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Case Report

MRI-negative myeloradiculoneuropathy following Covid-19 infection: An index case

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Abstract
Covid-19 associated several neurological manifestation in the form of Post-infectious transverse myelitis(TM) and para-infectious TM has been reported. A 54 years old female patient presented to us with acute retention of urine and upper motor neuron type of bilateral lower limb weakness in shock stage, after 12 days of covid-19 infection. MRI (3T) brain and spine showed no abnormality and Nerve conduction study showed acquired motor axonal polyradiculoneuropathy in bilateral lower limbs. We herein present an index case of MRI-negative myeloradiculoneuropathy following covid-19 infection.

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The neurotropism of SARS-CoV-2 in particular has been well demonstrated, affecting both the central and peripheral nervous system either in isolation or rarely simultaneously [1]. Myeloradiculoneuropathy as a neurological manifestation of Covid-19 has rarely been reported [2–5]. We herein present an index case of a middle-aged female with MRI-negative myeloradiculoneuropathy following Covid-19 infection.

A 54-year-old hypertensive female presented with complaints of paraparesis for last 15 days, started as acute urinary retention, followed by paraparesis from next day, simultaneously involving both sides, progressing to maximal weakness within 6 hours, and difficulty in turning in bed, along with girdle-like-sensation around umbilicus with diminished sensation below it, without any upper limb weakness or cranial nerve symptoms. Enquiry revealed history of fever, cough and anosmia 12 days prior to ictus which resolved uneventfully within 3 days and had positive RT-PCR results of nasopharyngeal swab for SARS-CoV-2.

Neurological examination was marked by spasticity of lower limbs except for hypotonia near both ankle joints, muscle power was diminished in both lower limbs along with truncal weakness [Medical Research Council grading, upper limbs(bilateral):5/5; lower limbs(bilateral):proximally 2/5 and distally 1/5], bilaterally knee jerks were exaggerated while ankle jerks were lost, upper limb jerks were normal, and plantar was bilaterally extensor. There was loss of all sensory modalities below T9 level. Other neurological examination was unremarkable. A syndromic diagnosis of myeloradiculoneuropathy was made.

Routine blood Investigations revealed normocytic anemia. MRI Brain and spine revealed no significant abnormality (Figs. 1 and 2). Nerve conduction study showed acquired motor axonal polyradiculoneuropathy in the bilateral lower limbs. Electromyography indicated neurogenic denervation pattern. Visual evoked potential was normal. CSF analysis showed pleocytosis with mildly elevated protein, neuroviral panel for viral DNA PCR was negative. Workup for primary CNS demyelination was unyielding (serum aquaporin-4 IgG, myelin oligodendrocyte glycoprotein antibody, oligoclonal band and IgG-index were negative). Targeted investigations directed for etiologies of Myeloradiculopathy were ruled out with appropriate investigations (serum vitamin B12,homocysteine, methylmalonic acid, folate, vitamin E,copper,HIV,hepatitis-B surface antigen, anti-hepatitis-C antibody, antinuclear antibody, anti-
double stranded DNA antibody, anti-sjögren’s-syndrome-related antigen A and B autoantibody, serum angiotensin converting enzyme, antineutrophil cytoplasmic antibodies, anti-phospholipid antibody and paraneoplastic antibody panel were negative) [6].

Patient was subjected to 5 days of pulse methylprednisolone therapy (1 gm/day). In the absence of significant improvement following steroid therapy, plasmapheresis was planned however patient’s kin refused consent. Immunoglobulin therapy (2 gm/kg) was instituted next with only mild improvement in the subsequent 1 month follow-up.

Acute transverse myelitis (ATM) is a rare neurological condition, however COVID-19-associated ATM cases haven’t been infrequent, mostly post-infectious and less commonly para-infectious, accounting for 1.2% of the neurological complications of coronavirus [1,7]. MRI of spinal cord taken acutely can be normal in up to 30% of cases, however persistence of absence of signal changes in spinal cord imaging beyond 3 weeks in the index case makes it a diagnostic difficulty [8].

