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Severe COVID Pneumonia Unmasking the Subclinical Myasthenia Gravis

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Abstract

Myasthenia gravis is an autoimmune neuromuscular junction disease characterized by weakness and respiratory failure. Novel Coronavirus COVID-19/SARS-COV-2) presents as fever, cough, breathlessness and most commonly associated with pulmonary infiltrates. Myasthenia gravis can be unmasked or exacerbated by an infection, drugs like (statin, hydroxyl chloroquine and antibiotics) and non-compliance to medications. Symptomatic COVID-19 increases the work of breathing, and myasthenia gravis causes early fatigue of respiratory muscles leading to respiratory failure. Here we are reporting an undiagnosed case of myasthenia gravis with myasthenic crisis unmasked by COVID-19. Our patient presented with respiratory distress and developed respiratory failure, which required mechanical ventilation. He did not respond to treatment and succumbed to death, despite adequate efforts. This indicates early suspicion of myasthenia and consideration for immunosuppression therapy in such patients for a better outcome.

Keywords: Myasthenia gravis; Novel Coronavirus (COVID-19/SARS-COV-2); Hydroxyl chloroquine; Respiratory failure; immunosuppression

Introduction

Myasthenia gravis is a neuromuscular junction disorder due to antibodies binding to acetylcholine receptors at the neuromuscular junction [1]. Myasthenia gravis presents as bulbar, respiratory, and ocular and limb muscle weakness, which worsens with activity [1]. Corona Virus Disease 2019 (COVID-19) from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can present with fever, cough, respiratory distress, diarrhea, and reduction of smell and taste sensations [2]. Muscle weakness and immune-modulating therapy in myasthenia gravis increase the chances of complications in COVID-19 infections [2]. Here we are reporting a case of COVID-19 unmasking myasthenia gravis without any previous symptoms of myasthenia gravis.

Case Presentation

A 45-year male, a known case of Type 2 diabetes mellitus for 8 years and hypertension for four years on ayurvedic (Unani) medications, came to emergency with a history of neck and tooth pain, slurring of speech and dysphagia for both solids and liquids, which was associated with nasal regurgitation for the last 12 days. He complained of facial asymmetry for the previous five days. There was no history of fever, headache, vomiting, Loss of consciousness or weakness of any side. He had no history of similar complaints in the past.

His blood pressure was 140/90 mmHg with a regular heart rate of 108 beats per minute on presentation. His oxygen saturation was 95% with room air, and respiratory rate was 22 breaths per minute. His blood sugar was 232 mg/dl, and he was afebrile. He was conscious and oriented, left side ptosis was present, gag and palatal reflex were absent, dysarthria with nasal twang was present, and rest of all other cranial nerves were intact. Tone and Power in all 4-limbs-5/5, sensory examination was within normal limits Cerebellar and meningeal signs were absent, no bladder or bowel incontinence, cardiovascular and abdominal examination was within normal limits

Investigations

His bedside ultrasound showed bilateral B lines in the lung posterolateral area. His screening echocardiography showed normal contractility, and abdominal ultrasound was within normal limits. His Hemoglobin was 14.7 g/dl, total leucocyte count was 11920 cells/dl, and platelet count was 1.9 lakh/dl. His Kidney and liver function tests were within normal limits (Table 1). His HbA1c was 11.9%. His imaging showed no infarct or bleed (non-contrast computed tomography of the head (NCCT) and magnetic resonance imaging (MRI). COVID-19 Real-Time-Polymerase Chain Reaction primers (RT-PCR) were positive. Acetylcholine receptor (AchR) antibody was positive. His chest x-ray Figure 1 showed bilateral lower zone infiltrates. His blood and urine cultures did not grow any organisms. His High-resolution computed tomography (HRCT) Figure 2 suggests bilateral basal segments infiltrates with no thymoma features. His procalcitonin and C-reactive protein levels were 44 ng/dl (<0.05) and 112/dl (mg/dl) respectively. His D-dimer values were 4.4 gm/dl (<500 ng/dl). His beside 2-dimensional echocardiography was done in bed side, which was normal. His cultures of blood and sputum were sterile. His serum procalcitonin levels and C-reactive protein levels initially decreased to 1.5 ng/dl (<0.05) and 8.6/dl(mg/dl) and again increased to 38 ng/dl(<0.05) and 162/dl (mg/dl). His cultures repeated again from blood and sputum which were sterile after 48 hours of incubation.

