

COVID-19 and Sudden Cardiac Death in a Young Man with Myasthenia Gravis

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ABSTRACT

Myasthenic patients are expected to develop more severe COVID-19 respiratory symptoms compared to the general population because of both respiratory muscle weakness and the possibility of an immunocompromised state related to immunotherapy. During a pandemic like COVID-19, such situation requires meticulous attention, as the entire population is potentially at risk of exposure. However, there is no data on best management for myasthenic patients with COVID infection.

Although pneumonia has been reported as the most common cause of death in COVID-19 patients, sudden cardiac death has also been described in the literature as a possible COVID-19 related mortality cause. Physicians should assess the patient's cardiac functions as precisely as possible, in addition to the respiratory condition, in order to prevent such incidents. Furthermore, as the cardiac system of myasthenic patients might be negatively influenced by their background, their cardiac system may be even more vulnerable during COVID-19, which should be noted by medical teams. Reporting such cases can be helpful to develop protocols for treating myasthenic patients during the COVID-19 pandemic.

Here, we present a 37-year-old man with generalized myasthenia gravis who was admitted to our hospital due to dyspnea. He developed severe respiratory distress in few hours and subsequently died of sudden cardiac death.

KEYWORDS: Myasthenia gravis; COVID-19; Sudden cardiac death

ABBREVIATIONS

MG: Myasthenia Gravis; SCD: Sudden Cardiac Death; COVID-19: Coronavirus Disease of 2019; SSRI: Selective Serotonin Reuptake Inhibitor; ABG: Arterial Blood Gas; ICU: Intensive Care Unit; RT-PCR: Reverse Transcription-Polymerase Chain Reaction; SARS-Cov2: Severe Acute Respiratory Syndrome Coronavirus 2; CT: Computed Tomography; LDH: Lactate Dehydrogenase; IVIG: Intravenous Gamma-Globulin; EKG: Electrocardiography.

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INTRODUCTION

MG (Myasthenia Gravis) is a chronic autoimmune disorder caused by autoantibodies against the nicotinic acetylcholine receptors on the postsynaptic membrane at the neuro muscular junction. It is characterized by skeletal muscle weakness and fatigability, which typically increase with exercise [1]. Other commonly presented symptoms include diplopia, ptosis, and difficulty in swallowing. Approximately 20% of MG patients will experience myasthenia crisis, i.e., weakness of upper airway muscles leading to airway obstruction and aspiration. Myasthenic crisis usually happens within the first year of illness [2]. According to a study conducted by Liu C, et al. on 2195 myasthenic patients, the estimated mortality rate was 5.88% at a 10-year follow-up. The most determinative death-related factors of MG are found out to be the severity of the disease at the beginning, the presence of acetylcholine receptor antibodies, and the occurrence of thymic pathology [3]. MG patients may also experience fluctuations in heart rate, which is mainly associated with autonomic dysfunction rather than the presence of cardiac conducting system pathology. Meanwhile, SCD (sudden cardiac death) has also been reported in some cases without a discovered definite connection [4].

Since the initial reports on the COVID-19 (coronavirus disease) cases in Wuhan, China, in December 2019, COVID-19 has rapidly become a global concern as it has spread all the world over. Nevertheless, little is known about its potential effect on MG patients. During this global pandemic, myasthenic patients are considered high risk not only due to the weakness of their respiratory muscles but also because of taking immunosuppressive medications [5].

The mortality rate of COVID-19 has been reported approximately 5.7% [6], which is primarily caused by pneumonia and acute respiratory distress [7]. Underlying

diseases like high blood pressure, cardiovascular and cerebral disorders, diabetes, hyperlipidemia, and chronic renal failure increase mortality [8].

SCD has also been reported in the literature as an infrequent COVID-19-related death cause [9]. Prolongation of the QTc from the baseline average is mainly due to prescribed medications for COVID-19 patients, such as hydroxychloroquine and azithromycin [10]. Moreover, the viral infection itself can cause myocarditis and subsequently SCD.

Herein, we present a young man suffering from MG who experienced SCD following COVID-19.

CASE PRESENTATION

On April 3rd, 2020 a 37-year-old male was brought to the BuAli hospital, Tehran, Iran complaining about mild exertional dyspnea from six hours prior to his admission. He mentioned a background of generalized MG for the previous six years. His initial presenting symptoms were ptosis and weakness. As a result, he was treated with Pyridostigmine. The patient also stated a positive history of hypertension, Hashimoto thyroiditis, and depressive disorder, for which he has been receiving levothyroxine, losartan, and SSRI (selective serotonin reuptake inhibitor) respectively in the last six years.

