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ATYPICAL VARIANT OF GUILLAIN-BARRE SYNDROME FOLLOWING COVID-19 PNEUMONIA

Neurology

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ABSTRACT

Background- Coronavirus disease 2019 (COVID-19) has been shown to be associated with a lot of neurological complications, of which Guillain-Barre syndrome (GBS) is an important post-infectious or para-infectious sequelae.
We present a 42-year-old female with sudden onset weakness along with tingling sensation in both lower limbs.
She suffered from Bilateral pneumonia secondary to COVID-19 17 days earlier and symptoms of weakness started 7 days after discharge from the hospital NCS and CSF studies were performed which confirmed Atypical variant of GBS.
MRI Whole spine was done to rule out any other causes.
Patient was started on IVIG and needed Ventilatory care Patient unfortunately had a fatal outcome.

KEYWORDS

Guillain-Barre Syndrome, Post-COVID 19, Neurology.

INTRODUCTION

The COVID-19 outbreak started at the end of 2019 in Wuhan, the capital of Hubei province, in China. The novel coronavirus was designated as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Neurological manifestations have been described in one third of patients with COVID-19. Some of these neurological symptoms have proved to be quite specific, e.g., loss of smell or taste, but other ones are non-specific, e.g., headache, dizziness, or reduced level of consciousness ().

However, whether the neurological symptoms associated with SARS-CoV-2 are attributable to secondary mechanisms (i.e., multi-organ dysfunction or systemic inflammation), an abnormal immune response or the direct injury of the virus is still unknown.

Several case reports have suggested a relationship between the occurrence of Guillain–Barré syndrome (GBS) and a previous SARS-CoV-2 infection, which preceded the GBS onset by up to 4 weeks. Therefore, a post-infectious dysregulation of the immune system, triggered by SARS-CoV2, appears to be the most probable cause.

GBS is classically described as an Acute symmetrical demyelinating areflexic ascending polyradiculoneuropathy with flaccid paralysis.
Although most commonly GBS has been described secondary to GI infections such as C.jejuni various reports of GBS have come to light during the COVID-19 pandemic which were preceded by a COVID-19 infection.

GBS if detected early has good prognosis specially the demyelinating variant AIDP (Acute inflammatory demyelinating neuropathy) and other variants which include AMSAN (Acute motor sensory axonal neuropathy) and AMAN(Acute motor axonal neuropathy) which are axonal variants have a relatively poor outcome.

Miller-Fischer syndrome characterised by Bilateral ophthalmoparesis, ataxia without any weakness is another rare variant of GBS

Conversely, a pathological study on post-mortem human brain tissues found that anosmia and dysgeusia, described in up to 20% of patients, are more likely due to the direct viral invasion of the olfactory nerve and bulb (2). In addition and in line with this observation, a COVID-19 patient with anosmia showed magnetic resonance imaging (MRI) abnormalities in the olfactory bulb and in the inferior frontal lobe, as a conceivable result of the direct invasion of SARS-CoV-2 through the olfactory pathway via trans-synaptic retrograde spreading (3).

Case Presentation:

A 42 year old female presented to our hospital with sudden onset weakness along with tingling numbness in both lower limbs.

Sensory symptoms of paraesthesia were present since 2 days and the weakness gradually started progressing over 2 days when the patient noticed an inability to get up from her bed and was then brought to the hospital.

There was no associated fever, trauma and did not have bowel/bladder involvement.

The patient suffered from COVID 19 Bilateral Pneumonia 20 days ago and was treated for the same, 7 days after discharge the patient developed symptoms of weakness and tingling numbness in both lower limbs.

She was conscious oriented on admission and the patient's oral temperature was 37.1◦C, O2 saturation was 94% on Room air, pulse rate was 118 beats per minute, and blood pressure was 150/80 mm Hg , respiratory rate was 16 per minute Power was 1/5 in both lower limbs on presentation and power was 3/5 in right upper limb and 5/5 in left upper limb at presentation according to Medical Research Council (MRC) scale.

There was loss of pain, temperature, vibration in both lower limbs while the following sensations were intact in both the upper limbs.

Superficial and deep reflexes were completely absent in both lower limbs and hyporeflexia (1+) was found in both upper limbs.

Cranial nerves were intact on presentation. Cerebellar signs were absent and gait could not be assessed due to lack of power in both lower limbs. Higher mental functions were normal and no involuntary movements were seen.

Her NCS were done on day 2 of symptoms, the findings were suggestive of Atypical variant of Guillain-Barré syndrome.

MRI of the cervical spine along with CSF studies were performed to rule out any alternative causes of paraparesis.

