Progressive Fulminant Necrotizing Myelitis in COVID-19 Infection; Case Report of a Rare Complication

Sir,

A wide variety of neurological complications have been reported regarding SARS-CoV-2. Previous studies suggested several mechanisms for CNS involvement in SARS-CoV-2. Acute longitudinal extensive transverse myelitis (LETM) with necrotizing changes is a rare neurological complication of COVID-19. Our case is a rare form of necrotizing myelitis after Covid-19 with an upward progression in the subsequent control MRIs. The study was approved by the Iranian Ethics Committee under the code, IR.RUMS.REC.1399.246, in accordance with Helsinki Criteria.

A 54-year-old immunocompetent man was admitted to the emergency unit due to shortness of breath, cough, and fever for a few days. The patient himself was a neurologist and was otherwise healthy. He had no history of autoimmune diseases within his family.

A chest computed tomography was performed for COVID-19 infection, which showed bilaterally ground-glass and alveolar opacities [Figure 1]. The COVID-19 RT-PCR test on nasopharyngeal samples was positive. On examination, he was febrile (temperature: 38.4°C) with a pulse rate of 74 beats per minute and a respiratory rate of 24 per minute. The oxygen saturation was 82 while he was breathing ambient air.

The patient received a combination of interferon beta-1a QOD and remdesivir for 5 days. The patient’s condition deteriorated, and clinical findings, including respiratory parameters and findings of lung CT scan, showed progressing COVID-19 pneumonia; thus, treatment with tocilizumab (Actemra)...

Figure 1: Inspiratory HRCT: Multifocal ground-glass opacities are seen in both lung fields
400 mg TDS was performed for 1 day. Dexamethasone 8 mg/TDS was prescribed for the patient.

As his clinical condition worsened, he was prescribed plasma therapy in the second week. A few hours after the second convalescent plasma infusion, the patient experienced an acute intensive and stabbing pain in his back and abdominal area together with numbness and weakness in his lower limbs. His weakness continued to progress in a way that after 2 hours, he developed paraplegia as 0/5 MRC in the lower limbs as well as urinary retention. There was a spinal shock pattern and anesthesia under T2 level in the trunk.

**Figure 2:** Extensive abnormal signal intensity and swelling at upper thoracic cord (in T2 image-a) from T1 to T8. The patchy high signal intensity in T1 images (b) could be due to hemorrhage. Abnormal signal intensity at bilateral (more in the right side) occipital lobe sulci on FLAIR sequence (c)

**Figure 3:** Upward progression of the lesion to lower level of C6 3.5 months later (a) with thoracic cord enhancement in that time (b) and more upward progression to lower part of C4 6 months later (c)

**Figure 4:** Regression of upward progression to C6 9 months later (upper level of the lesion above C6) (a), T1 hypointense lesion in the lower cervical and thoracic cord (necrotizing lesion) (b), Two enhanced lesions in T1 view 9 months later (c)
The patient underwent a magnetic resonance imaging (MRI) of the brain and spinal cord. As expected, MRI of the thoracic spine, with and without contrast, showed extensive T2-signal abnormality extending from T1 to T8 with a patchy hyperintense lesion in T1-image in the involved cord, suggesting micro hemorrhages. Diffuse enlargement of the cord was also seen in this region. Post-contrast sequences did not demonstrate a mass-like enhancement. Some peripheral enhancement was observed in the cord. Based on clinical and MRI features, we diagnosed an acute longitudinal extensive transverse myelitis (LETM) with hemorrhagic and necrotizing changes. Accordingly, intravenous methylprednisolone pulse therapy (1000 mg/day) was administered for 5 days without any significant clinical effect in the third week. Thus, treatment with intravenous immunoglobulin (IVIG) was initiated in the fourth week. Due to severe allergic reactions including generalized rash, dyspnea, and hypertension crisis after the 35-g infusion, we decided to stop the treatment.

Following the severe adverse reaction to IVIG, the patient underwent therapeutic plasma exchange (PE) in the fourth week, which could not be continued after the fourth session due to hemodynamic instability under treatment. After that, in addition to sensorimotor neurologic deficits, the patient presented severe signs of autonomic dysregulation with hypotension and tachyarrhythmia, which were treated with intravenous hypertonic fluids and oral fludrocortisone that persist till now in changing position.

In the second MRI 1 month later, there was an extensive abnormal signal intensity and swelling at the upper thoracic cord without obvious enhancement from T1 down to T8 level in favor of longitudinal extensive myelitis. In brain MRI, there was an abnormal signal intensity at bilateral (more on the right side) occipital lobe sulci on FLAIR sequence suggestive of inflammation. Following the severe adverse reaction to IVIG, the patient received a course of IVIG in the fourth week. Due to severe allergic reactions including generalized rash, dyspnea, and hypertension crisis after the 35-g infusion, we decided to stop the treatment.

The COVID-19 RT-PCR test was negative. All serologic tests for laboratory evaluation and diagnosis of autoimmune vasculitis were normal [Table 1].

The patient had physiotherapy without any improvement. After 3 months, he was unable to walk, and autonomic dysfunction.

