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Case report

Case series: COVID-19 in patients with mild to moderate myasthenia gravis in a National Referral Hospital in Indonesia

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ABSTRACT

Background: During the COVID-19 pandemic, patients with myasthenia gravis (MG) are most likely to be affected by this situation. Corticosteroids and immunosuppressant agents increase the risk of severe infection. Furthermore, viral infection and some medications in COVID-19 may exacerbate MG symptoms.
Case description: We presented three patients with MG who contracted COVID-19. All of the patients had a favourable outcome. Only one patient who was not treated with corticosteroids or immunosuppressant therapy experienced deterioration of MG symptoms, while the other patients who received immunosuppressant therapy did not develop MG exacerbation. Surprisingly, azithromycin did not provoke myasthenic crisis (MC) in patients with normal MGFA classification.
Conclusion: Using immunosuppressant agents may not lead to MG deterioration and may not be related to unfavourable outcomes.

1. Introduction

Coronavirus disease 2019 (COVID-19) has developed rapidly into a global pandemic. New COVID-19 cases have continued to rise in Indonesia, especially in Jakarta, the capital, which has a dense population. As in other studies of patients with autoimmune disorders, myasthenia gravis (MG) patients are at increased risk of contracting severe COVID-19. Long-term immunosuppressive treatments in MG are predicted to increase the risk of serious infection. [1] Therefore, this population may be at risk of developing severe COVID-19 infection. Corticosteroid treatment in MG may act as a double-edged knife, as it gives an advantage in some stages of COVID-19 infection but can also worsen it. [2] On the other hand, some treatments for COVID-19, such as hydroxychloroquine [3] and azithromycin, are widely known to exacerbate MG symptoms or even cause myasthenic crisis.

There have been some case reports regarding COVID-19 in MG patients. [4–7] The course of disease and outcomes varied greatly. More than 50% of MG patients hospitalized due to COVID-19 had severe courses and that led to death in 30% of patients. [5] COVID-19 may precipitate myasthenic crisis [6]. However, some cases had favourable outcomes. [4] [7] Here, we present three MG patients admitted with COVID-19 between July and October 2020. To the best of our knowledge, this is the first reported case series of resolved COVID-19 in MG patients in South-East Asia.

2. Case 1

This was a 25-year-old woman with an eight-year history of seropositive MG without episodes of severe exacerbations who was well controlled with 180 mg/day of pyridostigmine. Eight days before hospital admission, she developed fever, dry cough, muscle pain, and difficulty swallowing solid food. Subsequently, four days later she had diarrhoea.

Upon admission, she had fever, anosmia, and dry cough and was haemodynamically stable. The myasthenic symptoms were bilateral ptosis, nasal speech, difficulty swallowing, fatigue in chewing solid food, and mild weakness of neck flexion and shoulder abduction. The MG composite score was 9, and the MGFA classification at admission was IIIB (See Table 1). The SARS-CoV-2 PCR test by naso-oropharyngeal swabs was positive. Serum C-reactive protein, procalcitonin, and D-

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dimer levels were unremarkable. Although chest X-ray was normal, chest CT scan showed ground glass opacity (GGO) in both lungs (Fig. 1A, B).

She was admitted to the high care unit (HCU), supported with O_2 2 L/min by nasal cannula, and her O_2 saturation was 98%. She was treated with vitamin C 500 mg/day, *N*-acetylcysteine 600 mg/day, and ceftriaxone 2 g/day for 6 days. Azithromycin 500 mg/day was given only for one day by the internist and was stopped after consulting the neurologist regarding azithromycin-induced deterioration potential in MG. Pyridostigmine 240 mg/day was continued. Her myasthenic symptoms resolved on the 5th day, and she was transferred to theisolation ward without routine O_2. She was discharged on the 14th day and continued to undergo home self-quarantine for the next 2 weeks.

