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Case Series

COVID-19 associated myelitis: case series

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ABSTRACT

The coronavirus pandemic brought with it a wide range of clinical presentations. Earlier, the respiratory symptoms comprised most of the clinical picture. However, as more and more people got infected, many atypical presentations came into the limelight, especially the neurological manifestations. Spinal cord complications are widely reported, with COVID-19 associated myelitis constituting a big part. Through this report, we bring you a series of cases of COVID-19 associated myelitis to add to the already available data. We report four patients, two of whom developed longitudinally extensive myelitis (three or more vertebral segments). The other two suffered from multisegmented short-segment myelitis (less than three vertebral segments). COVID-19 myelitis can be seen during COVID-19 illness and post COVID. We aim to familiarize the medical community with this entity so that there is a minimum delay between the onset of the symptoms in the patient and the management of this complication, as the treatment is often gratifying.

Keywords: Myelitis, COVID, Longitudinally extensive transverse myelitis, Short-segment myelitis

INTRODUCTION

COVID-19 virus can lead to a wide range of neurological manifestations and diseases and affect both the central and peripheral nervous systems.[1] Spinal cord complications are widely reported worldwide with COVID-19 illness. These include COVID-19 associated myelitis, acute flaccid myelitis, as a component of acute disseminated encephalomyelitis (ADEM), spinal hematoma, and anti-myelin oligodendrocyte glycoprotein (MOG) antibodies associated demyelination, neuromyelitis-optica spectrum disorder, and epidural abscess.[2-7] Myelitis cases reported in patients with COVID-19 have presented similarly to the non-COVID-19 associated myelitis. The clinical picture, cerebrospinal fluid (CSF) profile, blood investigations, and magnetic resonance imaging (MRI) findings of the spine are the primary modalities for establishing the diagnosis. Although the mechanism is still under debate, it is high time to recognize these spinal cord complications in COVID-19 patients early to aid in prompt diagnosis and treatment.

CASE SERIES

A 45-year-old male patient presented to the emergency with urinary disturbances in the form of difficulty in passing urine. He was tested positive for COVID-19 illness with the nasopharyngeal RT PCR at the time of admission. COVID-19 antibodies were found to be negative. CSF examination showed a cell count of 88/mm^3, predominantly lymphocytes, with a protein level of 65 mg/dl and glucose levels of 60 mg/dl. MRI spine depicted short segment T2 hyperintensities in the cervical and thoracic region (Figure 1 and 2). He was treated with methylprednisolone 1 gm i/v once a day for five days, following which he started recovering well.

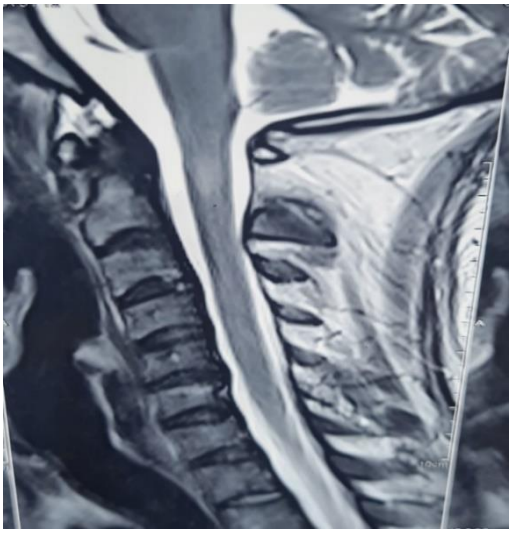

Figure 1: Short segment hyperintense signal in the upper cervical cord on sagittal T2W image (case 1).

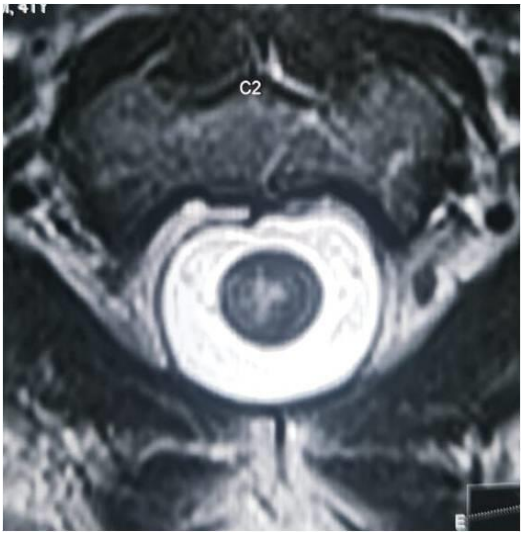

Figure 2: Axial T2W image showing hyperintensity in the central aspect of cervical cord (case 1).

A 32-year-old female patient presented to the emergency with bilateral weakness of the lower limbs with bladder and bowel involvement. She was tested positive for COVID-19 illness about two weeks ago. Nasopharyngeal PCR at the time of the admission was negative. COVID-19 antibodies were found to be positive. CSF examination showed a cell count of 56/mm^3, predominantly lymphocytes, with a protein level of 96 mg/dl and glucose levels of 54 mg/dl. MRI spine depicted short segment T2 hyperintensities in the cervical region (Figure 3). She was treated with methylprednisolone 1gm i/v once a day for five days, following which she started recovering well.

