Case Report

Guillain-Barre Syndrome Associated with COVID-19 infection

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ABSTRACT

Guillain-Barré syndrome (GBS), the prototypic infection-triggered autoimmune disease, presents as an acute polyradiculoneuropathy. With increasing neurological manifestations of COVID-19 being recognised, a vigilance for early diagnosis and therapy is required. Here we report a diagnosed case of Guillain-Barré syndrome (GBS) associated with COVID-19.

Introduction :

COVID-19 disease caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV 2) typically presents with upper or lower respiratory symptoms. There have been few, but definitely increasing, reports of neurological complications. It has been noted that there are both central and peripheral nervous system complications. A few observational series of Guillain Barre syndrome and its variants are reported.[1,2]

Case Report :

A 52 year old male came to our medical college hospital with progressive ascending lower and upper extremity weakness. His symptoms started 7 days before admission. He also had a history of COVID-19 infection (confirmed by RT-PCR) 20 days before onset of his neurological symptoms. He was hospitalised for a duration of 10 days, as his HRCT-thorax showed features of atypical viral pneumonia, CORADS 6, CTSS 9/25. During hospitalisation he received injection remdesvir, steroids, anticoagulants, antibiotics and Oxygen therapy by nasal prongs. He didn't require non-invasive or invasive ventilation.

On admission at our hospital, patient general physical examination, including vital signs were normal. Neurological examination showed decreased motor power, MRC grade 2/5 in all four limbs and deep tendon reflexes were absent. Rest of the neurological examination was normal including cranial nerves and respiratory efforts.

Based on the history and examination, a provisional diagnosis of acute onset flaccid quadriparesis was kept. On investigations, serum electrolytes were normal (serum potassium 4.0 mmol/L), thyroid function tests were normal and there were no abnormalities on complete blood counts, liver and kidney function tests. Motor nerve conduction study (MNCS) showed prolonged distal latency, grossly reduced compound muscle action potential (CAMP) amplitude with reduced conduction velocity in both tibial, peroneal and median nerves and grossly reduced sensory nerve action potential (SNAP) amplitudes on both ulnar and median nerves suggestive of severe grade axonal more than demyelinating sensory motor polyneuropathy affecting both lower and upper limbs. Cerebrospinal fluid (CSF) study had no cells, proteins 56 mg/dL and sugars 65 mg/dL. His total antibody titre for SARS-CoV-2 was 14.49 units (positive result).

Clinical history, examination and findings on electrodiagnostic studies led to the clinical diagnosis of Guillain Barre syndrome associated with COVID-19. Patient was started on intravenous immunoglobulin therapy at a dose of 2 gm/kg over 5 days. Patient did not receive ventilator support. Over a course of 18 days of hospital stay, patient's power improved to MRC 4/5 in all four limbs.

Discussion :

Of the six corona viruses known to infect humans, two of them (SARS-CoV 2002-03 and MERS-CoV 2012) have led major epidemics of respiratory disease in the past, however both have reports of

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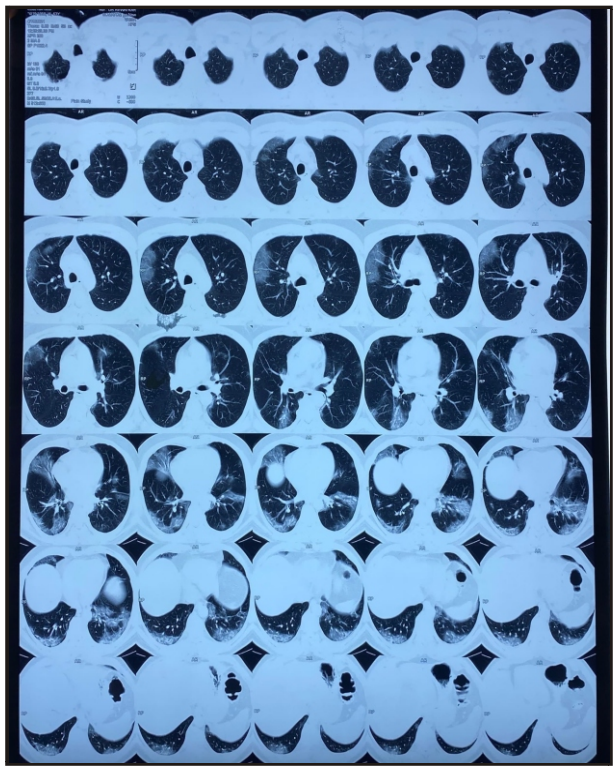

Motor Nerve Studies

UPPER LIMB

Nerve: Right N1: Median R1: APB N2: R2:

Site	Lat1 (ms)	Lat2 (ms)	Dur (ms)	Amp	Area	Segment	Diff (ms)	Dist (mm)	NCV (m/s)
Wrist	5.10	29.06	23.96	3.4 mV	19.6 mVms	Wrist - Elbow	5.11	225	44.03
Elbow	10.21	31.25	21.04	2.8 mV	17.8 mVms				
Lt Median Wrist									
Elbow									

Nerve: Left N1: Median R1: APB N2: R2:

