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Clinical short communication

Description of 3 patients with myasthenia gravis and COVID-19

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1. Introduction

Concern regarding patients with myasthenia gravis during the COVID-19 pandemic is twofold; firstly, as a result of immune suppression, they could be more severely affected, and secondly that there would be a high incidence of MG exacerbation, especially with respiratory failure [1]. Furthermore, treatment considerations in MG with COVID-19 are more complex. Steroids may have beneficial or detrimental effects on COVID-19 depending on the stage of infection. In the early stages, steroid treatment could prolong viremia and impair viral clearance, but in contrast, glucocorticoids inhibit immune cell migration and chemokines production and therefore could be beneficial during ARDS [2,3,8]. In addition, maintenance plasma exchange could expose patients to COVID-19 infection [4]. Lastly, some of the investigational drugs currently used to treat COVID-19 may exacerbate MG, such as hydroxychloroquine [5] and azithromycin [4].

Here we present the details and course of 3 patients (Table 1) with generalized AChR-Ab seropositive MG with COVID-19. To our knowledge, these are the first reported cases of resolved COVID-19 in MG.

2. Case 1

A 38-year-old woman with a 10 yr history of MG. She experienced two severe exacerbations in the past, both requiring invasive ventilation. At the time of COVID-19 infection she received maintenance IVIG, prednisone (25 mg once per day), and pyridostigmine (60 mg 5 times per day). She experienced worsening of her myasthenic symptoms over the month preceding COVID-19; consisting of fever and rigors, followed by malaise, myalgia and syncope resulting in minor head trauma.

Upon admission she had a fever of 38 °C, mild tachypnea shortness of breath and was hemodynamically stable. Myasthenic symptoms consisted of unilateral ptosis, hypophonic, nasal speech, and mild proximal limb weakness. Blood gases demonstrated normal pH (7.416) with mild hypocarbia (pCO2 34 mmHg), and creatine kinase levels were not elevated (57 IU/L). Chest CT demonstrated patchy ground glass opacities in the right lung, and head CT showed a fracture of the right temporal bone. RT-PCR for SARS-CoV-2 was positive with a CALL score of 6 [6].

She was admitted to the ICU where treatment was started with hydroxychloroquine (600 mg bid for one day, then 200 mg tid for 9 more days), lopinavir (400 mg bid) and ritonavir (100 mg bid) for...
BCV and NHFC. She was weaned off non-invasive support, and a few days later her respiratory parameters worsened. We hypothesized that these muscles had become preferentially fatigued due to the increased respiratory effort due to the infection and she responded within 24 h to continuous BCV and NHFC. She was weaned off respiratory support, and a few days later she was discharged with minimal residual myasthenic symptoms.

3. Case 2

A 66-year-old man, with a history of diabetes and hypertension, was diagnosed 1-year prior to COVID-19 infection with MG. Presentation was ocular, but became generalized within 3–4 weeks, at which point he required hospitalization and treatment with plasmapheresis and steroids. A subsequent relapse within 2 weeks of discharge required a second hospitalization for a course of plasmapheresis. He was discharged with steroids (increased gradually to 60 mg per day), azathioprine (increased gradually to 150 mg per day) and pyridostigmine. During March 2020 she presented with ageusia and anosmia, followed by fever of 38.8 °C, myalgia, cough, headache, rash, and chemoysis. She was abroad at the time, in an area with high COVID-19 prevalence, but without access to SARS-CoV-2 testing. COVID-19 was initially diagnosed clinically, but she later had serological testing which was positive for SARS-CoV-2 antibodies. Her symptoms resolved slowly over 2-weeks, without hospitalization or exacerbation of MG.