The proposed mechanisms in pathogenesis include: molecular mimicry, epitope spreading, bystander activation and polyclonal B-cell activation. In bystander effects, the pathogen directly invades the CSF or causes indirect damage through an immune-mediated process. Molecular mimicry related to cross-reacting of lymphocytic activation due to similar peptide sequence or three-dimensional structure self-antigen, and activation of auto-reactive lymphocytes during the inflammatory cascade in response to highly virulent pathogen as “bystander activation” serves as the two predominant mechanisms [1–3,7].

An acute immune-mediated polyradiculoneuropathy has been reported as most common form of peripheral nerve involvement in COVID-19. It is most likely secondary to a post-infectious immunopathogenesis rather than direct neuronal damage or a para-infectious mechanism. A predisposition to development of GBS and its variants related to host immunogenetic background and human leukocyte antigen (HLA) polymorphism in different populations has also been considered [1,2,5,9].
A simultaneous myelopathy with acute polyradiculoneuropathy has only rarely been reported in relation to Covid-19 infection (See Table 1). Myeloradiculoneuropathy is a frequently encountered clinical scenario with wide array of etiologies, which should additionally include Covid-19 infections [6,8]. A meticulous history-taking and clinical examination can greatly aid in the unfurling of multiple neuro-axis involvement in Covid-19 infections even in the absence of neuro-imaging evidence.

Fig. 2. MRI Spine T2 sagittal section showing no signal changes in cord.
Table 1
List of cases of Covid-19 infection with myelo-radiculo/neuropathy or MRI negative myelitis.

| Study | Concurrent LETM and GBS by Khera et al. [3] | Acute motor axonal neuropathy and Myelitis by Masuccio et al. [2] | Acute necrotising Myelitis and acute motor axonal neuropathy by Maidenuic et al. [5] | MRI negative Myelitis by Memon et al. [10] | Case of elsberg syndrome in the setting of SARS COV-2 infection by Abram et al. [4] |
|-------|---------------------------------------------|---------------------------------------------------------------|------------------------------------------------------------------|----------------------------------------|-----------------------------------------------|
| Age   | 11 yr                                      | 70 yr                                                        | 61 yr                                                            | 65 yr                                  | 68 yr                                         |
| Sex   | Female                                     | Female                                                       | Female                                                           | Female                                | male                                          |
| Country | India                                      | Italy                                                        | USA                                                              | USA                                    | USA                                           |
| Latency to development of neurological symptoms | Not specified | 5 days                                                       | 7 days                                                           | 9 weeks                                | Few months                                    |
| Neurological symptoms | Acute onset severe flaccid paraparesis | Difficult in walking with ascending paresthesia in all 4 limbs | Acute onset Paraparesis and urinary retention | Acute onset Paraparesis and urinary retention | Ascending numbness of lower limbs with genitourinary dysfunction No symptoms |
| Severity of covid infection | Mild (low grade fever only) | Moderate (fever, myalgia, anosmia, cough) | Mild (fever, runny nose) | Severe(Fever, cough, headache, taste loss, shortness of breath) | Normal MRI findings |
| Imaging findings (MRI findings) | Long segments intramedullary T2 hyperintensity signal from D7 to D10 without enhancement | Hyperintensity in post portion of spinal cord (C7-D1) | Patchy T2 hyperintensity within the central cord below foramen magnum proximal to C1–C2 | Cell count 20 Lymphocytes predominant Protein 81 Normal | A Hyperintense signal in the dorsal cord at T10 |
| CSF study | Not done | Normal cell count and normal protein | Cell count 20 Protein raised(87) Glucose normal | Normal MRI findings | Cell count 10, all RBC, no WBC Protein 34 |
| NCV findings | Motor axonal polyradiculopathy involving predominantly peroneal than tibial nerve | Reduction in motor amplitude, mild increase in distal latency and a B/L impairment of F waves | Acute motor axonal neuropathy with normal sensory conduction | Normal MRI findings | Normal distal motor and sensory conduction. Tibial and peroneal H-reflex response were absent in right lower limb |
| Therapy | Iv Methylprednisolone | Ivg | Iv Methylprednisolone | Iv Methylprednisolone | Iv Methylprednisolone |
|         | Ivg | Plasmapheresis | Plasmapheresis | Plasmapheresis | Plasmapheresis |
| Response | Good | No improvement | Partial improvement | Partial improvement | Poor |

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