Post COVID-19 Gullain-Barre Syndrome: An Emerging Neurological Complication

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Sir,

COVID-19 is a new disease that causes the recent pandemic since its outbreak in Wuhan, China in the year 2019 and affects more than 100 countries of the globe.¹ The virus belongs to family of Coronavirus and is a capsulated, non-segmented, positive RNA virus. It is primarily a respiratory syncytial virus that affects the upper and lower respiratory tract through angiotensin-converting enzyme-2 receptors.¹ It has the potentiality to invade other systems either directly or through inflammatory response. Since its outbreak there have been several reports on neurological manifestations that include stroke, encephalopathy, muscle injury, and Gullain-Barre syndrome (GBS).² Here we report a case of Post-Covid 19 GBS in view of its significance in the present pandemic situation in India.

A 45-year-old man presented to the Medicine Outdoor with chief complaints of tingling sensation of lower limbs followed by weakness of both lower and upper limbs of 5 days duration. His complaints started with tingling sensation on dorsum of feet that progressed upwards and within 12 hours he developed weakness of both lower limbs that progressed to affect both upper limbs within 24 hours. There was no involvement of bladder and bowel. About 15 days prior to this event, he had fever for 5 days with cough, sneezing, myalgia without anosmia and ageusia. He got relief of these symptoms with azithromycin and paracetamol without testing for Covid-19.

On examination, he was afebrile, pulse rate of 80/minute, Blood Pressure-130/80mm of Hg. In right arm supine posture, respiration rate-18/minute, oxygen saturation-97% at room air. Neurological examination demonstrated that there was no cranial nerve involvement. Muscle tone was normal in upper limb and hypotonia in lower limb. The muscle power was grade 3/5 in upper and 2/5 in lower limbs. All the deep tendon reflexes were absent. Bilateral plantar was unresponsive. There was no sensory deficit and no signs of meningeal irritation. Examination of other systems did not reveal any abnormality. In view of acute onset lower motor neuron type of quadriaparesis without sensory deficit and sphincter involvement with a preceding history suggestive of upper respiratory tract infection (URTI) 2 weeks before, a clinical diagnosis of Post-infectious Gullain-Barre syndrome (GBS) was made. Owing to recent Covid-19 pandemic investigations for Covid-19 along with other investigations were planned. Investigations showed Hb-13.0 gm%, total leukocyte count-8340/cumm, Differential leukocyte count- N:50%,  L:36%, E:11%, M-3%, B:0%; platelet count-340 thousand /µL, ESR (Westergren)-35 mm 1st hour. Biochemical investigations showed FBG-90.5mg/dl, urea-26.0mg/dl, creatinine-0.8mg/dl, sodium-136.0 mEq/L, potassium-3.7mEq/L, bilirubin-0.2 mg/dl, AST-25.0 IU/l, ALT-32.0 IU/l, Alkaline phosphatase-53.0 IU/l. X-ray chest PA view and HRCT scan of chest were normal. MRI of cervical spine was normal.

Rapid Antigen test and RT-PCR for Covid-19 were negative. Biomarkers showed CRP- 200.0 mg/l (normal <3mg/l), serum ferritin-919.0 ng/ml (normal 68.0-434.0 ng/ml in males), D-Dimer 0.9mg/ml (normal 0-0.5mg/l), serum LDH-767.8 IU/l. SARS-COV-2 IgM and IgG index was 0.73 and 13.93. Nerve conduction study was in consistent with demyelinating neuropathy with axonal degeneration. CSF analysis showed glucose 40.8mg/dl, an elevated protein 90.5mg/dl with no cells suggesting albumin cytological dissociation. Antiganglioside antibody was not tested. In view of the clinical presentation and electrophysiological findings suggest GBS with level 1 diagnostic certainty as per Brighton Criteria.³

The detection of serum IgG to SARS-CoV-2 which is in accordance with the time interval of antibody appearance i.e., within 13 median days of clinical onset suggested the antecedent Covid-19 that was limited to upper respiratory tract. Hence, final diagnosis of GBS after Covid-19 infection has been made and he was treated with intravenous Immunoglobulin at a dose of 0.4g/kg/day for 5 days with a total dose of 2g/kg. He improved symptomatically and could walk without support and was discharged after 7 days.

Knowledge regarding various clinical manifestations and complications of COVID-19 is essential for understanding the natural history of the disease. GBS is generally an acute, autoimmune, polyradiculoneuropathy that ensues few days to weeks after infection and vaccination with an incidence of 1-2 cases per 100,000 population annually.³ The common infective agents are C. jejuni, M. pneumoniae, H.influenzae, Epstein-Barr virus, Influenza A virus, and Zika virus. After the initial report, Covid-19 has been added as another emerging cause of GBS.⁴ The causal association between GBS and Covid-19 infection has been recognized after the rise in number of patients with GBS worldwide during the Covid-19 pandemic.

The clinical features, electrophysiological, and CSF analysis of post-Covid 19 GBS is like other
infective agents. Acute inflammatory demyelinating polyneuropathy, acute motor and sensory axonal neuropathy, and acute motor axonal neuropathy was found in 64.8%, 13.5%, and 2.7% respectively. In another review of 38 cases classical sensory-motor GBS, Miller Fisher syndrome, facial diplegia with sensory deficit was found in 78.9%, 13.2%, 5.3% respectively. Neurophysiological study showed demyelinating, axonal and mixed forms of disease with majority belonged to demyelinating type. Respiratory failure was found significantly (39.5% cases) among post COVID GBS. It may be due to respiratory muscle paralysis, associated Covid pneumonia, and direct affection of medulla oblongata by the virus causing dysfunction of cardio-respiratory centers.

The mechanism of GBS in Covid-19 is not clearly understood. In general, the mechanism has been attributed to molecular mimicry of the cell membrane antigen of the microorganism with the ganglioside component of nerve antigen that develop antiganglioside antibodies damaging the spinal roots and peripheral nerves. But antiganglioside antibodies were not detected among patients with post-Covid GBS. Direct invasion of Covid -19 has been postulated for the neurological deficits due its neuro invasive potential. But the absence of Covid-19 in the CSF does not favor this hypothesis. Affection of simultaneous neurological and respiratory symptoms in patients with GBS has been prompted to hypothesize the role of hyperinflammation with increased level of proinflammatory cytokines (cytokine storm) in the pathogenesis of GBS. This has been supported by the observation of endothelial damage by the cytokines. Therefore, axonopathy has been attributed to microvascular involvement.

The clinical course, electrophysiological study, response to treatment of the present case supported the diagnosis of GBS and satisfied the essential diagnostic criteria. In view of the ongoing Covid-19 pandemic similar cases likely to occur which require further research to elucidate the underlying pathogenesis.

References