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LETTERS TO THE EDITOR

MuSK-positive myasthenia may be triggered not only by SARS-CoV-2

We read with interest the article by Assini et al. [1], regarding a 77-year-old male who developed ptosis, diplopia, dysarthria and chewing difficulty 2 months after a mild infection with SARS-CoV-2, manifesting with fever and bilateral pneumonia (COVID-19), without necessitating continuous positive airway pressure, bilevel positive airway pressure, or mechanical ventilation. Evaluation revealed muscle-specific tyrosine-kinase (MuSK)-positive myasthenia gravis (MG; MuSK-MG), which did not respond to pyridostigmine but to azathioprine [1]. We have the following comments and concerns with regard to the article.

The first comment is that it remains unsubstantiated that SARS-CoV-2 triggered MuSK-MG. The statements that "the unusually late onset of MuSK-MG" and "the latency of 2 months between COVID-19 and onset of MG" favour the viral origin of MuSK-MG are no arguments in favour of this aetiology. On the contrary, the delay of 2 months between onset of COVID-MG and onset of MuSK-MG argues against a causal relation. It is also unclear why a late-onset at age 77 years should be an argument in favour of the viral hypothesis.

A second concern is that the treatment the patient received for COVID-19 was not detailed. We should know whether the patient received steroids, chloroquine, azithromycin, lopinavir, ritonavir or tocilizumab. It is well known that azithromycin may exacerbate MG [2] or may even trigger myasthenic crisis [3]. Chloroquine has been reported to induce MG [4] and to cause myasthenic syndrome [5]. There is also one report of a 71-year-old male in whom MG was exacerbated with ritonavir treatment. We should also be informed of the length of time for which any of these compounds was given.

A third point to note is that azathioprine cannot be made responsible for the rapid recovery of MuSK-MG. The beneficial effect of azathioprine does not become evident earlier than 3–6 months after starting the therapy, which is why MG patients usually receive steroids to bridge the latency period until azathioprine becomes effective. We should also be told whether steroids were given as well, and should be given an explanation for how azathioprine already exhibited a beneficial effect 2 months after initiation. A further argument against a beneficial effect of azathioprine is that it can be ineffective for the treatment of MuSK-positive MG.

A fourth concern is that Guillain–Barre syndrome (GBS), affecting the cranial nerves was not adequately excluded. It is well known that SARS-CoV-2 can trigger GBS, even weeks after COVID-19. Thus, we should know the results of nerve conduction studies and of cerebrospinal fluid investigations.

Since it was speculated that COVID-19 unmasked a previously non-symptomatic MG, we should know if the history was positive for clinical manifestations of a transmission disorder prior to COVID-19.

Although bulbar MG is frequently associated with affection of respiratory muscles, it is mentioned that respiratory muscles were not affected. Were lung function tests carried out to substantiate this statement?

Overall, the appealing report has a number of limitations, which should be addressed before concluding that SARS-CoV-2 caused MuSK-MG. The results of electrophysiological investigations should be provided, GBS should be excluded, and anti-COVID-19 drugs should be excluded as triggers of MuSK-MG.

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KEYWORDS

COVID-19, immunosuppression, myasthenia, neuromuscular transmission, SARS-CoV-2

CONFLICT OF INTERESTS

None.

AUTHOR CONTRIBUTIONS

JF: design, literature search, discussion, first draft, critical comments, final approval, FS: literature search, discussion, critical comments, final approval.

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