Site	Lat1 (ms)	Lat2 (ms)	Dur (ms)	Amp	Area	Segment	Diff (ms)	Dist (mm)	NCV (m/s)
Wrist	5.94	23.33	17.40	2.7 mV	13.5 mVms	Wrist - Elbow	4.68	225	48.08
Elbow	10.63	31.77	21.15	2.7 mV	19.5 mVms				
Lt Median Wrist									
Elbow									

Nerve: Right N1: Ulnar R1: ADM N2: R2:

Site	Lat1 (ms)	Lat2 (ms)	Dur (ms)	Amp	Area	Segment	Diff (ms)	Dist (mm)	NCV (m/s)
Wrist	2.60	24.17	21.56	4.9 mV	27.8 mVms	Wrist - Elbow	4.90	225	45.92
Elbow	7.50	29.27	21.77	3.6 mV	22.8 mVms	Elbow - Axilla			
Axilla						Axilla - Erb's			
Erbs									

Nerve: Left N1: Ulnar R1: ADM N2: R2:

Site	Lat1 (ms)	Lat2 (ms)	Dur (ms)	Amp	Area	Segment	Diff (ms)	Dist (mm)	NCV (m/s)
Wrist	2.60	23.75	21.15	5.0 mV	27.9 mVms	Wrist - Elbow	5.21	225	43.19
Elbow	7.81	29.27	21.46	3.7 mV	21.8 mVms	Elbow - Axilla			
Axilla						Axilla - Erb's			
Erbs									

LOWER LIMB

Nerve: Right N1: Peroneal R1: EDB N2: R2:

Site	Lat1 (ms)	Lat2 (ms)	Dur (ms)	Amp	Area	Segment	Diff (ms)	Dist (mm)	NCV (m/s)
Ankle	8.44	40.00	31.56	0.4 mV	2.5 mVms	Ankle - Knee	13.12	325	24.77
Knee	21.56	40.00	18.44	143.2 µV	562.4 µVms				

Nerve: Left N1: Peroneal R1: EDB N2: R2:

Site	Lat1 (ms)	Lat2 (ms)	Dur (ms)	Amp	Area	Segment	Diff (ms)	Dist (mm)	NCV (m/s)
Ankle						Ankle - Knee			
Knee									

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NOTE: THE RESULTS MAY BE CLINICALLY CORRELATED

occasional CNS and PNS diseases. A wide range of neurological diseases are associated with COVID-19, including the Cerebrovascular disease attributed to prothrombotic state of COVID-19, Encephalitis, Meningitis, Myelitis or CNS vasculitis, Acute Disseminated Encephalomyelitis, Guillain Barre Syndrome (GBS) and the commonly found loss of smell (Anosmia) and taste (Ageusia).

The neurological manifestations of COVID-19 could be the effects of direct viral invasion, para-infectious and post-infectious inflammation of nervous system and vasculature or complications of a systemic disease.[2]

Till date, the mechanisms responsible for involvement of peripheral nervous system in COVID are not well established. However, GBS is a prototype of infection-triggered autoimmune neurological disease with the common agents being viruses like influenza, enterovirus, cytomegalo virus, Epstein-Barr Virus, and bacteria such as campylobacter jejuni & mycoplasma pneumoniae.[3]

It is proposed that SARS-CoV involves a dual receptor attachment to surface of a respiratory cell mediated by spike (S) viral protein which binds to angiotensin converting enzyme (ACE-2) receptor and sialic acid containing glycoproteins and gangliosides on cell surfaces.[4,5] Gangliosides contain a disialosyl moiety- GD1b, GQ1b and GT1b or 2 gangliosides share epitomes with GM2 or a combination of GM2 and GM1 which can serve as antigens. When IgM recognises Gal (pl-3) Gal NAc moiety of GM1, which is found on surface of motor neuron, there can be a presentation of motor neuropathy like GBS.[6]

GBS presents as an acute polyradiculopathy with rapidly progressive, symmetrical limb weakness, areflexia, sensory symptoms, facial weakness and autonomic dysfunction. Several variants of GBS have been described in COVID-19 AIDP, AMAN, MFS, pharyngeal-cervical-brachial variant.

The time interval between onset of neurological disease after respiratory or systemic disease is not well established, however a case series reported a median duration of 7 days (range -7 to 24 days) with few patients presenting as GBS, later showing respiratory system involvement, implying physician

must have high index of suspicion for the disease association.[2]

WHO has provided COVID-19 case definitions[7] which defined GBS and other acute neuropathies associated with SARS-CoV infection as probable association when

1. Neurological disease onset within 6 weeks of acute infection,
2. Either SARS-CoV-2 RNA detected in any sample or antibody evidence of acute SARS-CoV-2 infection
3. No evidence of other commonly associated causes, are met.

Supplementing the proposed post-infectious inflammatory theory for disease causation is a good response to IVIg. It has been used in standard dose (2 gm/kg divided over 5 days). In presence of chloroquine, it is found that SARS-CoV viral spike protein cannot bind gangliosides to infect the target cells. However trials are needed to establish safety and benefit in adding the anti malarial drug to IVIg therapy in COVID-19 triggered GBS.[4]

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