The patient's vital signs upon his arrival are noted in table 1. Except for the mild crackles auscultated in the lower lobes of both lungs, all other physical examinations were normal. ABG (arterial blood gas) and laboratory blood tests were performed (The results are reported in Table 1 and Table 2). The Renal function test was normal, but an increase in liver enzymes was observed.

Time after hospitalization		Upon arrival	8 th hour	10 th hours
Patient complaints		Mild exertional dyspnea	Severe dyspnea	Severe respiratory distress, confusion
Vital signs	Temperature	37.8°C orally	37.6°C orally	36.9°C orally
	Pulse rate	92/min	105/min	91/min
	Respiratory rate	22/min	38/min	45/min
	Blood pressure	140/90 mmHg	120/80 mmHg	100/60 mmHg
ABG Results	PH	7.41	7.31	7.32
	PaO ₂	64.7	94.4	57.7
	PaCO ₂	39.9	57.9	46.2
	HCO ₃ ⁻	18	22	32
	Saturation	93.2% (In room air)	92.6% (5L/min O2 nasally)	95.2% (post intubation)

Table 1: Patient complaints, ABGs, and vital signs during the hospitalization course.

Lab data	D-Dimer	BUN	Cr	CRP	AST	ALT	LDH	Pr	TSH	T4	T3	WBC	HB	PLT
Unit	ng/ml	Mg/dl	Mg/dl	Mg/l	U/l	U/l	Au/l	gr/l	mU/l	ng/dl	pg/ml	/ μ l	gr/dl	ML
Result	1460	18	0.8	65	46	37	430	5	3.1	1.71	3273	3580*	10.5	2.1x10 ⁵

Table 2: Results of the blood tests upon arrival. *With 89% neutrophil. BUN: Blood urea nitrogen, Cr: Creatinine, CRP: C-reactive protein, AST: Aspartate aminotransferase, ALT: Alanine transaminase, LDH: Lactate dehydrogenase, Pr: Protein, TSH: Thyroid-stimulating hormone, T4: Thyroxine, T3: Triiodothyronine, WBC: White blood cell, HB: Hemoglobin, PLT: Platelet.

Due to patchy bilateral consolidation observed in the initial chest X-ray of the patient (Figure 1), he was transferred to ICU (intensive care unit). Upon ICU admission, Baseline ECG was within normal limits (Figure 2). In the following hours, dyspnea became gradually worse in so far as he developed with tachypnea and respiratory distress after 8 hours of his arrival. After applying 5 liters per minute O₂ mask, another ABG was requested, which showed respiratory acidosis. As a result, endotracheal intubation was performed, and RT-PCR (reverse transcription-polymerase chain reaction) for SARS-Cov2 (Severe acute respiratory syndrome coronavirus 2) was requested.



Figure 1: Initial admission posteroanterior chest radiography.

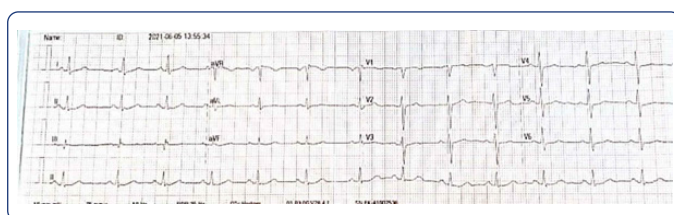


Figure 2: ECG showed normal sinus rhythm, normal axis, QTC intervals is 435 msec.

On the 9th hour of admission, chest CT (Computed tomography) was performed, revealing bilateral multifocal ground-glass opacities with consolidation and mild right pleural effusion (Figure 3). Then, thoracentesis has been performed for the patient, which results were as below: LDH (Lactate dehydrogenase) = 330 IU/L and protein = 4.6 g/L suggesting an exudative pleural fluid. We considered both infection and MG as the leading causes of the patient's respiratory failure, so he underwent plasmapheresis on the same day combined with 2g/kg/day IVIG (intravenous gamma-globulin). Moreover, he received Lopinavir/Ritonavir 400/100 mg and hydroxychloroquine 400mg in addition to the prophylactic anticoagulation. Echocardiography revealed normal cardiac function. Afterwards, the RT-PCR for SARS-Cov2 collected from the nasopharynx was reported positive. Despite all of these medical actions, no sign of recovery was depicted, and the patient's situation worsened as time was going on. Approximately 2 hours later, he suffered a cardiac arrest, and the cardiopulmonary resuscitation was unsuccessful, and he unfortunately died.

