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Acute Transverse Myelitis (ATM) and Guillain-Barre Syndrome (GBS) Overlap Syndrome in A COVID-19 Patient: A Case Report

Syed Hashim Ali Inam[1], Ayesha Malik[2], Manahil Chaudhry[2], Mohammad Abdullah[3], Zimar Arshad[4], Bismah Riaz[1]

[1]House Officer, Combined Military Hospital, Lahore, Pakistan.
[2]Medical Officer, Hameed Latif Hospital, Lahore, Pakistan.
[3]Resident Medicine, Combined Military Hospital, Lahore, Pakistan.
[4]Resident Radiology, Combined Military Hospital, Lahore, Pakistan.

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ABSTRACT

Acute transverse myelitis (ATM) and Guillain-Barre syndrome (GBS) are classified as myelopathy and radiculopathy, respectively, that rarely co-exist together, but when they do either concurrently or sequentially it is termed as ATM-GBS overlap syndrome. While a few cases have been reported, we report a case of the overlap syndrome in a patient with coronavirus disease 2019 (COVID-19). As per our knowledge, this is the first case to be reported. This case report documents this rare presentation which will add to the scarcity of previous literature on ATM-GBS overlap syndrome post-COVID-19 infection, and can facilitate clinicians in diagnosing similar cases whenever they occur.

Keywords: Acute Transverse Myelitis, COVID-19, Guillian Barre Syndrome.

INTRODUCTION

Acute transverse myelitis (ATM) is a type of inflammatory myelopathy that can present with various, progressive sensory and motor symptoms.[1] On the other hand, Guillain-Barre syndrome (GBS) is an immune-mediated neuropathy that can either cause a demyelinating or axonal neuropathy and has several variants.[2] The two diseases can rarely occur simultaneously as a radiculomyelopathy proving to be a diagnostic dilemma for any physician. Only a few cases of this aforementioned overlap syndrome have been reported to date.[3] A 2019, literature search by Fang Guo and Yong-Bo revealed 23 cases of ATM-GBS overlap syndrome, and later in the same year, another case was reported in Pakistan.[3,4] Etiologically, GBS can be preceded by numerous infectious agents, including Campylobacter jejuni, Mycoplasma pneumoniae, Mumps virus, Legionella, Influenza virus, Bartonella henselae, and Zika virus.[5-7] Since the onset of the COVID-19 pandemic, there have been several case reports of GBS in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) patients.[8-10] However, the SARS-CoV-2 virus causing ATM remains unreported.

Name & Address of Corresponding Author
Dr. Mohammad Abdullah
Resident Medicine
Combined Military Hospital,
Lahore, Pakistan
Email: mohammadabdullah_786@hotmail.com

Nonetheless, as per our knowledge, there has been no documented case of the ATM-GBS overlap syndrome in a patient of COVID-19 to this date.

CASE PRESENTATION

A 40-year-old, previously healthy male presented to the emergency department (ED) with complaints of low-grade fever, nausea, rhinorrhea, and generalized myalgias for the past one week. This was followed by bilateral, asymmetrical, distal lower limb weakness over the next three days, which rapidly progressed to quadriparesis of the flaccid type one day before presenting to the ED. He did not inform us of any other symptoms indicating respiratory compromise, bladder or bowel dysfunction, or those pertinent to autonomic dysfunction.

His general physical examination was remarkable for jaundice while the neurological system examination revealed widespread hypotonia and power of 3/5 in all four limbs, as per the medical research council (MRC) scale.[11] His deep tendon and superficial reflexes showed an active, normal response, and the plantar reflexes were down-going bilaterally. Additionally, his sensory system examination revealed diminished fine touch sensations in the lower limbs without a well-defined sensory level. The rest of the systemic examination was unremarkable. His past medical, surgical, drug and occupational history were also unremarkable. He had bodyaches for which he required repeated analgesics. As a part of the admission process, screening investigations for COVID-19 were

conducted. This included a nasopharyngeal swab for polymerase chain reaction (PCR) and a high resolution computed tomography (HRCT) chest. Other initial blood work was done as shown in [Table 1].

