</sup>Division of Neurology, University Hospitals of Geneva, Geneva, Switzerland

<sup>3</sup>Department of Clinical Neurosciences, Division of Neurology, Unit of Neuroimmunology and Multiple Sclerosis, University Hospitals Geneva, Geneva, Switzerland

**Correspondence to** Dr Annemarie Hübers, University Hospitals Geneva Department of Clinical Neurosciences, Geneva 1211, Switzerland; annemarie.hubers@hcuge.ch

**Contributors** AH and AML wrote the manuscript. AH and AML examined the patients and collected the clinical data. PHL reviewed the manuscript.

**Funding** The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests** None declared.

**Patient consent for publication** On hand.

**Provenance and peer review** Not commissioned; externally peer reviewed.

This article is made freely available for use in accordance with BMJ's website terms and conditions for the duration of the covid-19 pandemic or until otherwise determined by BMJ. You may use, download and print the article for any lawful, non-commercial purpose (including text and data mining) provided that all copyright notices and trade marks are retained.

© Author(s) (or their employer(s)) 2020. No commercial re-use. See rights and permissions. Published by BMJ.



**To cite** Hübers A, Lascano AM, Lalive PH. *J Neurol Neurosurg Psychiatry* 2020;**91**:1124–1125.

Received 22 April 2020

Revised 9 June 2020

Accepted 23 June 2020

Published Online First 10 July 2020

*J Neurol Neurosurg Psychiatry* 2020;**91**:1124–1125.  
doi:10.1136/jnnp-2020-323565

#### ORCID iD

Annemarie Hübers <http://orcid.org/0000-0002-3088-0366>

#### REFERENCES

- Jacob S, Muppidi S, International MG/COVID-19 Working Group, *et al.* Guidance for the management of myasthenia gravis (Mg) and Lambert-Eaton myasthenic syndrome (LEMS) during the COVID-19 pandemic. *J Neurol Sci* 2020;412:116803.
- Gajdos P, Simon N, de Rohan-Chabot P, *et al.* [Long-term effects of plasma exchange in myasthenia. Results of a randomized study]. *Presse Med* 1983;12:939–42.
- Lechien JR, Chiesa-Estomba CM, De Siati DR, *et al.* Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the coronavirus disease (COVID-19): a multicenter European study. *Eur Arch Otorhinolaryngol* 2020;117.
- Lighter J, Phillips M, Hochman S, *et al.* Obesity in patients younger than 60 years is a risk factor for Covid-19 hospital admission. *Clin Infect Dis* 2020. doi:10.1093/cid/cia415
- Wei X, Liu T, Bai H, *et al.* High dose IVIg as a therapeutic option for deteriorating patients with COVID-19. *Open Forum Infect Dis* 2020;48:1–6. eCollection 2020 Mar.