Journal of Cardiovascular Disease Research

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 05, 2022

COVID-19-ASSOCIATED GUILLAIN–BARRE SYNDROME: A CASE SERIES

AbujamIndrajit Singh[1], Rothangpui[2], M. Ratankumar Singh[2*], Gracefulda Hadem[3], Joydeep Sarkar[3]

[1]Assistant Professor, Department of Medicine, JNIMS, Imphal, Manipur, India.
[2]Associate Professor, Department of Medicine, JNIMS, Imphal, Manipur, India.
[3]Post graduate Trainee, Department of Medicine, JNIMS, Imphal, Manipur, India.

Corresponding Author: Dr M. Ratankumar Singh, Associate Professor, Department of Medicine, JNIMS, Imphal, Manipur, India.
Email: drmratan2007@gmail.com

ABSTRACT

COVID 19 since its emergence has created a turmoil across the globe and has taken innumerable lives worldwide. Apart from the respiratory manifestation, neurological manifestations also occupy a prominent feature with a special mention on Guillain–Barre syndrome (GBS). There are growing volume of reported cases of GBS associated with Covid 19. More than 220 patients with GBS have been reported thus far. We wish to share 6 cases of GBS associated with COVID 19 admitted in our institute. More intriguingly, one of the case develops GBS along with active COVID 19 symptoms. So what is the exact relationship with COVID 19 and GBS? Further studies are needed to get a clear answer.

Keywords:COVID-19, Guillain–Barre syndrome.

Introduction

SARS-CoV-2, since its discovery in December 2019[1] at Wuhan continues to linger, evolve, and astonish the researchers across the globe with its wealth of manifestation. Apart from respiratory involvement, neurological manifestation is also an important component of Covid 19 infection. While the neurological sequelae of the virus remain poorly understood, there are a growing number of reports of neurological manifestations of COVID-19. Initial reports from Wuhan showed 78 (36.4%) out of 214 patients admitted with COVID-19 had neurological symptoms ranging from anosmia, taste disturbances to cerebrovascular accident and seizures.[2] More beguilingly, there are growing reports of Guillain–Barre syndrome associated with COVID 19 infection from different parts of the world.[3-6] Here we are also reporting a case series of GBS associated with COVID 19 from our institute, Jawaharlal Nehru Institute of Medical Sciences, Imphal after getting full informed consent.

Case 1

On December 10, 2020, a 28-year-old, right-handed female was referred from a District Hospital to our centre with 1-week history of progressive limb weakness and foot dysesthesia. On the evening, prior to admission to the district hospital, she noted some difficulty standing unaided and noticed some tingling sensations in her feet. The next

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 05, 2022

morning, she was unable to stand and her arms felt weak for which she was taken to the district hospital.

Incidentally, she also reported a 1-week history of fever, cough, myalgia, and headache. On presentation to our institute, she was febrile, had tachycardia (heart rate 110 bpm), and bilateral crepitations on lung auscultation. Her oxygen saturation was 88% on room air with respiratory rate of 28 breaths/min. Limb examination revealed reduced tone with symmetrical weakness of 4/5 on the Medical Research Council (MRC) Power Grading scale in upper and lower limbs. She had diminished triceps reflexes and absent bicep, supinator, knee, and ankle reflexes bilaterally. Pinprick sensation was impaired to the right midfoot and left ankle, with intact cranial nerves. Bowel and bladder habits were normal.

After 72 h, her lower limb power had reduced to 3/5 proximally and 2/5 distally and all limb reflexes were absent. The overall impression was of a progressive flaccid symmetrical sensory and motor neuropathy.

On investigation, hemogram showed significant thrombocytosis (690 × 109/L) and a raised C-reactive protein (25 mg/L). Renal profile, electrolyte, serum thyroid, and clotting parameters were all within the normal range. Antinuclear antibody, antineutrophil cytoplasmic antibodies, virus screen (HIV, hepatitis B, and hepatitis C) were negative. Her chest X-ray on admission showed mild heterogenous infiltrates in bilateral lower zones. Her SARS-CoV-2 (COVID-19) nasopharyngeal swab RTPCR was positive, became negative for COVID-19 on 7th day of admission in our institute and she was shifted to non-COVID intensive care unit for further management.

CSF analysis revealed high CSF protein (73 mg/dl) with normal glucose and cell count, showing albuminocytologic dissociation. Nerve conduction study was done on day 12 of admissions which revealed reduced conduction velocity and prolonged distal motor latencies in motor and sensory nerves more prominently in the LL.

Case 2

A 29-year-old young male, chronic smoker, alcoholic and recently detected diabetes mellitus was referred on August 24, 2021, to our hospital from a local private hospital, with a history of acute-onset progressive ascending paralysis of both upper and lower extremities which started 10 days back. The patient has been quadriplegic 2 days before admission with facial and respiratory muscle weakness causing CO2 narcosis needing ventilatory support.