A 36-year-old female presented in the emergency with bilateral upper and lower limbs weakness with bladder and bowel involvement with a sensory level. She was tested positive for COVID-19 illness about four weeks ago. Nasopharyngeal PCR at the time of the admission was negative. COVID-19 antibodies were found to be positive. CSF examination showed a cell count of 24/mm^3, predominantly lymphocytes, with a protein level of 74 mg/dl and glucose levels of 48 mg/dl. MRI spine depicted longitudinally extensive T2 hyperintense lesion from C3 to T12 (Figure 4). She was started on methylprednisolone 1 gm i/v once a day for five days, but she did not significantly improve. Therefore, she was treated with IVIG (2 gm/kg over five days), following which she started recovering well.

Figure 3: Short segment hyperintense signal in the upper cervical cord on sagittal T2FS images image (case 2).

Figure 4: Long segment hyperintense signal in the dorsal cord on sagittal T2W image (case 3).

Figure 5: Long segment hyperintense signal in cervical and upper thoracic cord on sagittal T2W image (case 4).

A 38-year-old male presented in the emergency with bilateral upper and lower limbs weakness with bladder and bowel involvement. She was tested positive for COVID-19 illness about three weeks ago. Nasopharyngeal PCR at the time of the admission was negative. COVID-19 antibodies were found to be positive. CSF examination showed a cell count of 114/mm^3, predominantly lymphocytes, with a protein level of 92 mg/dl and glucose levels of 66 mg/dl. MRI spine depicted longitudinally extensive T2 hyperintense lesion from C3 to T3 (Figures 5 and 6). He was started on methylprednisolone 1gm i/v once a day for five days, but he did not show any significant improvement. Therefore, he was treated with IVIG (2 gm/kg over five days), following which he started recovering well.

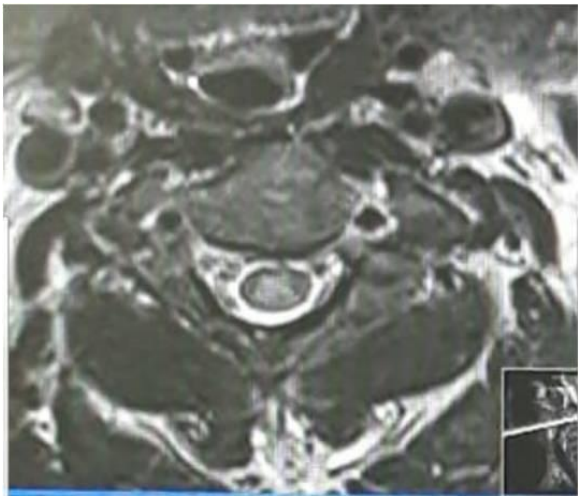

Figure 6: Corresponding axial T2W image showing hyperintensity in central aspect of the cord (case 4).

Table 1: Case details.

PT	Presenting feature	Naso-pharyng-eal RT PCR	RT PCR positive COVID-19 illness	COVID-19 Abs	CSF	MRI findings	Treatment
45 M	Urinary disturbances	Positive	Present	Negative	Cells- 88/mm^3; pred lymphocytes proteins- 65 mg/dl; glucose- 60 mg/dl	Short segment T2 hyperintensities in the cervical and thoracic region	Methyl prednisolone 1 g IV for 5 days
32 F	Paraparesis with bladder and bowel involvement	Negative	2 weeks back	Present	Cells- 56/mm^3; pred lymphocytes proteins- 96 mg/dl; glucose- 54 mg/dl	Short segment T2 hyperintensities in the cervical region	Methyl prednisolone 1 g IV for five days
36 F	Quadripare-sis with bladder and bowel involvement with sensory level	Negative	4 weeks back	Present	Cells- 24/mm^3; pred lymphocytes proteins- 74 mg/dl; glucose- 48 mg/dl	Longitudinally extensive T2 hyperintense lesion from C3 to T12	Methyl prednisolone 1 g IV for five days followed by IVIG (2 g/kg for five days)
38 M	Quadripare-sis with bladder and bowel involvement	Negative	3 weeks back	Present	Cells- 114/mm^3; pred lymphocytes proteins- 92 mg/dl; glucose- 66 mg/dl	Longitudinally extensive T2 hyperintense lesion from C3 to T3	Methyl prednisolone 1 g IV for five days followed by IVIG (2 g/kg) for five days

DISCUSSION

Myelitis is defined as an inflammation of the spinal cord which results in neurological manifestations involving sensory, motor, and/or autonomic dysfunction, not attributed to any compressive myelopathy.[8] The etiology of myelitis is extensive. It can be idiopathic but may be secondary to an infection (viral, bacterial, or fungal), vaccination, or a paraneoplastic disorder. It can also be a sequela to an immune-mediated illness like multiple sclerosis, neuromyelitis optica, anti-MOG related disease, sarcoidosis, lupus, Sjogren's syndrome, and vasculitis.[9,10]

