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COVID-19 and Guillain-Barre Syndrome: A Rare Case Report

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Abstract

Though the exact role of influenza like illnesses and vaccination in the development of Guillain-Barre Syndrome (GBS) has not been clear (debatable), Guillain-Barre Syndrome (GBS) has been considered to be an adverse reaction occurring as a result of vaccination since more than fifty years. GBS is an immune-mediated disorder of peripheral nervous system manifesting as one of the most common, most severe form of acute paralytic neuropathy. It is a rare but serious cause of acute neuromuscular paralysis, leading to weak muscular tone and gradual decline in reflexes. We reported a case of 52 year old male, who is chronic tobacco chewer and smoker for more than 20 years, with complaint of difficulty in walking (requiring support of two person) along with associated tingling numbness in both lower legs. The patient suffered from diarrhoea 10 days prior to hospitalization and low grade intermittent fever 5 days prior to hospitalization. Slurring of speech, drooping of saliva and difficulty in closing eyes were reported on 3rd day after hospitalization. RT-PCR (Reverse Transcriptase – Polymerase Chain Reaction) was reported as Positive for COVID-19 infection on 5th day after hospitalization. The electro diagnostic test revealed AMSAN variant of GBS. GBS is an immune mediated disorder and autoimmune disorder mechanism plays a vital role in its pathogenesis. It is not clear whether COVID-19 plays a role in production of antibodies against specific gangliosides. Further research is warranted in this direction to know the mechanism of GBS in patients with COVID-19.

Keywords: Guillain-Barre Syndrome, COVID-19, paralytic neuropathy, SARS-CoV, AMSAN.

Introduction

Corona viruses often cause multiple systemic infections of which respiratory complications are the primitive recognizable symptoms similar to Severe Acute Respiratory Syndrome coronavirus (SARS-CoV). Severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) which is a novel corona virus (COVID-19) was first detected in Wuhan City of Hubei province of China and is spreading around the globe leading to pandemic situation. The symptoms include fever, respiratory illness including cough and dyspnoea, headache, myalgia and diarrhoea.[1] Several studies across the globe have reported gastrointestinal symptoms and neurological symptoms as

well as acute cardiac damage and renal failure due to this infection.

Guillain-Barre Syndrome is an immune mediated disorder that causes acute inflammatory demyelinating polyradiculo-neuropathy. Of the total cases reported of GBS so far, nearly 1/5th cases develop permanent neurologic disabilities. Men have greater risk than women for developing GBS. Any kind of infection can cause GBS due to the immune-pathologic process leading to acute neuromuscular paralysis, muscular weakness and loss of reflexes.[2]

According to our literature review, we came across about only 9 cases published of Guillain-Barre Syndrome associated with COVID-19 infection of which one patient each has been reported from Iran[1], China[3], Spain[4], USA[5] and five patients were from Italy[6]. The Spanish team had reported Miller Fisher Syndrome and polyneuritis cranialis in COVID-19 patient.[4]

In this report, we present a case of hypertensive, type-2 diabetic, and COVID-19 positive patient with GBS (AMSAN variant).

Case Report

A 52-year old male tobacco chewer and smoker patient, with known case of essential hypertension and diabetes mellitus type-2, having history of tobacco use for more than 20 years, was admitted to emergency department, with symptoms of difficulty in walking (requiring 2 person support) with associated tingling numbness in both lower legs. 10 days before admission, patient suffered from diarrhoea (5-6 times/day) and lower grade intermittent fever 5 days prior to admission. On the 3rd day after admission, slurring of speech, drooping of saliva and difficulty in closing eyes was observed in patient on both sides suggesting bilateral Facial Nerve Palsy. An expert opinion of Oral and Maxillofacial Pathologist was solicited to confirm the bilateral facial nerve palsy. RT-PCR was reported to be positive for SARS COV-2 on 5th day of admission.

At the time of admission, patient had normal temperature, pulse 78 per minute, blood pressure 130/92 mm Hg, and respiratory rate 14 per minute with SpO2 98% at room air. On examination, there was decrease in bilateral air entry along with bilateral crepitations. Cardiovascular examination revealed normal S1 S2 sounds. Patient was conscious, oriented to time, place and person with intact higher functions, slurring of speech and Bilateral Facial Nerve palsy – Brackmann grade 4. The muscle tone was decreased in all 4 limbs.

Power	Right	Left
	Upper Limb 2/5 Lower Limb 3/5	Upper Limb 2/5 Lower Limb 3/5
Deep tendon Reflex	Absent	Absent
Plantar Reflex	Absent	Absent

Table 1: Table showing muscle power and reflexes.

Vibration and fine touch sensation were decreased bilaterally below ankle level. No spinal sensory level was detected. Cerebellar signs were absent and bowel bladder were normal and intact. Nerve conduction velocity study suggested severe generalized sensory motor mixed axonal demyelination. Cervical and brain MRI was suggestive of chronic small vessels ischemic changes (FAZEKA Grade 1).

