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Immunocompromised myasthenia gravis patient not infected with SARS-CoV-2 after close exposure — what is the risk of COVID-19?

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To the Editors:

Since the outbreak of the Coronavirus Disease 2019 (COVID-19) pandemic, there has been ongoing debate about the risk for immunocompromised patients of developing a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Among them are individuals with myasthenia gravis (MG) who often require immunosuppressive therapy, as well as symptomatic treatment. Immunosuppression may contribute to the treatment of MG exacerbations (e.g. plasmapheresis) or constitute a form of maintenance therapy (e.g. steroids or oral immunosuppressants) [1]. Due to the possibility of acute respiratory failure in the course of both MG and COVID-19, patients with the coexistence of these conditions may experience severe outcomes [2]. So far, it is known that SARS-CoV-2 can be transmitted between people via respiratory secretions, respiratory droplets and saliva of infected individuals, either through direct contact or by using contaminated objects. Unfortunately, people can infect others before developing disease symptoms. Therefore, the largest clusters of new cases are mainly observed within households [3].

We present a case report of a 42-year-old woman with a diagnosis of generalised myasthenia gravis who was exposed to three forms of immunosuppression and to a symptomatic infection with SARS-CoV-2 in the other members of her three-person household over a short period of time.

The patient experienced the first symptoms of MG in the form of ptosis in 2003. The diagnosis was established in the same year by the finding of disturbances of neuromuscular transmission in a repetitive nerve stimulation test, the presence of anti-acetylcholine receptor antibody in the serum, and persistent thymus in chest computed tomography. Three years later, the patient developed generalised MG. As her symptoms had been controlled satisfactorily with pyridostigmine bromide and the short-term oral prednisone therapy was used only during the disease exacerbation periods (a therapeutic regimen inconsistent with the treatment guidelines for MG), she decided not to undergo thymectomy.

In 2013, azathioprine was added to the treatment regimen due to the progression of fatigue and generalised weakness, but that drug was discontinued after three months because of gastrointestinal adverse events. In 2014, the patient became pregnant and used only pyridostigmine bromide. In 2017, due to MG exacerbation, steroid therapy was resumed, with a partial clinical improvement. Since June 2018, the patient has been using pyridostigmine bromide (420 mg/day), prednisone (20 mg/day), and mycophenolate mofetil (MMF) (1,000 mg/day).

On 16 February 2020, the patient was admitted to her local Neurology Department with a diagnosis of impending myasthenic crisis. For this reason, therapeutic cycles of plasma exchange were performed, with a total of 7,600 ml of plasma replaced, resulting in an improvement from class IVA (severe weakness predominantly affecting limb and/or axial muscles) to class IIA (mild weakness predominantly affecting limb and/or axial muscles), according to the clinical classification of the Myasthenia Gravis Foundation of America [4]. After the patient's discharge on 24 February, the pre-hospitalisation

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doses of prednisone and MMF were maintained to avoid another MG exacerbation, despite a potential risk of SARS-CoV-2 infection.

Unfortunately, on 10 April, the patient's 45-year-old husband, with a history of arterial hypertension, was diagnosed with COVID-19 after a five-day period of runny nose, dry cough without shortness of breath, low-grade fever, muscle pain, and loss of smell. The following day, the same infection was recognised in their five-year-old son, with a history of atypical dermatitis, who had been complaining of a dry cough, low-grade fever, vomiting and abdominal pain for two days. The diagnosis of COVID-19 in both cases was established on a basis of symptoms and virus detection in nasopharyngeal swabs by the use of real-time reverse-transcription polymerase chain reaction (rRT-PCR). As infected persons, the father and the son both underwent two weeks of isolation, and treatment with azithromycin for the first five days from the diagnosis. After the first week of isolation, both infected individuals had completely recovered, and three consecutive rRT-PCR tests of their nasopharyngeal swabs did not reveal the presence of the virus. During this time, despite the use of dual immunosuppressive therapy and a six-day period of daily contact with household members with the symptomatic SARS-CoV-2 infection, the woman was not infected: three rRT-PCR tests of her nasopharyngeal swabs were negative. Serum tests performed in the husband and son two months later revealed positive titres of IgG and IgA antibodies against SARS-CoV-2, with negative IgM titres. The woman was seronegative for SARS-CoV-2 in all three classes of antibodies analysed, and had not developed any symptoms of COVID-19.

Currently, no conclusive data is available on the risk of using immunosuppressive therapies in MG during the COVID-19 pandemic. The international MG/COVID-19 working group suggests the maintenance of current treatment and recommends that patients on immunosuppressive medications should practice extra-vigilant social distancing [2]. Anand et al. described the clinical course of COVID-19 in four hospitalised MG patients with acetylcholine receptor antibodies and concomitant diseases. Three of them were aged over 60 years and were using MMF (two at a daily dose of 2,000 mg and one at a dose of 1,500 mg) as well as prednisone (5 mg every other day, 15 mg every day, and 30 mg every day, respectively) before the SARS-CoV-2 infection was confirmed. MMF was maintained in all patients on admission, and the mildest course of COVID-19 was reported in the subject with the lowest baseline dose of this medication.

However, the authors did not disclose the circumstances nor the route of the SARS-CoV-2 infection [5]. Preliminary data suggests that the incidence and morbidity rates of COVID-19 in patients on immunosupressive therapies may not differ very much from those of the general population [6]. Nevertheless, it remains unclear which therapeutic strategy should be adopted in an immunosuppressed MG patient exposed to close contact with individuals infected with SARS-CoV-2. Furthermore, the question remains open as to whether the risk of SARS-CoV-2 infection is dependent on a dose of the immunosuppressive drug, and whether such treatment may have a potentially protective effect against this disease. It should also be noted that, compared to subjects reported by Anand et al., our patient used a lower MMF dose, was younger, and had no comorbidities other than MG, which certainly reduced her risk of developing the infection [5].

The presented case of an immunocompromised MG patient who was the only member of her three-person household not infected with SARS-CoV-2, presents the risk associated with immunosuppression in the times of the COVID-19 pandemic, a topic which still has not been fully determined.

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