A diagnosis of Guillain-Barre syndrome was made using the Brighton criteria as described below (10)

She was admitted with Bilateral pneumonia 17 days ago when RTPCR for COVID 19 was positive and HRCT thorax showing Bilateral Ground glass opacity (figure 1) suggestive of COVID 19 pneumonia. During that Time period treatment with Inj. Remdesivir 100mg 6 doses , Inj. Methylprednisolone 40mg BD, Inj. Low-Molecular weight heparin 0.4cc S/C BD along with broad spectrum antibiotics and Vitamin A/C/E was initiated, she did not complaint of any tingling or weakness during this time period and needed 5 litres of oxygen via simple mask for the initial 5 days of therapy.

CARP was followed to maintain adequate oxygenation and then on Day 10 the patient was discharged after 3 days of being afebrile and off oxygen therapy.

The Patient did not have any comorbidities like diabetes, hypertension, or any history of trauma or similar complaints in the past.

During the episode of weakness, the patient was started on IVIG (0.4g/kg/d) and received all 5 days of IVIG as the NCS was suggestive of Atypical GBS.

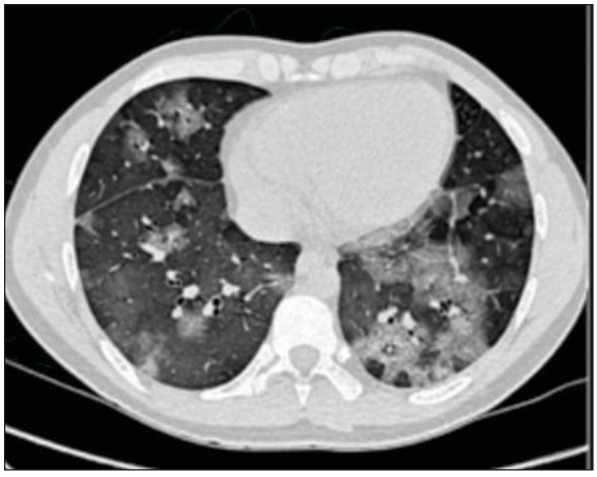
The laboratory examination results were follows: serum glucose 121 mg/dL; blood urea nitrogen: 21 mg/dL; creatinine 0.8 mg/dL; alanine aminotransferase 35 IU/L; aspartate aminotransferase 47 IU/L; sodium 135 mmol/L; potassium 4.3 mmol/L; white blood cell count 11,700 cells per microliter (neutrophils = 77.7%; lymphocytes = 14.4%); Erythrocyte sedimentation rate 72 mm/hour, haemoglobin 11.6 g/dL.

The patient was tracheostomised on day 10 of illness as the patient did not show any signs of spontaneous breathing and a prolonged Ventilatory course was expected.

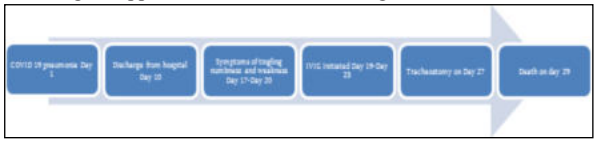
The power did not improve during the course of the illness and areflexia was noted throughout.

Sequential ABGA were done and did not reveal any abnormality.

Unfortunately the patient succumbed to complications of ventilatory care.



Ground glass appearance on HRCT thorax Figure 1



INVESTIGATIONS

The NCS was suggestive of Widespread Sensory-motor demyelinating + Axonal Polyradiculoneuropathy affecting all 4 limbs
An overview of the findings is described in the table below

Motor Nerve Conduction:
Right peroneal - EDB: Absent
Left peroneal - EDB: Absent
Right Tibial -AH : Prolonged Latency, Low Amplitude.
Left Tibial -AH: Prolonged Latency, Low Amplitude.
Right Median -APB: Prolonged Latency, Low Amplitude
Right ulnar : ADM: Prolonged Latency, Low Amplitude.

Sensory Nerve Conduction:
Right Sural : Absent
Left Sural: Absent
Right Median Digit 2: Prolonged Latency, Normal Amplitude, Low velocity.
Right Ulnar- digit 5: Absent

F wave study:
Right Tibial F wave: Absent
Left Tibial F wave: Absent
Right Median F wave: Absent