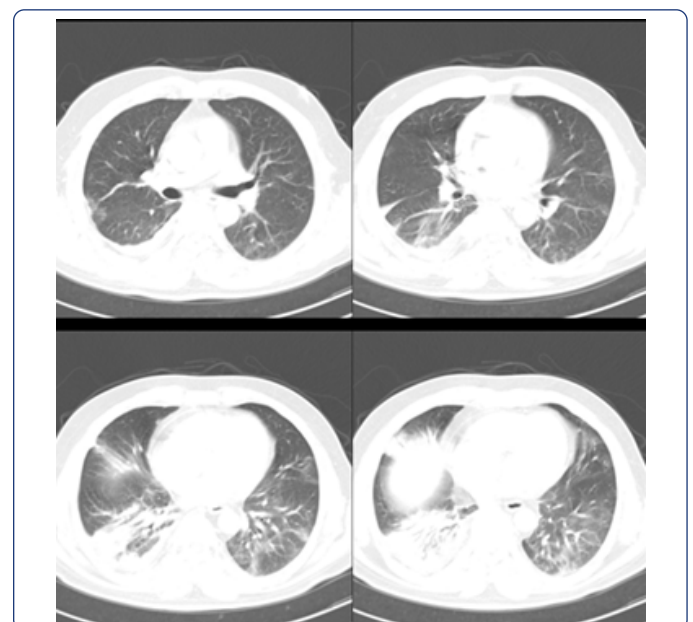


Figure 3: Chest spiral CT scan.

DISCUSSION

MG is an immune-mediated disorder, most commonly affecting middle-aged females, but it is known to occur at any age [11]. It predominately involves the destruction of the neuromuscular junction by the acetylcholine receptor-specific antibodies. MG is diagnosed on the basis of clinical, electrophysiological, and serological findings [12]. Cardiac muscle is also a target for autoimmune inflammation in MG. Cardiac manifestations of MG include: heart failure, cardiomyopathy, pericarditis, and arrhythmia [4]. In addition, SCD in MG patients has been reported in literatures; however, no definite association has been established yet. Infection is considered a common trigger for MG exacerbation.

Despite the higher likelihood of COVID-19 severe disruptive effects on MG patients, due to receiving immunosuppressive or immunomodulatory therapies and the weakness of respiratory muscles, in comparison with healthy population, no explicit association has been established, and this likelihood still remains debatable [13]. In addition to the infectious nature of COVID-19, its recommended therapies, such as azithromycin and hydroxychloroquine, may also lead to myasthenic exacerbation [14]. Most patients dealing with COVID-19 have a good prognosis, and a few patients (mostly elderly or people with comorbidities such as hypertension, diabetes, and chronic cardiac and renal disorders [15]) become critically ill. Although the COVID-19 mortality is mainly attributed to respiratory-related complications directly, cardiac consequences have recently been reported in the literature [9]. According to a study conducted by Zhou et al. in Wuhan, China studying 191 COVID-19 patients, at least 17% of cases were found to have an elevated troponin level, and 23% were distinguished to experience heart failure [16]. Moreover, myocarditis, atrial and ventricular arrhythmias as well as cardiogenic shock have also been reported [17].

In the beginning, the symptoms of the presented patient were mild. Unfortunately, his condition worsened within a few hours. Finally, he developed severe respiratory distress requiring endotracheal intubation. In addition to MG, the proarrhythmic effects of hydroxychloroquine which is prescribed for COVID-19, should also be considered as a possible cause of SCD. QT prolongation and torsades de pointes are common cardiac adverse effects of hydroxychloroquine [18]; nevertheless, the absolute risk of hydroxychloroquine causing SCD is minor and mainly observed among patients older than 60 years of age [19]. We did not have the ECG of the patient prior to his death, however, initial EKG (electrocardiography) was normal and did not show QT prolongation and torsades de pointes. In our case, myocarditis following viral infection could also be a cause of sudden cardiac death.

CONCLUSION

In conclusion, considering the disease process of the presented case and other similar reported cases [20], MG patients catching COVID-19 demonstrate different disease course compared with other COVID-19 cases. As a result, the unique evaluation and management for such patients seem necessary as MG patients are among the most vulnerable population, by means of explained throughout this report. It is also highly recommended to monitor cardiac condition in COVID-19 patients suffering from MG and admit them to ICU if possible. Moreover, repetition of blood gas appears necessary in order to forecast possible respiratory failure. Consultation with a cardiologist, EKG, echocardiography should be considered. Additionally, more studies are needed to make the disease process fully comprehensible. Reporting such cases can help the medical teams to be aware of the delicacy of treating COVID-19 patients with underlying diseases such as MG.

CONSENT

Written informed consent was obtained from the patient's family to publish this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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AUTHORS CONTRIBUTION

Maysa Ghayyem was the internist who has admitted the patient to the hospital and performed the treatment. Sara Haseli analyzed and interpreted the patient data regarding radiological findings, reviewed and edited the manuscript. Shekoofeh Yaghmaei prepared the draft of the manuscript and the tables. All authors read and proved the final manuscript.

CONFLICT OF INTEREST

None.

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