Case report

COVID-19 in Myasthenia Gravis: The Double Whammy

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Abstract

Coronavirus disease 2019 (COVID-19) co-infection in patients with myasthenia gravis has not been well described. Our primary aim is to describe the course of illness of a myasthenia patient who developed repeated episodes of myasthenic crisis along with severe COVID-19 infection. This case highlights the need to monitor the immune response to the infection accurately, and treatment of myasthenia gravis with COVID-19 should be tailored to the individual patient.

Keywords: COVID-19, Myasthenia gravis, Myasthenic crisis

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Introduction

Myasthenia gravis (MG) is an autoimmune disease that mainly affects the neuromuscular junction and results in fatigable weakness of the bulbar, limb, and ocular muscles. Myasthenic patients can stay in remission with treatment and show exacerbation with worsening disease symptoms. In some cases, the patient may experience a neurologic emergency characterized by respiratory muscle failure called a myasthenic crisis. This crisis is mainly precipitated by superadded infection. (1)

In the coronavirus disease 2019 (COVID-19) pandemic, patients with myasthenia gravis can be considered at high risk for poor outcomes due to immune suppressive therapy, existing respiratory weakness, exacerbation due to viral infection, and multiple drug exposure during treatment. (2) A myasthenic patient developed severe COVID-19 infection, secondary opportunistic infections, and prolonged post-COVID-19 illness. We present clinical evolution, disease progression, interventions, and radiological findings showing poor response to infection, which may persist for the variable period following COVID 19 infections resulting in multiple hospitalizations and poor outcomes.

Case Report

A 62-year-old female presented with 5 days' history of persistent cough, mild fever, worsening dysphasia, dysarthria, and dyspnea on exertion to the emergency department following a home quarantine period (Figure 1). She had a history of MG since 2009, which was diagnosed when she had developed sudden onset drooping of her left eyelid and slurring of speech and difficulty in swallowing. She also had developed

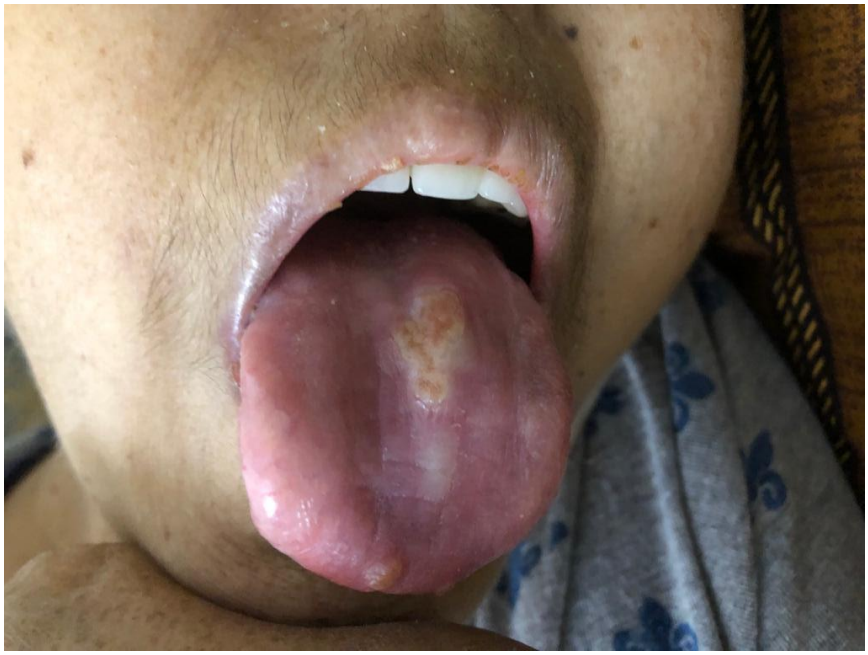

Figure 1. The Patient's Tongue Examination in Admission

Table 1: Immuno-profiling reports show immunosuppression and a significant decrease in lymphocytes.

S.No.	Investigation	Result	Reference values
1.	CD3 (% of total gated lymphocytes)	64.75	49.2-80
2.	CD4 (% of total gated lymphocytes)	43.25	21.5-48.8
3.	CD8 (% of total gated lymphocytes)	21.25	12.6-41.4
4.	CD3 (Absolute count (cell/µL)	358.02	800-2751
5.	CD4 (Absolute count (cell/µL)	239.14	600-1489
6.	CD4/CD8 ratio	2.03	0.68-2.73
7.	CD19 % (gated of lymphocytes)	15.2	7.2-31.1
8.	Absolute CD19 (Cells/ µL)	15.2	138-645

CD3 (% of total gated lymphocytes) 64.75 (49.2-80)
CD4 (% of total gated lymphocytes) 43.25 (21.5-48.8)
CD8 (% of total gated lymphocytes) 21.25 (12.6-41.4)
CD3 (Absolute count (cell/µL) 358.02 (800-2751)
CD4 (Absolute count (cell/µL) 239.14 (600-1489)
CD8 (Absolute count (cell/µL) 117.5 (254-1193)
CD4/CD8 ratio 2.03 (0.68-2.73).
%CD19 (gated of lymphocytes) =15.2 (7.2-31.1)
Absolute CD19 (Cells/ µL) =84.3 (138-645).

