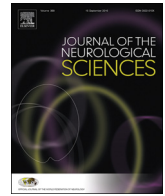




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Letter to the Editor

Diagnosing myasthenic crisis in SARS-CoV-2 infected patients requires adherence to appropriate criteria



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Letter to the Editor

With interest we read the article by Delly et al. about a 56 years old female with myasthenia gravis (MG) since 5y for which she received pyridostigmine (240 mg/d), prednisone (40 mg/d), and intravenous immunoglobulins (IVIG, 650 mg/kg within 2d every 2 weeks), and with undetermined mixed connective tissue disease for which she received chloroquine (400 mg/d), who developed myasthenic crisis with respiratory insufficiency during pneumonia due to infection with SARS-CoV-2 [1]. Though the patient received vancomycin, cefepime, and azithromycin and prednisone was increased to 80 mg/d, she lastly had to be intubated and required mechanical ventilation [1]. The patient recovered after 25 days under repeated courses of IVIG [1]. It was concluded that the index patient is the first in the literature experiencing a myasthenic crisis in association with a SARS-CoV-2 infection and that registries of MG patients with SARS-CoV-2 infection should be established [1]. We have the following comments and concerns.

The main shortcoming of the report is that the diagnosis “myasthenic crisis” is not well supported and substantiated. Missing are the application of clinical scores (e.g. MGFA severity score), serum levels of the acetyl-cholin receptor antibodies, lung function parameters, repetitive nerve stimulation, and single-fiber EMG results. It is also not reported if there was myosis or mydriasis. A myasthenic crisis is usually associated with mydriasis [2]. Respiratory insufficiency could be simply explained by pneumonia or could be due to other causes, such as brain stem involvement or drugs. It is also well known that chloroquine may cause secondary myopathy, why chloroquine-induced myopathy must be excluded [3]. We should know upon which criteria myasthenic crisis was diagnosed and which differential diagnoses were considered.

Assuming that the clinical deterioration truly represents a myasthenic crisis, possible triggers should be carefully assessed. In addition to the SARS-CoV-2 infection, possible triggers could be underdosing of pyridostigmine, increase of prednisone to 80 mg/d, discontinuation of oral pyridostigmine after intubation, azithromycin, chloroquine, or other drugs not mentioned in the report. From chloroquine and hydroxy-chloroquine it is well-known that they may induce development of MG or may worsen clinical manifestations of MG [4–8]. Also from azithromycin it is well known that it may worsen MG or even trigger a

myasthenic crisis [9,10]. Also from vancomycin it is known that it may trigger a myasthenic crisis [11].

The authors claim that the reported patient is the first with a myasthenic crisis in association with a SARS-CoV-2 infection [1]. This is not the case since several patients with deterioration of MG manifestations during an infection with SARS-CoV-2 have been reported [12]. There are also reports showing that MG does not exacerbate or worsen during an infection with SARS-CoV-2 [13].

A further shortcoming is that acetyl-cholin-esterase inhibitors were discontinued with the intubation. We should know why, for example, neostigmine, which can be given intravenously, was not applied. We also should know why plasma exchange was not considered.

We should know why chloroquine was resumed although it is meanwhile known that it is ineffective in SARS-CoV-2 infected patients. Also, it cannot be excluded that muscle weakness was due to chloroquine myopathy or that chloroquine deteriorated MG manifestations. Furthermore, it is not comprehensible why the patient received steroids during five years [1]. Steroids cause severe side effects, including myopathy, and should be given as bridging until immunosuppressants had become effective but not as long-term treatment. We should know why azathioprine, mycophenolate mofetil, cyclosporine, methotrexate, tacrolimus, rituximab, tocilizumab, or oculizumab were not given to save steroids. We should also know if IVIG were ineffective or not. Missing are the drugs the patient was taking in addition to the anti-MG medication.

Steroids should not be discontinued in symptomatic SARS-CoV-2 infected patients as there are indications that in-hospital mortality of SARS-CoV-2 infected patients is lower if treated with steroids compared to those not under glucocorticoids [14].

We also should know which type of connective tissue disorder was diagnosed in the index patient and if alternative treatments to chloroquine had been considered.

Overall, a myasthenic crisis should be diagnosed according to established criteria, severity of myasthenia should be quantified, alternative causes of respiratory insufficiency should be excluded before attributing it to SARS-CoV-2, all drugs an MG patient is regularly taking should be listed, steroids should not be given as a maintenance treatment of MG, and triggering agents such as chloroquine, azithromycin,

or vancomycin should be avoided in SARS-CoV-2 infected MG patients.

Declaration of Competing Interest

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