On physical examination, he was afebrile with blood pressure (BP) 118/80 mmHg, heart rate of 95 beats/ min, and maintaining oxygen saturation of 98% on Synchronized Intermittent Mandatory Ventilation, SIM-VC mode (mechanical ventilation). Neurologically he was fully conscious, with motor power showing weakness in all four limbs with a Medical Research Council (MRC) scale of 3/5 in proximal, 4/5 in distal of upper extremities, 2/5 in proximal, 3/5 in distal of lower extremities. Deep tendon reflexes were absent with generalized hypotonia. There was no bowel and bladder involvement.

Potassium level was normal with unremarkable complete hemogram except for the raised erythrocyte sedimentation rate (ESR) of 62 mm/h. HbA1C was 12.35 gm%. COVID-19-RTPCR (Reverse transcription polymerase chain reaction) was negative,

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 05, 2022

however, anti-SARS-CoV-2 – IgG positive (87.01 BAU/ml), and anti-SARS-CoV-2 – IgM were positive (2.35 BAU/ml). He was not vaccinated for COVID 19.
Noncontrast computed tomography of the brain was normal. Cerebrospinal fluid (CSF) analysis showed markedly elevated protein level of 323 mg % with normal cell count of 2 cell/ cu mm, showing characteristic albumin-cytologic dissociation of GBS. Nerve conduction study could not be done.

Case 3

On September 14, 2021, a 51-year-old female, post-COVID status, presented with weakness of both upper and lower extremities, slurring of speech, and difficulty swallowing for the last 5 days. Weakness is acute in onset, initially involve the distal muscles then gradually progress to involve the proximal muscles. She had no urinary or fecal incontinence. Two weeks prior to hospitalization, she suffered from mild-to-moderate COVID-19, symptomatic for around 1 week.

On examination, she was afebrile with BP 120/88 mmHg, heart rate of 86 beats/min, respiratory rate of 18/min, and oxygen saturation of 98% at room air. The muscle strength examination shows weakness in all four limbs, with a Medical Research Council (MRC) scale of 4/5 in proximal as well as distal group of upper extremity muscle and 3/5 in proximal and distal group of muscles of the lower extremities. Deep tendon reflexes were absent in lower extremities and reduced in upper extremities. There is lower motor neuron type bilateral facial nerve palsy. There was no bowel and bladder involvement. Laboratory examination results are unremarkable except for the raised ESR of 45 mm/1st h. CSF analysis showed characteristic albumin-cytologic dissociation of GBS with raised protein of 121 mg % and normal cell count of 3 cells/mm3.

Magnetic resonance imaging of the brain without contrast was within normal limit. Nerve conduction velocity study showed prolonged latency with reduced amplitude of motor nerve with decreased conduction velocity of sensory nerve, compatible with both axonal and demyelinating neuropathy.

Diagnosis of GBS were made and Intravenous immunoglobulin 0.4g/Kg/day for a period of 5 days was given for all the three described cases. All of them showed remarkable recovery with successful extubation of the second case and were discharged on stable condition.

Case 4

On 7th may, 2022 a 36-year-old male, non-diabetic, ocassional alcoholic and smoker patient presented to our outpatient department with the complaints of acute onset weakness of bilateral lower limbs for 2 weeks and tingling sensation of both upper and lower limbs for 1 week. He was haemodynamically stable and his KFT was within normal limit. Viral markers were negative.

Neurological examination revealed motor power of bilateral LL and UL of MRC 4/5, with pan areflexia. Bladder and bowel were normal.
CSF examination showed cell count of 2, with protein of 138 mg/dl, showing albumin-cytological dissociation.

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 05, 2022

Nerve conduction Study shows Predominant Axonal motor sensory peripheral neuropathy

MRI whole spine was normal. He also didn't have antecedent COVID symptoms. However, his

Anti-SARS-CoV-2 IgG (547.28 BAU/ml) was positive. There was no history of recent COVID vaccination.

Case 5

A 46years old occasional alcoholic, non-diabetic was admitted on 13thMay, 2022 with complain of weakness of upper limb and lower limb with tingling sensation mainly in the lower limb for 2 weeks. On evaluation he had motor weakness with MRC scale of 4/5 in upper limb and 3/5 in lower limb. Cranial nerves were intact and there was no bowel bladder involvement. There was no preceding COVID 19 symptoms. However his covid serology was positive with IgG of 491 BAU/ml. CSF analysis showed normal cell with mildly elevated protein of 58mg/dl. NCS done showed motor neuropathy of tested UL and LL nerves. MRI whole spine screening was normal. There was no further worsening of symptoms during hospitalisation.

Case 6

A 35 years old hypertensive non diabetic presented on 17th May 2022 Medicine OPD with history of recent onset weakness of all four limbs. On evaluation he was found to have motor power of MRC 4/5 in all the limbs with pan areflexia with no bowel and bladder involvement. There was no facial, bulbar and respiratory muscle involvement. There was mild transaminitis. Serum potassium level was normal. CSF analysis showed typical albumin-cytological dissociation with elevated protein level of 52 mg/dl with no cells. NCS done showed mixed motor sensory polyneuropathy. MRI brain and spine were normal. Even though he didn't have any symptoms of recent covid 19 infection, serum IgG titre of COVID 19 (848 BAU/ml) were markedly elevated with negative IgM. He received his last covid vaccination on September 2021.