His HRCT chest revealed typical changes compatible with COVID-19 infection with a computed tomography severity score (CTSS) of 11/40. Therefore, the patient was admitted to the COVID-19 intensive care unit (ICU). His vitals at the time of admission were within normal limits, with an oxygen saturation of 95% on room air. The COVID-19 PCR test was negative. Considering mild disease, no novel or targeted therapy for COVID-19 infection was started except for anticoagulation for deep venous thrombosis (DVT) prophylaxis.

Table 1: Laboratory test values

Test	Admission	Day 3	Reference Values
Complete Blood Picture			
TLC	11.8	9.4	4–11 x 109 / L
Hb	12.3	12.6	13.5 – 17.6 g/dL
Platelets	99	180	150 – 400 x 109/L
Liver Function Tests			
Total Bilirubin	120	21 umol/L	3 – 17 umol/L
S. ALT	166	451 U/L	0 – 42 U/L
S. ALP	341	200 U/L	65 – 300 U/L
S. Albumin	36	25 g/L	35-50 g/L
Serum Ferritin	>2000 ng/ml	>2000 ng/ml	15 - 200 ng/ml
CRP Q	48.3 mg/l	40.0 mg/l	<6.0 mg/l
D-Dimers	200-400 ug/ml	<200 ug/ml	<200 ug/ml

(L: litre, g/dL: grams/ decilitre, ng/mL : nanograms/ millilitre, ug/mL: micrograms/ millilitre, U/L: units/ litre, mg/L: milligrams/ litre)

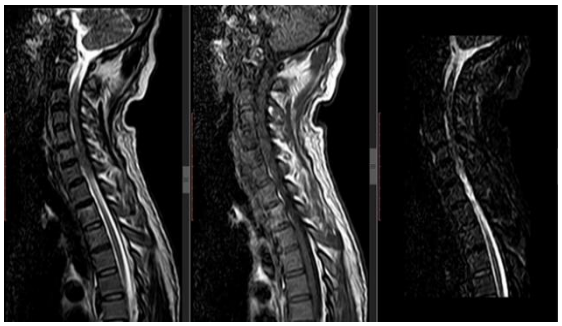

Figure 1: The image shows sagittal T1WI and T2WI slices of the cervical spine with the corresponding axial section through C2-3. Mild swelling of the cervical spinal cord noted with non-homogeneous T2WI hyperintensities, extending from C2 to C7 level. Obliteration of anterior and posterior CSF columns is also noted in this segment

Magnetic resonance imaging (MRI) brain and spine with contrast were ordered. The MRI brain was normal but the MRI spine revealed mild swelling of the cervical cord noted with non-homogenous T2 weighted image (T2WI) hyperintense signals in the cord extending from cervical vertebrae two (C2) to cervical vertebrae seven (C7). Obliteration of the anterior and posterior cerebrospinal fluid (CSF) columns was also noted in this segment, as illustrated in [Figure 1].

Keeping in view these findings, a diagnosis of acute transverse myelitis (ATM) was made and the patient was started on high dose corticosteroids (injection methylprednisolone 1 mg/kg/day). Daily motor, sensory, and respiratory system examination were done, along with a bedside single breath count and cough reflex assessment. However, on day four of treatment the patient's power deteriorated to 2/5 in all limbs. Due to the presence of normal reflexes, no bladder or bowel involvement, and no well-defined sensory level involvement, an alternate diagnosis was considered and his cerebrospinal fluid (CSF) analysis was carried out which showed albuminocytologic dissociation. After this, the team proceeded with an electromyography (EMG) and nerve conduction study (NCS) which revealed a severe acute motor and sensory neuropathy (AMSAN) variant of GBS. This is illustrated in [Table 2]