All these findings led us to provisional diagnosis of Acute Onset Sensorimotor Quadriparesis. The differential diagnosis included Acute Intermittent Demyelinating Polyradiculopathy (GBS – Post Viral Sequelae), Periodic Paralysis, Multifocal Motor Neuropathy and Porphyria.

Blood, CSF and Urine investigation findings are mentioned in table 2 and table 3.

Table 2:

CSF Analysis: (Albumino-cytological dissociation was seen)	
Protein	70 mg/dl
Glucose	120 mg/dl
Cells	4/mm^3
Polymorphs	1%
Lymphocytes	99%
Blood and Urine	
ESR	50 mm/hr.
HbA1C	8.2
Vitamin D	15.69
Vitamin B-12	415 pg./dl
S. Magnesium	1.6
LDH	454
Urine Glucose	+3

Table 3:

Day	Day 0	Day 4	Day 7	Day 9
Haemoglobin	12.8	12.7	12.1	13
WBC	10.62	8.32	6.87	6.89
Neutrophil / Lymphocyte	71 / 16	60 / 29	70 / 20	54 / 30
Neutrophil: Lymphocyte Ratio	4	2.06	3.5	1.8
Platelets	240	219	230	313
S. Creatinine	0.72	0.76	0.72	0.75
S. Potassium	4.6	4.2	3.8	4.1
SGPT	34	-	131	135
SGOT	48	-	67	54
Total Proteins	7.6	-	09	9.3
Albumin	4.3	-	3.3	3.9
C – Reactive Protein	2.4	28.18	33.66	0.6
Ferritin	313.4	342	383	-
D-Dimer	0.51	0.63	0.80	0.80
PT/INR/APTT	14.8/1.08	-	19.9/1.48	13.5/0.97
APTT	26.5	-	27.2	26.6

HRCT scan showed multiple ground glass opacities confined mainly to bilateral lower lobes predominantly in Right lower zone (CORADS-4)

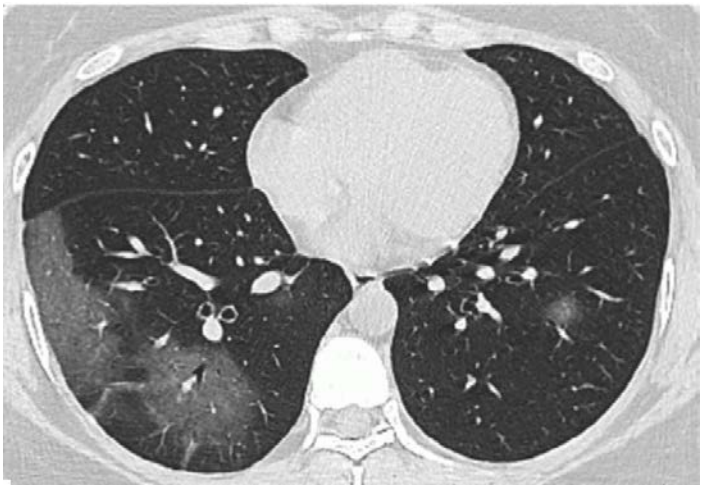

Figure 1: HRCT scan showing multiple ground glass opacities.

All these findings were consistent with Covid Pneumonitis admitted with GBS (AMSAN) in a known case of Essential Hypertension and Diabetes Mellitus Type-2.

Discussion

The novel corona virus is from the beta corona virus subgroup of Coronaviridae family and is comprised of an enveloped single stranded Ribonucleic acid (RNA) genome. Genetically it is similar to SARS-CoV and Middle East Respiratory Syndrome coronavirus (MERS-CoV) in its sequence but there are some differences which make it to be considered as novel or new virus.[7] The human receptor for SARS-Cov2 may be angiotensin converting enzyme receptor 2 similar to SARS-CoV.[8] The main cause of death in patients affected with novel corona virus is acute respiratory distress syndrome (ARDS) along with overwhelming shock from a surge of cytokines.[5] The complications that occur after the COVID-19 infection are not fully understood or studied at present.

Guillain-Barre Syndrome is a life threatening disorder with frequent morbidities, even with the best available treatment. The proposed mechanism for associated GBS in bacterial or viral infections is the autoimmune response wherein the antibodies to surface glycoproteins of pathogen also act on the similar protein structures of

peripheral nerve (molecular mimicry) leading to neurological involvement.[9]

Neurotropism is one of the common feature of this novel corona virus and this virus enters brain possibly through olfactory nerves and spreads to brain areas like thalamus and brainstem which may lead to loss of smell sensation (anosmia).[10] An understanding of exact mechanism of SARS CoV2 induced neurological manifestations is still under research and is in a very early stage. However, neurological symptoms associated with COVID-19 are reported by Mao et al.[11] Other beta coronavirus like SARS and MERS infections have reported neurological manifestations including myopathy, polyneuropathy, GBS and stroke.[12]

Considering the temporal association, we believe that COVID-19 infection might have triggered the neurological manifestations and was responsible for the development of Guillain-Barre Syndrome in our patient. Our findings were consistent with those of Zhao H et al.[3] and Sedaghat Z et al.[1] who also reported GBS associated with COVID-19 infection. There have been nine reported cases so far that suggested possible association of GBS with COVID-19 infection.

