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SARS-CoV-2 may unravel metabolic myopathy mistaken for myasthenia

El SARS-CoV-2 puede desentrañar la miopatía metabólica confundida con la miastenia

Dear Editor,

With interest we read the article by Maresma et al. about an 86yo male with a previous history of arterial hypertension, diabetes, atrial fibrillation, and hyperuricemia who was admitted for COVID-19 manifesting with bilateral pneumonia.[1] He was treated with azithromycin, ceftriaxone, and steroids intravenously.[1] On hospital day-4 he experienced generalised fatigue, proximal muscle weakness of the lower limbs, bilateral ptosis, hyporeflexia, and dysarthria.[1] He was diagnosed with seronegative myasthenia gravis (MG) and treated with pyridostigmine, steroids, and immunoglobulins.[1] The study has a number of limitations and raises the following comments and concerns.

We do not agree with the diagnosis MG. The patient was tested negative for AchR-antibodies and anti-MUSK antibodies. The results of repetitive nerve stimulation (RNS), edrophonium (tensilon) test, and single fibre electromyography (SF-EMG) were not provided. Furthermore, antibodies against LRP4, agrin or titin were not determined. More likely than MG the patient suffered from a mitochondrial disorder (MID), which exacerbated upon the viral infection or the myotoxic treatment applied. Myotoxic is azithromycin, which may trigger or exacerbate MG and steroids, which may cause mitochondrial myopathy. Arguments for a MID are the previous history of arterial hypertension, diabetes, hyperuricemia, atrial fibrillation, and QT-prolongation.

Missing is an extensive family history. Since MIDs are inherited from the mother in case of a causative mtDNA variant or from the father or mother in case of a nuclear variant, we should know if either the father or mother were clinically affected or if any other first degree relative had developed clinical manifestations of a MID.

Since MIDs are frequently multisystem disorders, MID patients should be prospectively investigated for multiorgan involvement. Of particular interest are the MRI of the brain electroencephalography, and cardiologic investigations. Cardiac involvement may manifest as cardiomyopathy or arrhythmias as in the index case. Cerebral MRI with contrast medium should exclude a cerebral cause of muscle weakness, such as Bickerstaff encephalitis, immune encephalitis, acute, disseminated encephalomyelitis (ADEM), or viral encephalitis. How did the authors exclude Guillain Barre syndrome with involvement of the cranial nerves, increasingly recognised as a complication of COVID-19?[2,3]

The patient had received steroids already on hospital day-1 for SARS-CoV-2 associated pneumonia, which he received again for suspected MG. We should be told how to explain that he developed MG under an anti-MG treatment.

We do not agree with the statement that no other cases of SARS-CoV-2 triggered MG have been reported.[1] The first study that demonstrated MG due to an infection with SARS-CoV-2 was published by Restivo et al. who reported three cases of SARS-CoV-2 triggered MG.[4] Since then, SARS-CoV-2 triggered MG had been reported also by others.[5]

Overall, the interesting report has limitations which should be addressed before concluding that SARS-CoV-2 may trigger MG. Since the diagnosis MG remains poorly supported, it cannot be excluded that the index patient indeed had a MID, which worsened after application of macrolids and steroids. Myotoxic drugs should be avoided in SARS-CoV-2 infected patients as they may exacerbate or worsen pre-existing NMD.

Author's contribution

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

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Conflicts of interest

The authors declare no conflicts of interest.

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