The last 3 cases of GBS were admitted on the month of May with almost similar clinical presentation. There was no facial, respiratory muscle involvement and relatively stable as compared with first 3 cases. They were managed conservatively with no further neurological worsening. All of them were serologically positive for COVID 19 infection.

Discussion

Guillain-Barre syndrome (GBS) is an acute-onset, immune mediated polyradiculoneuropathy that may affect sensory, motor and autonomic nerves. Even though considered relatively rare with an annual incidence of 1.11 per 100,000,[7] we are witnessing increasing reports of GBS associated with COVID 19. The incidence of GBS was 0.42% in a large Italian study of 1200 patients admitted with SARS-CoV-2, substantially higher than the normal population.[5]

Infection and re-infection by Campylobacter jejuni, human herpes virus, CMV and EBV account for about 20-30% of the cases. Other viruses like HIV, Zika, H1N1 and Hepatitis-E are also implicated as the causative agents, besides recent immunizations.[8.9] A number of

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 05, 2022

mechanisms have been proposed to explain the pathogenesis of post-COVID-19 GBS, which include systemic inflammation and immune dysregulation . The most probabilistic theory is that of molecular mimicry between the spike glycoprotein and ganglioside proteins,where antibody directed against spike protein damaged the ganglioside, manifesting as classical post infectious GBS.

However there are reports of possible direct COVID 19 invasion of neurons causing GBS like syndrome, which may explain in one of our cases where paralytic features appear along with active COVID 19 symptoms. While Para infectious neuropathies may develop as an unusual hyperimmune response which is the hallmark of severe or critical COVID illness, they could also represent a direct toxic or neuropathic effect from SARS-COV. Similar description is reported with demonstration of SARS-COV RNA in CSF.[10]

The clinical manifestations of GBS are varied, from mild limb weakness to respiratory muscle involvement requiring mechanical ventilation. Studies have found that the severity of GBS is associated with the causative organism, demonstrated by the higher rates of severe axonal forms following C. jejuni infection.[11] As such, it is important to further look at the link between COVID-19 and GBS to help with diagnosis, prognostication, and institution of early immunological therapy if indicated. SARS COV -2 could well be an another important new viral trigger of GBS. If this is so, we may encounter increased incidence of GBS with time. More importantly we need to remain vigilant to detect GBS at early stage.

Financial support and sponsorship:
Nil.

Conflicts of interest:
There are no conflicts of interest.

References

1. Lu H, Stratton CW, Tang YW. Outbreak of pneumonia of unknown etiology in Wuhan, China: The mystery and the miracle. J Med Virol 2020;92:401-2.
2. Mao L, Jin H, Wang M, Hu Y, Chen S, He Q, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. JAMA Neurol 2020;77:683-90.
3. Zhao H, Shen D, Zhou H, Liu J, Chen S. Guillain-Barré syndrome associated with SARS-CoV-2 infection: Causality or coincidence? Lancet Neurol 2020;19:383-4.
4. Sedaghat Z, Karimi N. GuillainBarresyndrome associated with COVID-19 infection: A case report. J ClinNeurosci 2020;76:233-5.
5. Toscano G, Palmerini F, Ravaglia S, Ruiz L, Invernizzi P, Cuzzoni MG, et al. Guillain-Barré syndrome associated with SARS-CoV-2. N Engl J Med 2020;382:2574-6.
6. Virani A, Rabold E, Hanson T, Haag A, Elrufay R, Cheema T, et al. Guillain-Barré Syndrome associated with SARS-CoV-2 infection. IDCases 2020;20:e00771.
7. Asiri S, Altwaijri WA, Ba-Armah D, Al Rumayyan A, Alrifai MT, Salam M, Almutairi AF. Prevalence and outcomes of Guillain-Barre syndrome among pediatrics

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 05, 2022

in Saudi Arabia: a 10-year retrospective study. Neuropsychiatric Dis Treat 2019 Mar 1;15:627e35.

8. Hughes RA, Cornblath DR. Guillain-Barre syndrome. Lancet 2005 Nov 5;366(9497):1653e66.
9. Van den Berg B, Walgaard C, Drenthen J et.al Guillain-Barre syndrome: pathogenesis, diagnosis, treatment and prognosis. Nat Rev Neurol 2014 Aug;10(8):469e82.
10. Khan F, Sharma P, Pandey S, Sharma D, Vijayavarman V, Kumar N, et al. COVID-19-associated Guillain-Barre syndrome: Postinfectious alone or neuroinvasive too? J Med Virol 2021;93:6045-9.
11. Willison HJ, Jacobs BC, van Doorn PA. Guillain-Barré syndrome. Lancet 2016;388:717-27.