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LETTERS TO THE EDITOR

Comment on "Predictive factors for a severe course of COVID-19 infection in myasthenia gravis patients with an overall impact on myasthenic status and survival" by Jakubíková et al.

Dear Editor,

We read with interest the report by Jakubíková et al. [1] on predictive factors affecting myasthenia gravis (MG) and survival in severe COVID-19 patients at two centers in the Czech Republic.

Although the study was certainly conducted with good methodology, our careful reading raised some points of discussion.

First, we were impressed by the number of patients enrolled. The authors should provide information regarding the global incidence of COVID-19 in the Czech Republic and the prevalence of MG at the two centers in Prague and Brno during the pandemic.

Second, it was unclear to us whether the study was conducted cross-sectionally or with a prospective or retrospective design. The time course and interplay of neurological and respiratory symptomatology between MG and COVID-19 are difficult to understand using a cross-sectional design. The duration of follow-up would be interesting to know.

Third, the authors should specify whether patients were followed and treated in a neurology ward or in an intensive care unit, because MG patients might receive different treatments in the two settings [2]. Interestingly, among the 93 patients with confirmed COVID-19 infection and MG, only 34 were hospitalized. Surprisingly, no patient was in Stage V according to the Myasthenia Gravis Foundation of America classification [2], that is, in myasthenic crisis (MC), either before, during, or after the infection.

Finally, Jakubíková et al. [1] do not provide radiological details to better define the severity of COVID-19 infection, especially for cases falling into categories scored as 5 and 6. Radiological findings, in our view, are crucial. Different radiological and functional patterns have been described during the course of COVID-19 respiratory failure: patients with lung damage who fulfill acute respiratory distress (ARDS) criteria (type H) and patients with "non-ARDS" (type L) respiratory failure, with lower lung parenchymal involvement [3]. Patients with the more critical "pattern H" exhibit widespread bilateral lung consolidations on computed tomography (CT) scan and an alteration of gas exchanges often requiring immediate mechanical ventilation (MV). In such cases, respiratory worsening can be plausibly attributed to SARS-CoV-2 infection and not to MG, whereas the detection of atelectasis on CT scan in patients with minimal parenchymal consolidation (type L) could suggest a diaphragm dysfunction due to exacerbation of MG or a MC (i.e., myasthenic crisis).

Another important issue concerns the prognostic role of forced vital capacity (FVC) prior to infection in MG patients affected by COVID-19 pneumonia. This result needs comments. Although many patients with generalized MG have a restrictive pattern on pulmonary function testing and evidence of ventilatory muscle weakness, FVC may provide a less sensitive measure than maximal static respiratory mouth pressure and dynamic maneuvers such as maximal voluntary ventilation [4]. MG is characterized by fluctuating weakness and fatigability, which may be reversible after rest, involving specific muscle groups, namely, respiratory muscles. This feature could make static respiratory functional measurements less reliable in predicting prognosis than in other neuromuscular diseases (i.e., amyotrophic lateral sclerosis or muscular dystrophies), where the weakness is progressive and not subject to fluctuations.

Finally, the authors [1] stated that long-term use of oral corticosteroids (CS) before COVID-19 increased the risk of severe pneumonia and therefore they suggest avoiding increased dosage during SARS-CoV-2 infection. This assumption is currently unproven and requires caution. Although it is true that high-dose CS, especially given intravenously, should be used with caution, as it can worsen weakness in as many as one third of nonventilated MG patients, oral CS given for months followed by low doses often for years are the first-line immunotherapy recommended for patients who cannot be adequately treated with symptomatic anticholinergic inhibitors.

CS, although related to several adverse effects, are effective treatment in MG, with impact on autoimmune mechanisms by various manners: by binding the glucocorticoid receptor, by suppressing the glucocorticoid receptor-mediated apoptosis of autoreactive cells, and by the release of proinflammatory cytokines [2,4]. In addition, the recent RECOVERY trial, a randomized, controlled, open-label study [5] clearly showed that among hospitalized patients with COVID-19, the use of dexamethasone (at a dose of 6 mg once daily) resulted in significantly lower 28-day mortality than usual care in subjects who were receiving oxygen and MV. Therefore, we should encourage the use of this treatment in cases falling into this category, regardless of the underlying disease, until there is no other

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evidence from randomized trials. Jakubíková et al. [1] propose some interesting conclusions; however, essential data validated by large longitudinal studies are missing. Currently, cautious statements are advisable about predictive factors of outcome in MG during COVID-19 infection.

KEYWORDS

COVID-19, myasthenia gravis, myasthenic crisis

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

AUTHOR CONTRIBUTIONS

Giuliana Galassi: Conceptualization (equal), data curation (equal), formal analysis (equal), methodology (equal), supervision (equal), writing–original draft (equal), writing–review & editing (equal). **Alessandro Marchioni:** Data curation (supporting), investigation (supporting), writing–original draft (equal), writing–review & editing (equal).

ETHICAL APPROVAL

This article does not contain any studies with human participants or animals performed by any of the authors.

DATA AVAILABILITY STATEMENT

The datasets generated and analysed during the study are available-from the corresponding author on a reasonable request.

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