3. Case 2

This was a 49-year-old man with a four year history of MG. He had been treated with pyridostigmine 180 mg/day and azathioprine 100 mg/day as routine MG treatment. Acetylcholine receptor antibody was never tested. He used to have unilateral ptosis that had been resolved for the last 3 years. One week before admission, he had fever and dry cough intermittently. Upon admission, his temperature was 37.8 °C, and he had no cough and was haemodynamically stable. There were no myasthenic symptoms during admission to the hospital or during hospitalization. His MG composite score was 0. The SARS-CoV-2 PCR test by naso-oropharyngeal swabs was positive. Chest X-ray showed left pleural effusion and infiltrates in bilateral lower lungs (Fig. 1C). The blood test showed increased CRP (35.7 mg/L), SGOT and SGPT levels (101 u/L and 148 u/L, respectively), and D-dimer (537 ng/mL). His O_2 saturation was 96–98% with O_2 2 L/min by nasal cannula intermittently. He was treated with azithromycin 500 mg/day for 5 days, vitamin C 3000 mg/day and paracetamol 1500 mg/day. Pyridostigmine and azathioprine were continued since his condition was stable and there was no deterioration. He was discharged 14 days after the SARS CoV-2 PCR test was negative.

4. Case 3

This was a 42-year-old woman with a 6-year history of MG who was treated with pyridostigmine 240 mg/day, methylprednisolone 4 mg/day, and mycophenolate mofetil 720 mg/day. Her myasthenic symptom was bilateral ptosis. For the last week before admission, she had fever, cough with mucus and tiredness. Physical examination revealed fever (38 °C), bilateral ptosis, and ronchi at bilateral lower chest auscultation. The MG composite score was 1, and the MGFA class was I. The SARS-CoV-2 PCR test by naso-oropharyngeal swabs was positive. Chest X-ray showed left pleural effusion and infiltrates bilaterally perihilar and paracardial. Blood tests showed leukocytosis with neutrophil dominance and increased CRP (167 mg/L). Her O_2 saturation was 96–98% with O_2 2 L/min by nasal cannula intermittently. She was treated with 200 mg/day hydroxychloroquine and 600 mg/day *N*-acetylcysteine for 7 days. The methylprednisolone dose was increased to 16 mg/day, and pyridostigmine and mycophenolate mofetil were continued as routine daily doses. She was discharged 14 days after the SARS-CoV-2 PCR test was negative. Her myasthenic symptoms did not deteriorate during hospitalization.

5. Discussion

Patients with autoimmune conditions such as MG are thought to be more prone to severe infection, including viral upper respiratory infection. Immunosuppressant treatment, such as corticosteroid and nonsteroid agents, increases the risk of infection in MG patients. [1] On the other hand, viral upper respiratory infection may lead to MG exacerbation. [8] The mechanism includes activation of the immune system triggered by infection, followed by enhanced T-cell signalling and upregulation of cytokines and proinflammatory molecules. [9] Among all three cases, none of them showed severe MG exacerbation, myasthenic crises during hospitalization, or severe COVID-19.

Despite continuing steroid and nonsteroid immunosuppressants in case 2 and case 3, those patients had favourable outcomes. Although the methylprednisolone dose was increased in case 3, her MG symptoms did not deteriorate, and COVID-19-related symptoms resolved. On the other hand, Case 1, who was not on corticosteroids or immunosuppressants, experienced deterioration in her MG symptoms. Corticosteroids can be beneficial for improving MG as well as COVID-19 symptoms. [2] Long-term use of steroids in MG does not worsen COVID-19. [4] Using immunosuppressant agents in MG during the COVID-19 pandemic remains a challenge. A report from Brazil of MG patients with COVID-19 who were already on immunosuppressants showed favourable outcomes. On the other hand, 4 out of 5 patients who died did not receive immunosuppressant agents. [5] Immunosuppressant therapy is likely to be beneficial in COVID-19 cases with MG by reducing hyperinflammation and cytokine storms. [10] Therefore, corticosteroid and immunosuppressant agents should be continued in MG patients with or without SARS-CoV-2 infection. Despite these results, MG patients should practice vigilance and take extra precautions to reduce the risk of contracting COVID-19.

Azithromycin and hydroxychloroquine have been considered to contribute to MG exacerbation. [3,8] Cases 2 and 3 did not show any deterioration of MG symptoms during hospitalization despite administration of azithromycin and hydroxychloroquine. Thus, azithromycin

Table 1
Characteristics of patients with MG with COVID-19.

