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COVID-19

The Janus faces of SARS-COV-2 infection in myasthenia gravis and myasthenic crisis

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To the Editor

With interest we read the article by Rodrigues et al. [1] focusing on myasthenic exacerbations and crisis (MC) in patients infected by SARS-CoV-2. The report concluded that the mortality rate associated with COVID-19 might be considerably higher than for MC due to other causes, reaching the impressive rate of 50% [1]. This work retrospectively includes 8 adults with myasthenia gravis (MG) admitted at two hospitals in Brazil with confirmed diagnosis of COVID-19 infection [1]. Although the study was conducted with good methodology, a careful reading raises key questions. Is this high death rate due to multiorgan failure or to COVID-19 pneumonia or to enhanced autoimmune dysregulation or to concurrent treatments exacerbating MG?

My first concern is the following: none of the 8 patients according to the pre-admission state met the diagnostic criteria of MC [2, 3], but there was worsening of weakness, which required mechanical ventilation (MV) in 6 patients. Missing are the clinical scores at the admission time (i.e. Myasthenia Gravis Foundation of America, MGFA severity score) [2].

Second, did the authors consider the involvement of more than 50% of the lung on computed tomography (CT-scan) an accepted criteria for severity in COVID-19 pneumonia? This method should be taken cautiously, because it may lead to overuse of CT-scan, which is certainly the routine imaging modality for diagnosis COVID-19 pneumonia. Indeed, CT-scan findings of some patients may not be consistent with their clinical symptoms [4]. In the 5 patients who had no lung involvement above 50%, the neurological worsening could be attributed simply to SARS-CoV-2 infection ? Indeed, it is well known that viral infections are major external causal factors in nearly all autoimmune disorders, as well as a confirmed trigger of MC, through an augmentation of T cell signaling causing a pro-inflammatory environment due to a hyper-reactive antiviral immune response and epitope spreading [3] .

Third, among 3558 patients with MG registered in the French database for rare disorders, 34 (0.96%) had COVID-19; by the end of the study period, 28 patients recovered from COVID-19, 1 remained affected, and 5 died [5]; only high MGFA class before COVID-19 was independently associated with severe COVID-19 factors, and the type of MG treatment had no effect on severity [5]. Interestingly, Murthy et al. [6] showed distinct differences between patients with MC and those with respiratory failure due to pulmonary complications of COVID-19: the patients with MC were young women in high grade MGFA Class, whereas subjects with respiratory failure due to pulmonary complications of COVID-19 were elderly men with stable disease state, pharmacological remission or MGFA Class I. Initial severity and worsening of myasthenic weakness was the only differentiating clinical feature between the two types of respiratory failure [6].

Notably, out of the 8 cases of Rodrigues et al. [1], 2 who do not need MV were taking steroids (CS) and among the survivors from death, most used CS chronically; on the other hand, 4 of those mechanically ventilated received dexamethasone. The views on the use of CS during COVID-19 infection evolved with the time and some authors [7] claim that their use remains controversial, although important studies point to benefits [8]. In Sole' et al. series [5], CS were not significantly associated with poor COVID-19 outcome, but had no protective effect (whatever the dose was used). The RECOVERY trial [8] 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.

Fourth, the authors gave intravenous immunoglobulin (IVIG) and plasma exchange (PE) as therapy to 5 out of

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8 cases; interestingly, 3 did not receive treatment for MG exacerbation, while they were taking CS, tocilizumab, and antibiotics [1]. Largely, before the COVID-19 pandemic outbreak, the treatment for MC either impending or manifest has been based on PE and IVIG [3]. We fully agree with Rodrigues et al. [1] that IVIG or PE treatment should be tailored to patient clinical profile, but a shared component between the immunopathogenesis of COVID-19 and MC is cytokine dysregulation, which promotes the increase of pro-inflammatory cytokines and chemokines, that attack organ systems, particularly the lung, leading to the acute respiratory distress syndrome (ARDS) [3]. While we treat our patients, we have to keep in mind that a shared component between the immunopathogenesis of COVID-19 and MC or MG exacerbations is the cytokine dysregulation, which promotes the increase of pro-inflammatory cytokines and chemokines attacking organ systems [3]. By concluding, there are several therapeutic dilemmas, which Rodrigues et al. [1] pointed out including the side effects of treatments, like IVIG and PE. Ongoing experiences will be helpful.

Declarations

Ethical approval and Informed consent None.

Conflict of interest The author declares no competing interests.

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