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SARS-COV-2 IN PRE-EXISTING AUTOIMMUNE MYASTHENIA GRAVIS: AN INSTITUTIONAL EXPERIENCE – CASES PRESENTATION

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ABSTRACT

The impact of SARS-CoV-2 on pre-existing chronic neuromuscular junction disorders like myasthenia gravis (MG) is not known. We report three patients with pre-existing acetylcholine receptor autoantibody-positive myasthenia gravis who were infected with SARS-CoV-2. We observed the clinical course of these patients during hospitalization, none of the three patients had an exacerbation of peripheral myasthenia syndromes like ptosis, extra-ocular muscle weakness, bulbar or limb weakness during hospitalization. Therapy for MG was not altered during hospitalization for any of the patients. While two of the patients had a favorable outcome, one succumbed to the complications of SARS-CoV-2. Our findings suggest that the clinical course of MG remains unaffected during course, however outcome is variable depending on severity of SARS-CoV-2. Further large observations are needed to define best management and treatment principals and determinants of outcomes in this unique patient population of co-occurrence of SARS-CoV-2 and myasthenia gravis.

Keywords: COVID-19, myasthenia gravis, neuroimmunology, neuromuscular disorders, immunosuppression

INTRODUCTION

SARS-CoV-2 infection has caused a global health crisis and apart from respiratory system involvement, it has been found to significantly affect the nervous system- directly or indirectly [1-3]. The impact of SARS-CoV-2 on pre-existing chronic neuromuscular junction like myasthenia gravis (MG) is not known. We describe the clinical course and outcomes of three patients with pre-existing MG, infected with SARS-CoV-2.

MATERIALS AND METHODS

This observational study was carried out in the Department of Neurology in a teaching hospital in central India from 15th September 2020 to 15th November 2020. The patients included were known or pre-existing patients of autoimmune Myasthenia Gravis with current hospital admission for SARS-CoV-2 infection. They were diagnosed positive for SARS-CoV-2 based on positive nasopharyngeal swab RT-PCR, in the setting of clinical symptoms and supportive CT chest findings. The diagnosis of autoimmune MG was confirmed by reviewing the symptoms, autoantibody status and electrophysiological testing done at the time of receiving the diagnosis.

CASES PRESENTATION

Patient 1

71 years old male patient, hypothyroid was diagnosed as autoimmune MG 8 months prior. He was on Tab Omnacortil 20 mg daily, Tab Pyri-

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dostigmine 60 mg twice daily and Tab Mycophenolate Mofetil 360 mg twice daily. He had a relatively stable course during hospitalization and was treated with Remdesvir therapy. He needed intermittent oxygen inhalation at 2-4 litres/minute flow rate. He had no exacerbation of peripheral myasthenia syndromes like ptosis, extra-ocular muscle weakness, bulbar or limb weakness during hospitalization. Therapy for MG was not altered during hospitalization. He was discharged within 7 days of admission.

Patient 2

63-years-old male, diabetic and hypothyroid patient was diagnosed as autoimmune MG 52 months prior. His symptoms were well controlled on Tab Azathioprine 50mg twice daily and Tab Pyridostigmine 60 mg twice a day. He developed fever, cough and throat pain and testing showed he was positive for SARS-CoV-2. He was admitted to the hospital on day 6 of onset of symptoms and needed high flow oxygen via non re-breathing mask for maintaining arterial oxygen saturation. As he developed increased respiratory distress, he was maintained on non-mechanical ventilation with BiPap. The patient had a cytokine storm and was administered Tocilizumab, Remdesvir and intravenous Immunoglobulin therapy. The patient gradually improved and was continued on 8-10 litres of oxygen inhalation via non-rebreathing mask. He had no exacerbation of peripheral myasthenia syndromes like ptosis, extra-ocular muscle weakness, bulbar or limb weakness during hospitalization. Therapy for MG was not altered during hospitalization.

Patient 3

68-years-old male patient, diabetic and hypertensive was diagnosed as autoimmune MG fourteen months prior. His symptoms were well controlled on Tab Wysolone 20 daily, Tab Azathioprine 50 mg twice daily and Tab Pyridostigmine 6 0mg thrice a day. He developed fever with cough and testing showed he was positive for SARS-CoV-2. He was admitted to the hospital on day 7 of onset