	Case 1	Case 2	Case 3
Age (sex)	25 (F)	49 (M)	42 (F)
History of MG (y)	2	4	6
Chronic MG treatment	Pyridostigmine	Pyridostigmine, azathioprine	Pyridostigmine, methylprednisolone, mycophenolate mofetil
MGCS at admission	9	0	1
MGFA before COVID-19	I	0	I
MGFA classification at admission	IIIb	Normal	I
MGCS at discharge	3	0	1
MGFA classification at discharge	IIa	Normal	I
MG symptoms during COVID-19	Ptosis, nasal speech, shoulder and proximal limb weakness	None	Ptosis
COVID-19 symptoms	Fever, anosmia, dry cough, myalgia, diarrhoea	Fever, dry cough	Fever, cough with mucus, tiredness
COVID-19 medication	Vitamin *C*, *N*-acetylcysteine, ceftriaxone, azithromycin (discontinued)	Azithromycin, vitamin C, paracetamol	Hydroxychloroquine, *N*-acetylcysteine
Outcome	Discharged home	Discharged home	Discharged home

Note: MGCS: myasthenia gravis composite score, y: years.

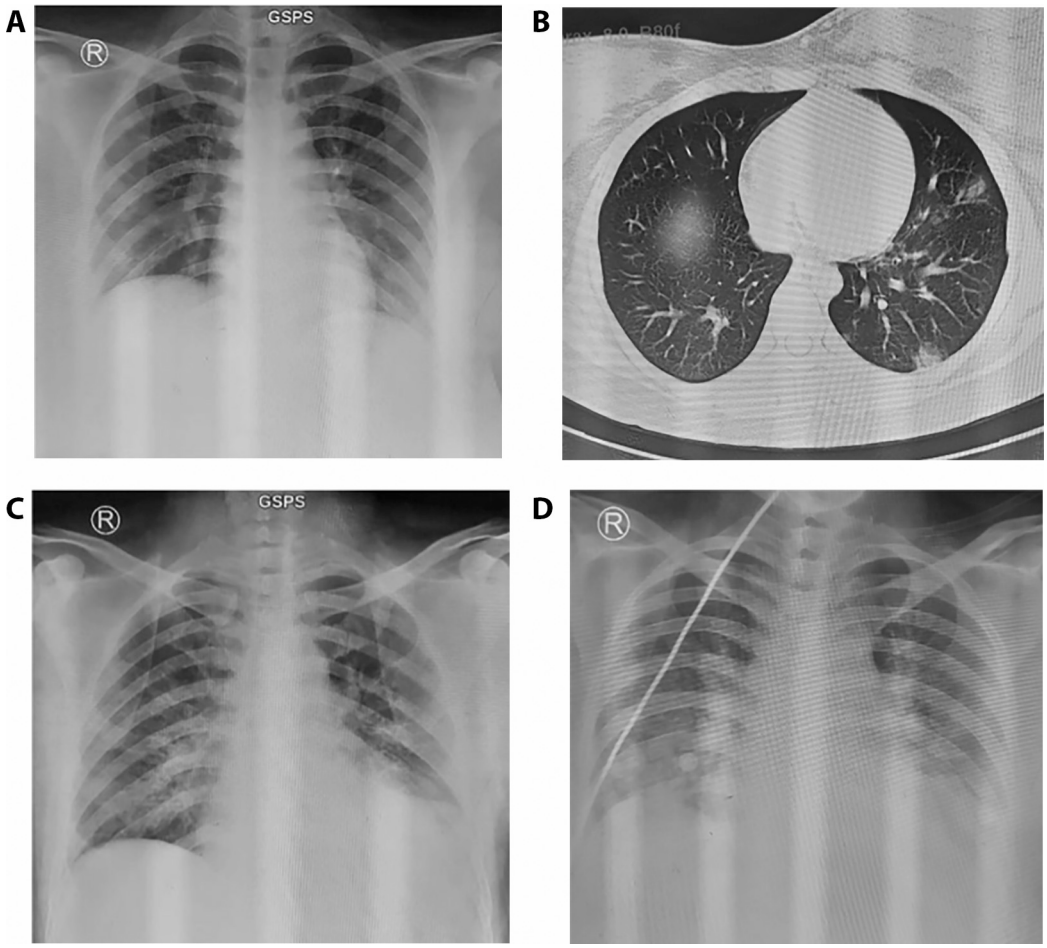

Fig. 1. Chest X-ray of Case 1 was normal (A). Chest CT scan of case 1 showed ground glass opacity (GGO) in bilateral lower lungs (B). Chest X-ray of case 2 showed left pleural effusion and infiltrates in bilateral lower lungs (C). Chest X-ray of case 3 showed left pleural effusion and infiltrates bilaterally perihilar and paracardial (D).

and hydroxychloroquine may not be harmful in MG patients with mild MGFA classification but still require caution.

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