The treatment plan in our patient included antibiotics (Ceftriaxone and Azithromycin) with complete COVID standard of care as well as injectable IVIG 2gm/kg divided over 5 days and oral Pregabalin 75 mg 1 od. The outcome of treatment plan was that the 2 person support was weaned off and the power as well reflexes became normal again. At the time of discharge, patient was having residual tingling sensations in bilateral lower limb.

The rationale behind IVIG treatment was that in a multicentre, double-blind, randomized, controlled study, the hyper immune globulin was used to treat patients with severe H1N1 infection in 2009 and it was found that the use of h-IVIG in the treatment of severe H1N1 within 5 days from onset of symptoms was associated with reduction in viral load and reduction in mortality. In previous studies of SARS and MERS, IVIG treatment has exhibited various clinical benefits with good tolerance.[13] The uncommon effects of H-IVIG treatment like rash, hypotension and anaphylaxis[13] were not detected in our patient. Use of immunoglobulin treatment, thus, can be an additional therapy to standard antiviral treatment in COVID-19 patients.

The comparison of findings in nine reported cases of GBS associated with COVID-19 and the findings in our case is enlisted in Table 4.

Parameters	9 Case Reports of GBS with COVID-19	Our patient (In NCH Surat)
Age	23 to 75 years (Mean age 62.5 years)	52 years
Sex	Male: Female = 75%:25%	Male
Symptoms	GBS symptoms started between 5-24 days after COVID-19 symptoms in all But in one case, COVID-19 symptoms started 7 days after GBS onset	GBS symptoms 5 days after onset of COVID-19 symptoms
Respiratory failure	5 patients (55%) develop respiratory failure 4-6 days after GBS onset	Did not develop
B/L Facial Palsy present	6 patients (66%) develop facial palsy mild to severe	Present
Anti-ganglioside antibodies	1 Miller Fisher Syndrome patient – Anti GQ antibodies positive 4 patients (44%) tested	Cannot be tested

	negative 3 patients (33%) testing not done	
CSF study	Proteins level ranged from 40 mg/dl to 193 mg/dl (median 101.5) 5 patients (55%) showed albuminocytological dissociation	Protein: 70 mg/dl Glucose: 120 mg/dl Cells: 4/mm^3 Polymorphs: 01% Lymphocytes: 99% Albuminocytological dissociation seen.
CSF-RT-PCR for COVID-19	All patient negative	Cannot be tested
GBS neuropathy type	Axonal – 3 Demyelinating – 3 Not reported - 3	Axonal
MRI Brain	1 patient showed Facial nerve enhancement bilaterally 2 patients showed Caudal nerve root enhancement	Normal
Treatment	8 patients – IVIG 1 patient – IVIG + Plasma therapy	IVIG 2g/kg iv total dose divided over 5 days
Outcome	2 in ICU + Mechanical Ventilation at 4 week 4 – sent to Rehabilitation facility 3 – Discharged with complete resolution	Discharged

Table 4: Comparison of findings in nine reported cases of GBS associated with COVID-19 and the findings in our case

Zika Virus outbreak in French Polynesia between October 2013 and April 2014 showed a 20-fold increase in GBS (41 patients with GBS had anti-Zika virus IgG or IgM).[14] In 2015, in the Brazilian state of Bahia, 42 GBS cases were reported, including 26 (62%) with a history of symptoms consistent with Zika virus infection.[15] However, the extensive evidence of Zika virus and GBS[16-18] makes it relevant to study and decipher if COVID-19 is also associated with GBS. (Table 5)

Characteristics	GBS and Zika Virus	GBS and COVID-19
Temporal relationship	In 48% cases, Zika symptoms paralleled to GBS	COVID-19 symptoms preceded GBS by 5-24 days
Possible mechanism	Other peri infection mechanism	Post infection aberrant immune response
B/L Facial Palsy present	62% cases	66% cases
Dysphagia	53.5%	20% (very low)
CSF Testing	In 10% patients, RT-PCR was positive	All cases RT-PCR was negative
CSF Protein levels	116 mg/dl (IQR= 67-171)	101 mg/dl (IQR= 51-145)

Table 5: GBS in Zika virus and COVID-19 infection

Conclusion

Influenza and similar like illnesses have been always considered as risk factors for GBS. In 2016, we completed hundred years of first description of GBS and in this century, we have understood the molecular mechanisms of pathogenesis of this disease and have developed new approaches for treatment. Clinicians are at a risk of confirmation bias when assessing patients with shortness of breath during the COVID-19 pandemic and such pandemics, requires high suspicion of GBS. As like Zika Virus and H1N1 virus, COVID-19 virus can also be a causative factor for GBS. Also in selected patients of COVID-19 pneumonia, IVIG can be used as an adjuvant treatment.

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