TABLE 1. *Patients characteristics*

	Patient 1	**Patient 2**	**Patient 3**
Gender	Male	Male	Male
Age (in years)	71	63	68
Duration of diagnosis of MG	8 months	52 months	14 months
Antibody status	AChR Ab +	AChR Ab +	AChR Ab +
MGFA disease clinical classification at time of SARS-CoV-2 diagnosis	I	I	I
thymoma-history/present	No	No	No
MG treatment at home	Tab Omnacortil 20 mg daily, Tab Pyridostigmine 60 mg twice daily, Tab Mycophenolate Mofetil 360 mg twice daily	Tab Azathioprine 50 mg twice daily, Tab Pyridostigmine 60 mg twice a day	Tab Wysolone 20 mg daily, Tab Azathioprine 50 mg twice daily, Tab Pyridostigmine 60 mg thrice a day
Pre-existing comorbidities	Hypothyroidism	Diabetes, Hypothyroidism	Diabetes, Hypertension
SARS-CoV-2 presenting symptom	Fever, cough	Fever, cough, throat pain	Fever followed by cough and dyspnea
Treatment of SARS-CoV-2 administered during hospitalization	Remdesvir	Tocilizumab, Remdesvir, iv Ig	Tocilizumab, iv Ig
ICU admission during SARS-CoV-2	No	Yes	Yes
Respiratory support provided during hospitalization	Intermittent oxygen inhalation	High flow oxygen via non re-breathing mask, followed by BiPAP	High flow oxygen via non re-breathing mask, followed by BiPAP, followed by Endotracheal Intubation and prone mechanical ventilation
Evidence of exacerbation of MG	None	None	None
Duration of hospitalization	7 days	36 days	5 days
Outcome of patient	Discharge	Discharge	Death

TABLE 2. *Laboratory and radiological parameters*

Parameter		Normal Value	Patient 1	Patient 2	Patient 3
Hemoglobin (gm/dl)		13-17	12.5	13.2	14.1
White cell count (per cmm)		4,000-11,000	8200	5000	27,300
Neutrophils (%)		40-70	81	87	94
Lymphocytes (%)		20-45	11	9	4
Monocytes (%)		2-10	8	4	2
Eosinophils (%)		1-6	0	0	0
Basophills (%)		0-1	0	0	0
Platelet count (no./cmm)		1.5-4.5	4.28	1.67	1.24
Mean corpuscular volume (fL)		80-96	89.6	88.7	87.2
Mean corpuscular hemoglobin (pg)		27-34	28.2	28.8	27.5
Creatinine (mg/dl)		0.7-1.2	1.05	0.87	1.1
Blood urea (mg/dl)		15-40	35	41	142
Prothrombin time (seconds)		14	14	14	16
INR			1.0	1.0	1.1
Activated partial-thromboplastin time (seconds)		28-32	30	28	32
D-Dimer (mg/dl)		< 250	398.3	345	Ø1000
Serum ferritin (ng/ml)		10-291	459.1	281.9	721.0
Lactate Dehydrogenase (U/L)		313-618	427	346	372
ESR (mm/hour)		0-9	28	19	30
C-RP (mg/dl)		<0.6	4.8	2.4	4.8
IL-6 (pg/ml)		0-6.4	44.27	62.34	37.10
HbA1c (%)		3-6	5.4	7	6.34
CT Chest	Percentage lung involvement		25-30%	80-85%	
	CORADS		6	6	
	CT severity score		9/25	18/25	

of symptoms and needed high flow oxygen via non re-breathing mask for maintaining arterial oxygen saturation. The patient deteriorated rapidly while being hospitalized, developed hypoxemic respiratory failure and was administered intravenous Immunoglobulin at the dose of 400mg/kg/day for 3 days and subsequently succumbed to the disease. He was intubated and on mechanical ventilatory support on the day of death. He had no exacerbation of peripheral myasthenia syndromes like ptosis, extra-ocular muscle weakness, bulbar or limb weakness during hospitalization.

The clinical course of these patients was observed during hospitalization and the details of the same are mentioned in table 1. The laboratory and CT chest findings of the patients are mentioned in table 2.

None of the patients had an exacerbation of peripheral myasthenia syndromes like ptosis, extra-ocular muscle weakness, bulbar or limb weakness during hospitalization. Therapy for MG was not altered during hospitalization for any of the patients.

Depending on the symptoms, level of the serum inflammatory markers and CT chest findings, specialized therapies were administered to the patients. There was no relation of ultimate patient outcome with the duration of MG symptoms, previous therapy of MG, and the pre-existing comorbidities. Further, the outcome of these patients depends on the levels of serum inflammatory markers, percentage of lung involvement and CT severity score for SARS-CoV-2.

DISCUSSION

Infections are a known common trigger for myasthenic exacerbations [4]. Theoretically, there is a higher risk of experiencing severe manifestations of SARS-CoV-2 due to the common use of immunosuppressive drugs and potential respiratory failure in relation to respiratory muscle weakness. Additionally, experimental therapies for SARS-CoV-2 like azithromycin and hydroxychloroquine may also trigger a myasthenic exacerbation [5,6].

In our patients, we had no exacerbation of myasthenic symptoms which is a very noteworthy ob-

servation, as respiratory infections are known to be the most common precipitant of respiratory failure and crisis in myasthenia patients [7].

Previous use of steroids plus immunosuppressive therapies did not seem to determine an unfavorable outcome in our patients. Though immuno-suppressed patients could be at a higher risk for a more severe COVID-19 course, growing evidence shows that immunosuppression might play a protective role, reducing the immune response that leads to an inflammatory cytokine storm and to clinical deterioration [8,9].

CONCLUSIONS

Our series is limited by the small number of patients and short duration of follow-up, which did not include the postinfectious period, a time of risk for myasthenic exacerbation. Larger and longer observations are needed to more fully understand: whether patients with MG face special risks from SARS-CoV-2 infection or treatments, whether baseline therapies impact risk and best principals for management and treatment of SARS-CoV-2 in patients with MG.

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