Table 2: EMG/ NCS Report

EMG	NCS (Nerve Conduction Study)	Conclusion
Very occasional involuntary activity seen, fibrillations +, PSWS+. Very few MUAPs with very discrete recruitment seen in bilateral posterior tibialis and deltoid. No involuntary activity is seen and normal recruitment MUAPs in the right masseter.	Low CMAP motor amplitudes with increased latencies in: • Bilateral tibial nerve • Common peroneal nerve • Right Ulnar nerve and Median nerve With decreased conduction velocity. Absent sensory amplitudes in: • Bilateral Sural nerve • Right Ulnar nerve • Left Median nerve Prolonged F wave minimum latency in bilateral tibial nerve.	The electrophysiological data is suggestive of "severe acute axonal motor and sensory neuropathy" (AMSAN) with: axonal involvement ++ ongoing denervation +

*MUAP= Motor unit action potential, CMAP= Compound muscle action potential, PSWS= Positive sharp waves

After this was established, without further delay the patient was started on plasmapheresis (PLEX) on an alternate days. After the second session, the patient and team noticed some clinical improvement in power. A total of five sessions of PLEX were conducted on alternate days.

Our patient was treated with both, steroids and PLEX, modalities that have a proven role in ATM and GBS, respectively. After the culmination of the treatment, the patient showed marked improvement and currently has power 4/5 in all limbs, the sensations returned to normal and overall the patient was ambulatory with support.

DISCUSSION

The symptomatology of GBS and ATM differ such that, GBS is characterized by symmetrical ascending weakness of the limbs, hyporeflexia, or areflexia and is a common cause of acute, progressive flaccid paralysis.[1] ATM, on the other hand, is an inflammation of the spinal cord characterized by motor, sensory, and autonomic disturbances.[2] The occurrence of Guillain Barre syndrome (GBS) and acute transverse myelitis (ATM), either concurrently or sequentially, is defined as ATM-GBS overlap syndrome.[12] In our case, the overlap syndrome was in adjunct to the AMSAN variant of GBS, a sub-type associated with poorer outcomes.[4]

Multiple case reports have reported GBS post-infection to the SARS-CoV-2.[8-10] This may be due to the virus's neurotrophic and neuro-invasive characteristics.[13] Our patient was diagnosed as a probable case of COVID-19 based on the HRCT findings and elevated acute phase reactants as shown in [Table 1].

A study by Ai et al. in Wuhan, China reported a significant number of people who were highly likely, or probable cases of COVID-19, which simultaneously had negative PCR reports.[14] They concluded the HRCT chest as a primary tool for detection,[14] which is why we labeled our case as COVID-19 positive. Another noticeable finding was an elevated bilirubin level and physical findings of jaundice which has been described by Paliogiannis et al. who reported a statistically significant finding of altered bilirubin levels in COVID-19 patients.[15]

Our patient was 40-year-old, while the reported mean age at onset of ATM-GBS overlap syndrome, according to a case series involving 23 patients, was 21.3 years old.[3] A similar report of a 34-year-old male of ATM-GBS overlap was reported at a local hospital in Pakistan.[4] The other contrasting differences in their case and ours was the presence of hyporeflexia and paraparesis involving the lower limbs at the time of presentation, in their patient.

Due to the rarity of the overlap syndrome, no well-defined treatment guidelines exist. The first-line treatment for ATM is corticosteroids and GBS is intravenous immunoglobulins (IVIG).[16] It has been stated that there is no statistically significant difference in treatment outcomes between patients treated with IVIG versus plasmapheresis in GBS patients.[2] In our setup, due to increased cost, there is an unavailability of IVIG, therefore, plasmapheresis was carried out which seemed to have worked based on patient recovery.

CONCLUSION

In conclusion, our patient had the imaging features of ATM with clinical features and electrophysiological tests that suggested GBS. In turn, recovery was seen when he was treated for both the diseases, and a diagnosis of ATM-GBS overlap syndrome was deduced. While this overlap syndrome has been reported previously, as per our knowledge and review of existing literature, this is the first to be reported in a patient of COVID-19. Therefore, we conclude that COVID-19 can cause ATM-GBS overlap syndrome in previously healthy patients.

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