Radiologically based on MRI, myelitis can be divided into short-segment myelitis and longitudinally extensive myelitis. Myelitis is defined as short segment myelitis when the length of the T2 hyperintense lesion on sagittal MRI images is present over less than three vertebral segments. On the other hand, when the size of the lesion extends to three or more vertebral segments, it is referred to as longitudinally extensive transverse myelitis (LETM). A typical example of short segment myelitis is multiple sclerosis, whereas long segment transverse myelitis is seen in neuromyelitis optica, MOG antibodies associated demyelination (MOGAD), sarcoidosis, paraneoplastic, para or post-infectious, and post-vaccination.[10]

We are reporting four cases of COVID-19 myelitis. Our first patient had presented with urinary disturbances only with positive nasopharyngeal COVID-19 polymerase chain reaction (PCR) (asymptomatic COVID-19 illness). MRI showed short segment T2 hyperintensities in the cervical and dorsal cord. Similarly, T2 hyperintense small segment lesion was observed in the cervical cord of our second patient, who had presented with paraparesis. Our third patient complained of upper and lower limb weakness with bladder bowel involvement two weeks after being diagnosed with COVID-19 illness. MRI of this patient showed a LETM from C3 to T12. The fourth patient presented with quadriparesis, with a LETM from C3 to T3 on the MRI spine. None of our patients' MRI spine depicted contrast enhancement. The axial T2 MRI images in all patients showed either complete or central T2 hyperintensities in the spinal cord. MRI brain was normal in all four patients. Their CSF findings showed lymphocytic pleocytosis, mild elevation in proteins with normal glucose, and were negative for all stains, pan-neurotropic virus panel, Covid -19 PCR, and Oligoclonal bands. Blood investigations like antinuclear antibodies (ANA), cytoplasmic antineutrophil cytoplasmic autoantibody (C-ANCA), perinuclear anti-neutrophil cytoplasmic antibodies (P-ANCA), angiotensin converting enzyme (ACE), anti-MOG immunoglobulin G (IgG), and aquaporin-4 antibodies were insignificant. Three patients have myelitis 2-4 weeks following COVID-19 illness except for the first patient in which it was the presenting feature of COVID-19 illness.

Over the past two years, multiple cases have been reported pointing toward the coronavirus yet being another possible cause of myelitis.[6,11,12] These have been found in association with acute COVID-19 illness and the covid vaccination. Although several neurological manifestations have been associated with COVID-19, transverse myelitis has emerged as a separate entity, comprising at least 1.2% of the overall neurological complications.[6] In most of these cases, the myelitis associated with COVID-19 infection has been shown to exhibit a long-segment involvement of the spinal cord, although there have been reported cases with short segment myelitis.[6,11,13] Although most of the patients are seen 1 to 4 weeks following COVID-19 illness but rarely neurological manifestations like myelitis can be the presenting feature of COVID-19 illness.[14]

The onset of symptoms is usually acute, and it progresses gradually over a few hours to days. As in our reported patients, the clinical presentation may be with quadriparesis, paraparesis, pain, paraesthesia, dysesthesia, bladder or bowel dysfunction, and even sexual dysfunction.[11] Although the classic signs of transverse myelitis aid in establishing a definite diagnosis, an MRI spine plays a significant role, especially with the exclusion of any underlying spinal compression. MRI spine also helps in demarcating the exact segment involvement.[10]

The nadir between acquiring the infection and the onset of myelitis cannot be ascertained because the disease is asymptomatic in many cases. However, multiple reports have shown the symptoms arise in about 2-4 weeks of confirmed COVID-19 diagnosis. The exact etiopathogenesis of COVID-19 associated myelitis has not been established yet. The mechanisms which have been proposed to play a role in the development of this entity include the direct neurotropic and neuroinvasive effect of COVID-19 and aberrant immune response leading to para-infectious and post-infectious myelitis. COVID-19 infection is known to cause a cytokine storm resulting in increased interleukins (IL-6, IL-1), and tumor necrosis factor (TNF)-alpha levels, which may activate glial cells and trigger demyelination.[15] Except for the first patient, all our other patients of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2)-associated myelitis had long latency periods suggesting a post-infectious origin which is thought to be due to molecular mimicry, epitope spreading, and bystander activation, and polyclonal B-cell activation.[2,6,16]

In spite of poorly understood mechanisms, patients with COVID-19 myelitis respond similarly to those with classic myelitis. This is why the quick realization of the diagnosis becomes essential here, as it would result in immediate medical attention, eventually resulting in a better prognosis. We treated our patients with methylprednisolone 1 gm i.v. per day for five days, followed by IVIG 2 gm/kg over five days if the response to steroids was unsatisfactory.

CONCLUSION

Myelitis is not an uncommon neurological manifestation of COVID-19 infection. It can be longitudinally extensive transverse myelitis that is commonly described in the

literature or sometimes can be short segment myelitis. It is usually seen during or after COVID infection but sometimes can be a presenting feature. Clinical picture, CSF analysis, serology studies, and MRI imaging aid in diagnosis and timely treatment provide gratifying results in most patients.

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