Variable	Reference Range, Adults,	Day 1	Day 3	Day 6
	This Hospital			

Hemoglobin (g/dl)	13.5-17.5	14.75	14.97	14.04
White-cell count (per µl)	4500-11,000	11920	17847	14600
Differential count (per µl)				
Neutrophils	1800-7700	10489	16,062	13,286
Lymphocytes	1000-4800	1120	1427	902
Monocytes	200-1200	210	317	392
Eosinophils	0-900	94	30	11
Basophils	0-300	6	10	9
Platelet count (per µl)	150,000-400,000	197000	250000	183200
Urea nitrogen (mg/dl)	8-25	32	40.5	41.4
Creatinine (mg/dl)	0.60-1.50	0.87	0.92	0.89
Sodium (mmol/liter)	135-145	135.4	127	131.9
Potassium (mmol/liter)	3.4-5.0	4.5	3.8	4.3
Chloride (mmol/liter)	100-108	91.5	82.2	88
Total bilirubin (mg/dl)	0.3-1.2	0.41		0.39
Direct bilirubin (mg/dl)	0-0.2	0.2		0.21
Alanine transferase (U/L)	00-0-35	33		41.4
Aspartate transferase (U/L)	0-35	23.3		44.3
Alkaline phosphatase (U/L)	30-120	243.7		164
Gamma glutamoyl transferase(U/L)	0-38	34.2		34.3
Total protein (g/dl)	6.6-8.3	6.8		7.1
Albumin (g/dl)	3.5-5.2	4.2		3.66
Globulin (g/dl)	2.5-3.2	2.5		3.44
Glucose (mg/dl)	70-110	192		
C-reactive protein (mg/liter)	44	8.5	26	162
Erythrocyte sedimentation rate (mm/hr)	0–13	44		
D-dimer (ng/ml)	<500		4400	
Prothrombin time	11-13.5 sec	13.2	14.8	
INR	0.8-1.1	0.98	1.1	
Viral Markers (HIV, antiHbsAg, antiHCV)		Non-reactive		
Procalcitonin(ng/dl)	112	1.5		38
HbA1c	<6.5%	11.40%		

Table 1: Laboratory investigations.

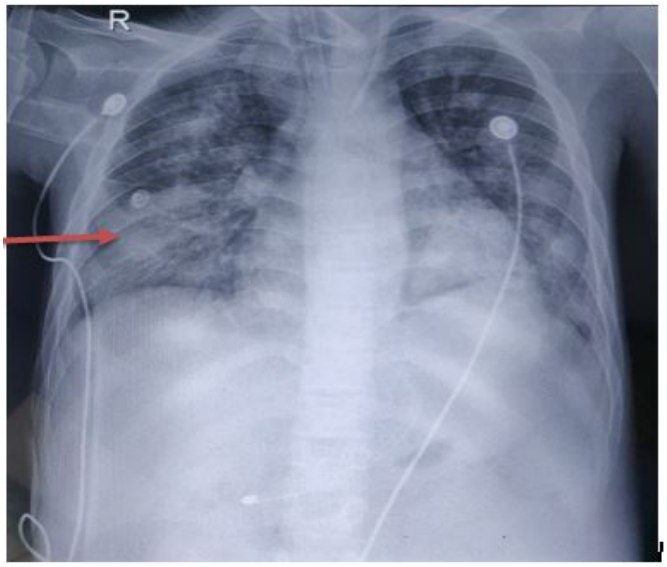

Figure 1: chest x-ray anteroposterior view showing bilateral lung heterogeneous infiltrates.

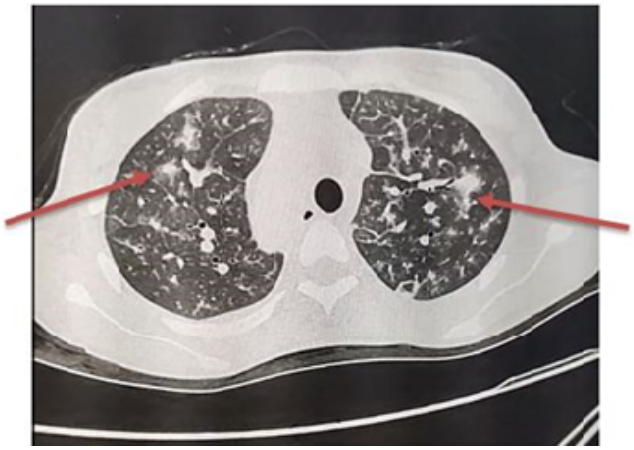

Figure 2: HRCT thorax showing bilateral infiltrates suggestive of COVID pneumonia.