H reflex:
Right Tibial H reflex: Absent
Left Tibial H reflex: Absent

Motor Conduction

Nerve	Distal latency, ms	Amplitude, mV	Conduction velocity, m/s	F latency, ms
Right median nerve				
Wrist–abductor pollicis brevis	9.1 (normal ≤3·8)	2.2(normal ≥4)	..	Absent F (normal ≤31)
Antecubital fossa–wrist	10.2	1.8	38 (normal ≥50)	..
Right ulnar nerve				
Wrist-abductor digiti minimi	4.8 (normal ≤3·0)	3.2 (normal ≥6)	..	..
Below elbow–wrist	5.2	2.1	44 (normal ≥50)	..
Left tibial nerve				
Ankle-abductor hallucis brevis	8.2 (normal ≤5·1)	1.2 (normal ≥4)	..	Absent F (normal ≤56)
Popliteal fossa–ankle	17·11	4·80	43 (normal ≥40)	..
Right tibial nerve				
Ankle-abductor hallucis brevis	7.6 (normal ≤5·1)	1.8 (normal ≥4)	..	Absent F (normal ≤56)
Popliteal fossa–ankle	15·95	6·00	43 (normal ≥40)	..
Left peroneal nerve				
Ankle-extensor digitorum brevis	Absent (normal ≤5·5)	Absent (normal ≥2)	..	..
Below fibula–ankle	Absent	Absent	Absent (normal ≥42)	..
Right peroneal nerve				
Ankle–extensor digitorum brevis	Absent (normal ≤5·5)	Absent(normal ≥2)	..	..
Below fibula–ankle	Absent	Absent	Absent (normal ≥42)	..

Sensory Conduction

Nerve	Site	Amplitude, µV	Conduction velocity ,m/s
Right median nerve	Digit 2–wrist	19·9 (normal ≥18)	42 (normal ≥50)
Right ulnar nerve	Digit 5–wrist	Absent (normal ≥18)	Absent (normal ≥50)
Left sural nerve	Calf–posterior ankle	Absent (normal ≥6)	Absent (normal ≥40)
Right sural nerve	Calf–posterior ankle	Absent (normal ≥6)	Absent (normal ≥40)

CSF analysis done on day 3 of illness revealed 12 cells (all Lymphocytes) and protein levels of 45.4% (10-45) suggestive of mild pleocytosis and not revealing any Albumino-cytological Dissociation, sugar of 63 mg% (40-80) Chloride of 117mEq/L (108-118).

MRI of the spine did not reveal any abnormality.

DISCUSSION:

Since the beginning of the pandemic several reports have tried to study the neurological impact of COVID 19 (4). A strong association has been noted between COVID 19 and GBS (5).

For GBS triggered by SARS-COV-2, it is hypothesized that the attachment of SARS-CoV-2 to cell surfaces is mediated by the viral spike (S) protein, which binds to angiotensin-converting enzyme 2 Receptor and also to gangliosides containing sialic acid residues, including the GalNAc residue of GM1 (11,12). It has been suggested that cross-reactivity between the viral protein–associated gangliosides

and peripheral nerve gangliosides as the result of molecular mimicry.

The age group 55±17 years as noted by Abu-Rumeileh et. Al (6) was consistent with our case report although a significant male preponderance was noted in their study.

Symptoms of GBS were noted after 17 days in this case and a median (IQR): 14 (7–20), min 2–max 33 days] (6) was reported in other studies The patient was in ARDS during the episode of COVID 19 and many such cases have dyspnoea and/or pneumonia (63.8%, 46/72) as per Abu-Rumeileh et. Al (6) study.

Typical ground glassing opacity on HRCT thorax was noted.

Acute onset paraparesis was the defining symptom of the case along with tingling numbness which was also observed in reports by Rahimi et.al (7).

Cranial nerve involvement was not seen at onset or during the course of illness, although autonomic involvement was present at the onset which was a rare finding as only 16.7% (12/72) cases reported autonomic involvement.

As autonomic involvement was predominant the Patient was administered IVIG as opposed to Plasmapheresis for the treatment of GBS.

The NCS findings were atypical as most reports showed a predominant AIDP pattern (6,7,8) and this case showed a widespread Sensory-motor demyelinating + Axonal Polyradiculoneuropathy affecting all 4 limbs.

CSF study did not reveal any albumin-cytological dissociation which was noted in most case reviews (6,7), this can also be attributed to the fact that the CSF was studied on day 3.

Hasan et.al (8) reported 65.3% cases had a good outcome (GBS Disability score <2) in their metanalysis, whereas review by Sriwastava S et.al (9) reported recovery of 70.4% cases Ventilatory care was needed for 21.7% (6) and death occurred in 5.8% of the cases (6).

Death was noted in 5 patients by Sriwastava S et.al (9) 3 had AIDP and 2 patients had AMAN/AMSAN.

In spite of optimal management the patient succumbed.

CONCLUSION:

COVID 19 has presented with Multi-system involvement over the pandemic but clinicians should remember that neurological involvement with GBS although rare, is a potentially treatable and has a good prognosis if diagnosed early and treated aggressively.

Subtle symptoms of tingling numbness in lower limbs should be evaluated promptly for symptoms of GBS and early interventions should be carried out to stop the progression of this fatal disease.

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