weakness in her upper and lower limbs. She was started on pyridostigmine. She also had a history of diabetes mellitus, hypertension, and hypothyroidism and was receiving treatment. She became positive for COVID-19 in August 2020. Her neurological examination showed restricted extraocular muscle movements, bilateral ptosis, and proximal muscle weaknesses of limbs. The patient was diagnosed to be in a myasthenic crisis. Her CECT-thorax showed bilateral infiltrates and ground-glass opacities with bronchiectasis, while the blood tests showed a dysregulated immune response. (Table 1) Due to respiratory failure, the patient was put on mechanical ventilation and was started on intravenous immunoglobulins. Subsequently, she improved and was extubated 5 days after receiving mechanical ventilation. Later, she was

discharged after receiving conservative management for 10 days.

In September 2020, she was readmitted with progressive respiratory distress. She was given an additional dose of intravenous immunoglobulin. The repeat CECT thorax did not reveal any new findings. She was restarted on oral steroids and immunosuppressant (azathioprine). Oral steroids were stopped within 2 months. The patient was well and remained asymptomatic till December 2020. Later, she developed acute onset of slurring of speech and inability to produce syllables using tongue which increased as the day passed. Her COVID-19 test remained positive though she didn't need any oxygen support and recovered. In January 2021, she had a repeat episode of slurring of speech difficulty in deglutition (more to liquids than solids) associated with cough and expectoration. A few days later she also developed high-grade fever with shivering and was diagnosed with urinary tract infection with the growth of E. coli on culture. She also developed oral candidacies (Fig. 1). She was managed with antibiotics and anti-fungal and was discharged. In March 2021, she was again admitted to the hospital with respiratory distress and required invasive mechanical ventilation. Subsequently, she expired due to septic shock and multiorgan failure.

Discussion

MG is a subtype of autoimmune disease where the body produces autoantibodies directed against postsynaptic acetylcholine receptors resulting in muscle weakness (1, 3). It is mainly treated with long-term immunosuppressive medications, IV immunoglobulins, and plasmapheresis (1, 3, 4). In some patients, it may progress to respiratory muscle weakness resulting in respiratory failure called a myasthenic crisis requiring intensive care admission and treatment. (5, 6) Various factors cause MG exacerbation, and infection is the most important (5, 6).

Managing COVID-19 infection in MG patients can be challenging as infections are known to precipitate MG crisis, they are prone to infection due to chronic immunosuppressive therapy, and respiratory failure can be seen in both conditions further complicating the management. (2) There is no scientific evidence suggesting stopping pyridostigmine in MG patients with COVID-19 unless there is any clinical indication. (7) Changing or withholding immunomodulatory therapy risks disease relapse or exacerbation. Hence, the decision to continue or stop should be tailored to each patient based on specific risks and benefits. (7,8)

Various studies have described the outcome in MG patients with COVID-19. Županić et al. (9) in their case series have demonstrated a favorable outcome in this cohort of patients. They also demonstrated that IVIG can be given safely and effectively in treating MG exacerbation in COVID-19 patients. In their cohort study, Antonio et al. (10) concluded that the baseline immunosuppressive therapy may not be associated with poor outcomes and should be continued. Saied, Z. et al. (11) too confirmed the same finding in their case series. Jakubíková M et al. (12) evaluated clinical features and outcomes in MG patients with COVID-19 and found that severe COVID-19 in MG patients was associated with long-term corticosteroid treatment, older age, presence of malignancy, and recent rituximab treatment. Solé G et al (13) in their registry-based cohort study demonstrated that COVID-19 had a limited effect on most of the patients, and immunosuppressive medications and corticosteroids are not risk factors for poorer outcomes.

The patient described in our case report was on pyridostigmine when she contracted COVID-19 infection. Her MG was relatively controlled with treatment, and at baseline, she didn't have any respiratory dysfunction. Later, she went into a myasthenic crisis and had a prolonged duration of illness. She received oral steroids, IVIG, and azathioprine but expired due to septic shock and hypoxemia.

Conclusion

Due to limited evidence, the cause for persistent COVID-19 infection in patients with COVID-19 is still unclear. MG patients due to immune dysregulation are at risk of developing severe and prolonged COVID-19 illness requiring multiple hospitalizations. Treatment of MG patients with COVID-19 needs to be customized according to the individual patient. Most

clinical decision and intervention needs to be done on a case-to-case basis depending upon the severity of MG and COVID-19. Immunomodulatory therapy involving corticosteroids, IVIG, and immunosuppressants should be based on collaborative decision-making models.

Acknowledgment

None.

Conflicts of Interest

The authors declare that there are no conflicts of interest.

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