4. Case 3

A 42-year-old woman, with a 14 yr history of generalized MG who had experienced two major exacerbations in the past, both requiring intubation in ICU, in 2010 and 2014. In the past, she received azathioprine, and, subsequently Rituximab. Her last dose of Rituximab was more than 3 years before COVID-19 infection. At the time of infection she received monthly IVIg, prednisone (10 mg once per day), and pyridostigmine. During March 2020 she presented with ageusia and anosmia, followed by fever of 38.8 °C, myalgia, cough, headache, rash, and chemoysis. She was abroad at the time, in an area with high COVID-19 prevalence, but without access to SARS-CoV-2 testing. COVID-19 was initially diagnosed clinically, but she later had serological testing which was positive for SARS-CoV-2 antibodies. Her symptoms resolved slowly over 2-weeks, without hospitalization or exacerbation of MG.

5. Discussion

Despite immunosuppressive therapy, all patients had a favorable outcome. Our preliminary observations are that treatment with hydroxychloroquine and anti-retroviral therapy, increasing steroid doses and switching maintenance plasmapheresis with IVIg were all tolerated well.

Of the 3 patients described, MG exacerbation occurred only in one. In this case, exacerbation of MG began prior to COVID-19 infection, and required non-invasive ventilator support.

Interestingly, exacerbation of ventilation parameters occurred whilst limb muscles were actually improving. Selective exacerbation of the respiratory muscles could be a feature of drug-related MG exacerbation [7] or may be due to increased respiratory effort due to the pneumonia; prophylactic pressure support could prevent fatigue and potentially avoid the need for invasive ventilation.

In addition, corticosteroids have recently been shown to reduce mortality in COVID-19 patients requiring respiratory support [8] and could therefore be particularly beneficial in myasthenic patients suffering from this infection.

We suggest that immunosuppressive therapies, and in particular steroids, should be continued in MG patients with COVID-19. IVIg may be a good alternative interim solution to maintenance plasmapheresis, during active COVID-19 infection.

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**Table 1**

Characteristics of patients with myasthenia gravis and COVID19.

| Case | Year of MG diagnosis | MG symptoms during SARS-CoV-2 infection | Treatment received for COVID 19 infection | Outcome |
|------|----------------------|----------------------------------------|------------------------------------------|---------|
| 1    | 2010                 | Ptosis, respiratory muscle weakness, proximal limb weakness | Plasmapheresis, hydroxychloroquine, lopinavir, ritonavir | Discharged home. Recovered at home |
| 2    | 2019                 | None                                    | None                                     | No change |
| 3    | 2006 N/A             | None                                    | None                                     | Discharged home. |
Funding

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

References

[1] A.C. Guidon, A.A. Amato, COVID-19 and neuromuscular disorders, Neurology (2020). https://doi.org/10.1212/WNL.0000000000009566.

[2] C. Perricone, P. Triggianese, E. Bartoloni, et al., The anti-viral facet of anti-rheumatic drugs: lessons from COVID-19, J. Autoimmun. (2020) 102468.

[3] B. Russell, C. Moss, G. George, et al., Associations between immune-suppressive and stimulating drugs and novel COVID-19—a systematic review of current evidence, Ecancermedicalscience 14 (2020) 1022.

[4] International MGC-WG, Jacob S, Muppidi S, et al. guidance for the management of myasthenia gravis (MG) and Lambert-Eaton myasthenic syndrome (LEMS) during the COVID-19 pandemic, J. Neurol. Sci. 412 (2020) 116803.

[5] D. Varan, H. Kucuk, A. Tufan, Myasthenia gravis due to hydroxychloroquine, Reumatismo 67 (2016) 125.

[6] D. Ji, D. Zhang, J. Xu, et al., Prediction for progression risk in patients with COVID-19 pneumonia: the CALL score, Clin. Infect. Dis. (2020), https://doi.org/10.1093/cid/ciaa414.

[7] Z. Argov, F.L. Mastaglia, Endocrine and toxic myopathies, in: D. Hilton-Jones, G. Karpati, K. Bushby, R.C. Griggs (Eds.), Disorders of Voluntary Muscle, 8 ed, Cambridge University Press, Cambridge, 2010, pp. 471–483.

[8] Effect of Dexamethasone in Hospitalized Patients with COVID-19—Preliminary Report. vol. 22 Jun 2020 (preprint). https://www.medrxiv.org/content/10.1101/2020.06.22.20137273v1.full.pdf.