Differential diagnosis

In the emergency department, based on his presenting complaints like acute onset progressive dysarthria, dysphagia with nasal regurgitation and dyspnea possibility of posterior circulation stroke with COVID pneumonia/aspiration pneumonitis was suspected. Still, his normal NCCT and MRI brain ruled out a stroke. He was also suspected of motor neuron disease (bulbar palsy), as his MRI brain did not show any bulbar palsy features, and there were no complaints of distal weakness/muscle cramps. Another differential in view of cranial nerve palsy, other diagnoses like diabetic cranial neuropathy was suspected, but as his tests were positive for myasthenia gravis, it was ruled out. Because of ptosis and dysphagia, myasthenia gravis was suspected. His AchR antibody, Icepack test and Neostigmine test were positive. During course of hospital stay he developed shock possibility septic shock was suspected as his echo was within normal limits.

Results

His inotropic requirement increased progressively and his respiratory compromised due to COVID with Myasthenia crisis, and he succumbed to death on day 8 of hospital admission can be interpreted as countries failing to develop practices and different perspectives on the correct parameters in epidemic management.

Discussion

Novel Coronavirus (COVID-19/SARS-COV-2) with myasthenia gravis is considered a high-risk case is given the risk of respiratory failure [3]. COVID 19 causes multiple neurological manifestations like encephalopathy, myalgia, headache, cerebrovascular disease, immune-mediated neuropathy, and rhabdomyolysis [4]. COVID 19 causes worsening or exacerbation of myasthenia of gravis through multiple mechanisms likes cross-reaction between viral proteins and acetylcholine receptor subunits due to the similarities between the viral epitopes and components of the neuromuscular junction. Another mechanism is a break in immunologic self-tolerance [5].

Inpatient with myasthenia gravis, infection is the most common trigger for exacerbations, and given global pandemic of COVID-19, myasthenia patients are at very high risk [6]. Other than infection, a drug like Chloroquine, levofloxacin, azithromycin and statins worsen myasthenia gravis due to neuromuscular blockade and worsens the respiratory failure [7]. In patients of myasthenia, one should be cautious while selecting drugs. Given the global pandemic of COVID-19 liberal use of hydroxychloroquine, aminoglycosides and fluoroquinolones should be avoided [7]. In our patient, also we initially started him on azithromycin, levofloxacin and hydroxychloroquine, but were stopped once we suspected myasthenia.

Diagnosis of myasthenia gravis through bedside test like ice pack test, edrophonium stimulation test, then a serologic demonstration of antibodies against specific receptors (AChR-Ab, MuSK-Ab, or LRP4) and confirmation through the electro physiological methods (repetitive nerve stimulation test and single fibre electromyography) [8]. In our case patient had clinical features of myasthenia gravis, acetylcholine receptor antibodies positive. We were unable to do electrophysiological tests due to the patient's critical condition and due to the COVID pandemic.

COVID-19 with myasthenia gravis patient should be electively intubated, and immunosuppression with steroids, intravenous immunoglobulin and plasmapheresis should be given. Other types of immunosuppressive therapy should be decided on a case to case basis [9]. Intravenous immunoglobulin acts through multiple mechanisms like blocking T cells differentiation and cytokine production. IVIG also decreases the acetylcholine receptor antibodies and complement activation [10].

In our case, we started him on Pyridostigmine, steroids and IVIG and changed his antibiotics. His high-resolution computerized tomography showed bilateral infiltrates with no evidence of thymoma. He was planned for plasma therapy and other immunosuppression therapy. Due to the limited availability of other antibiotics and immunosuppression due to diabetes mellitus, the patient developed sepsis and septic shock with the increasing inotropic requirement. His respiratory failure worsened leading to type 1 respiratory failure due to severe pneumonia and diaphragmatic weakness.

Conclusion

Early aggressive therapy required for patient with myasthenia gravis with COVID-19 to avoid poor outcome and precipitation of myasthenia crisis due to respiratory distress. Early pulse therapy would have helpful in patient with severe pneumonia with autoimmune disorders.

Myasthenia gravis and COVID-19 are associated with an increased risk of ventilator-associated pneumonia, difficulty in weaning and ventilator dependence. Hence early aggressive antibiotics and immunosuppression therapy would be warranted.

Myasthenia gravis should be considered/suspected in patients with respiratory failure with ptosis and/or characteristic fluctuation of symptoms, and treatment should be individualized. Close monitoring of the patient's respiratory status and early intubation to avoid severe hypoxia due to respiratory muscles' fatigue.

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