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Case Report

Miller fisher syndrome – A rare complication of covid-19 infection

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ABSTRACT

The COVID-19 virus can present with various neurological signs and symptoms involving both the central and peripheral nervous systems. Miller Fisher syndrome (M.F.S.), a variant of Landry Guillain Barre Syndrome (L.G.B.S.), presents with ataxia, areflexia, and ophthalmoplegia. It can develop during and after COVID-19 illness. We are reporting a case of the Miller Fisher variant of L.G.B.S. following a COVID-19 infection. We found no difference in clinical presentation, electrophysiological studies, severity, recovery, and treatment in our patient compared to a non-covid related M.F.S. Our goal is to add a case of the COVID-19-associated Miller Fisher variant of L.G.B.S. to already existing limited literature through this case report.

1. Introduction

COVID-19 is associated with multiple neurological complications like encephalopathy, encephalitis, myelitis, Guillain Barre syndrome, dysgeusia, anosmia, and stroke.[1] Different L.G.B.S. variants (including the Miller Fisher variant) have been reported during and after COVID-19 illness. Miller Fisher syndrome usually presents with ophthalmoplegia, ataxia, and areflexia.[2] In addition, some patients with the Miller Fisher variant develop limb weakness or respiratory muscle weakness resulting in M.F.S.-L.G.B.S. overlap syndrome. Miller Fisher Syndrome can also present as a case of acute ophthalmoplegia without ataxia.[3] Some authors proposed that M.F.S., L.G.B.S. with ophthalmoplegia, acute ophthalmoparesis, acute ataxic neuropathy, and Bickerstaff Brainstem Encephalitis are part of the anti-GQ1b IgG antibody syndrome spectrum.[4,5]

2. Case

A 70-year-old male presented in emergency with complaints of progressive ptosis in the right eye, binocular diplopia, and difficulty maintaining balance while walking for the last three days. 16 days back, he got discharged from the hospital, where he got treated for COVID-19-associated pneumonia. The patient reported no weakness in the upper and lower limbs, sensory complaints, dysphagia, nasal regurgitation of liquids, or bowel or bladder involvement. He had bilateral asymmetrical ptosis, bilateral complete external ophthalmoplegia with a preserved normal pupillary response, and bilateral facial weakness on examination. He had generalized areflexia along with gait ataxia. The rest of the neurological examination, like Higher Motor function, remaining Cranial nerves, motor strength, sensory examination, and finger-to-nose test, were within normal limits.

Possibilities of myasthenia gravis, brain stem stroke, Miller Fisher variant of L.G.B.S., space-occupying lesion

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in the brainstem and Polyneuritis cranialis were considered, and the patient was investigated accordingly.

2.1. Investigations

Routine investigations were within normal limits. Nerve Conduction Studies (N.C.S.) showed impersistent F waves. The repetitive nerve stimulation test was found to be normal. CSF showed albumino-cytological dissociation (2 WBCs, all lymphocytes, Protein= 195mg/dl, Glucose = 62 mg/dl). The rest of the CSF examination was negative for stains, culture, and pan neurotropic virus panel, including the COVID-19 PCR.

M.R.I. brain with optic nerve cuts showed no significant abnormalities, and Myasthenia gravis serology tests were negative. COVID-19 antibodies (IgG) came out to be positive, and nasopharyngeal COVID-19 PCR was negative. Serum anti-ganglioside antibodies, including anti-GQ1b, were negative.

The patient was diagnosed with the Miller Fisher-variant of Guillain Barre syndrome and was treated with IVIG 2gm/kg over five days, then followed by a tapering dose of steroids over 28 days. The patient improved significantly with improvement in balance, ptosis, and diplopia over the next eight weeks.

3. Discussion

Miller Fisher syndrome, a rare variant of Guillain Barre syndrome, is an acute autoimmune disorder of peripheral nerves classically involving the eyes resulting in ophthalmoplegia, loss of deep tendon reflexes, and an ataxic gait.[5] M.F.S. usually follows an acute diarrhoeal illness with Campylobacter jejuni or a respiratory infection with Haemophilus influenzae due to cross-reactivity with the nerves and destruction of the myelin sheath, the axons, or both.[5] There is now enough data available to link the development of M.F.S. to COVID-19 infection. We are describing a classical patient of M.F.S. 16 days after the COVID-19 infection. Like our case, most reported cases are where patients developed MFS-like signs and symptoms two to three weeks after being diagnosed with COVID-19 illness. However, data is available where the M.F.S. signs and symptoms have been the presenting feature of patients with COVID-19 infection.[6] In the systemic review of seven patients by Li.Z et al., the prominent symptoms of COVID-19-associated M.F.S. were perioral paresthesias, ataxia, blurred vision, ophthalmoplegia, generalized areflexia, and other neurological features like weakness.[6] The latency between COVID-19 virus infection and M.F.S. onset in our case favors post-infectious immune-mediated phenomenon. However, Zhao et al.[7] proposed in their study that L.G.B.S., associated with SARS-CoV-2, might also follow the pattern of a para-infectious profile.[8] The exact mechanism of M.F.S. following Covid-19 infection is still under investigation, but the most likely notion seems to be molecular mimicry. It is still unclear whether COVID-19 acts in a certain manner that induces the production of antibodies against specific gangliosides, which are usually seen with various variants of G.B.S. Other plausible mechanisms include the direct neuropathogenic effect of the COVID-19 virus on the nervous system or dysregulated immune response, especially in para-infectious M.F.S.[6,9] But so far, COVID-19 PCR has not been isolated from the CSF of M.F.S. patients.[6,9,10]

Our patient has negative anti-ganglioside antibodies, including anti-GQ1b antibodies. There are similar reports of negative anti-GQ1b antibodies in the literature indicating a distinct immune process or different antigen target from a non-COVID M.F.S. case.[8–10] A study published in November 2020 by Senel M. et al. observed a significant increase in phosphorylated neurofilament heavy chain protein (pNfH) in the CSF and neurofilament light chain (N.F.L.) protein in the blood of a patient who developed M.F.S. following COVID infection. He postulated that measurement of N.F.L. might be considered to detect early involvement of the central and peripheral nervous system in such patients after COVID infection.[8]

From a clinical perspective, the COVID-19-associated M.F.S. presents similarly to the classical M.F.S. Patients respond equally well to intravenous immunoglobulins and plasmapheresis when compared with non-COVID cases. Most patients make a full recovery. Prompt diagnosis is required to correctly and timely manage this entity, with watchful observation for any impending respiratory muscles involvement. A doctor should consider this possibility when encountering similar neurological presentations after a COVID-19 infection. Such neurological presentations can also be a presenting feature of COVID-19 illness.

4. Conflict of Interest

The author declares no potential conflicts of interest with respect to research, authorship, and/or publication of this article.

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