### Table 1: Hematologic and immunologic variables

| Variable             | Result | Reference Value | Unit      |
|----------------------|--------|----------------|-----------|
| WBC                  | 3.3    | 4.0-10.0       | 10³/mL    |
| RBC                  | 4.5    | M: 4.5-6.3     | 10³/mL    |
| Hgb                  | 11.4   | M: 14-17.5     | g/dL      |
| HCT                  | 34     | M: 42-51       | %         |
| PLT                  | 76     |               | <6/mL     |
| CRP Quantitative     | 110    | 150-450        | 10²/mL    |
| Tests                |        |                |           |
| Lupus                |        | 42.2           | coagulation|
| Anticoagulation      |        |                |           |
| Anti-MOG <1/10 (negative) | IFA   | titer         |
| Anti-Optic Nerve     |        |                |           |
| Anti-MAG <1/10 (negative) | IFA   | titer         |
| Anti-Myelin <1/10 (negative) | IFA   | titer         |
| Anti-Aquaporin 4 (NMO IgG) <1/10 (negative) | IFA   | titer         |
| Anti-Cardiolipin Ab IgG | 2.76  | EIA            | GPL/ml    |
| Anti-Cardiolipin Ab IgM | 2.61  | EIA            | MPL/ml    |
| Anti-Phospholipid Ab (IgG) | 2.08  | EIA            | AU/ml     |
| Anti-Phospholipid Ab (IgM) | 1.85  | EIA            | AU/ml     |
| C3                   | 126.8  | mg/dl          | Immunoturbine |
| C4                   | 21.9   | mg/dl          | Immunoturbine |
| CH50                 | 82     | %              | EIA       |

### Table 2: Adult post-COVID-19 LETM cases comparison in the literature

| Characteristics          | Case1 Fumery | Case2 Baghbaniyan | Case3-4 Advani (2) | Case5 Solota | Case6 Lee | Case7 Azin | Case8 Sarma | Case9 Lisnic | Case10 Chow | Case11 Zoghi | Case12 Maidenuic |
|--------------------------|--------------|-------------------|-------------------|-------------|-----------|------------|------------|-------------|-------------|-------------|----------------|-----------------|
| Age (years)              | 38           | 53                | 47-67             | 69          | 35        | 35         | 34         | 28          | 27          | 60          | 38              |
| Sex                      | F            | F                 | M-F               | F           | F         | M          | M          | M           | M           | F            | F               |
| Day of onset             | 11           | 12                | 10-21             | 8           | 6         | 12         | -          | -           | -           | 14           | 14              |
| Sensory Level            | T4           | T11-T12           | T10-?             | -           | T8        | T2         | -          | -           | -           | -            | -               |
| Sequel                   | No           | Minor             | Severe            | Severe      | No        | Severe     | No         | Minor       | No          | Moderate     | Minor           |
| Length of lesion         | cervicothoracic | T8-T10           | C2-T2             | Medulla to C7-T6 | -        | C6-T8      | C4-T5      | Medulla-C4  | T7-T10      | FM to T1     | -               |
| Enhance                  | No           | -                 | Yes               | Patchy      | No        | Yes        | No         | -           | Patchy      | -             | Patchy         |
| Brain                    | NAD          | NAD               | NAD               | NAD         | NAD       | NAD        | NAD        | NAD         | NAD         | Internal capsule & corpus Callosom | NAD            |
such as orthostatic hypotension and hypertension attacks still bother him. Weakness in upper limbs (4/5–3/5), especially in the distal part of the left hand, was added to his presentation in the fourth month. After the third MRI, another pulse therapy with methyl-prednisolone was prescribed for 5 days. Treatment with rituximab was initiated in the fifth month. In the fourth MRI, there was an upward progression in cord hyper intensity to C4 level 6 months later [Figure 3c]. After MRI, we recommended again cord biopsy and cerebrospinal fluid examination and another plasmapheresis course that was not accepted by the patient. In the fifth MRI 9 months later, there is some regression in upward progression from C4 to C6 but patchy enhancement still is seen in some parts of involved cord [Figure 4a–c].

There may be an autoimmune reaction continuity after para infection event as a post-infection process. Our patient showed extensive longitudinal myelitis in MRI with symmetric bilateral weakness of lower extremities, which is characteristic of acute LETM. There is a wide range of potential causes related to longitudinally extensive myelitis with a variety of autoimmune, demyelinating, infectious, vascular, and neoplastic etiologies.^[4,5^]

The incidence of myelitis is unknown in patients with COVID-19 infection. The first case of acute transverse myelitis in a patient with COVID-19 was reported from Wuhan.^[6^] Till the current date of this case report, more than 10 reports of patients with COVID-19-associated myelitis have been published in the literature [Table 2].^[7^] However, there are only two reports of patients with necrotizing and hemorrhagic changes of COVID-19 myelitis.^[8,9^] CSF findings of patients with LETM in the context of coronavirus infections are not specific, and COVID-19 RNA was not detectable in the CSF of patients with COVID-19-associated myelitis.^[7^] CNS involvement in COVID-19 infection was supposed to be an autoimmune/inflammatory syndrome induced by adjuvants (ASIA syndrome) rather than a direct invasion of virus into the CNS.^[10^]

Although previous studies reported favorable outcomes for COVID-19-associated myelitis, treatment with corticosteroids, IVIG, and PE^[8,10^] there are some investigations in which these therapies were not effective on COVID-19 patients with LETM, and myelitis may progress to complete flaccid paraplegia. Our patient refused to take cord biopsy and CSF examination, making our para clinical exam incomplete. There are two ideas for the management of the patient, one is conservative management and the other is treatment with cyclophosphamide or rituximab to stop the progression of the disease. This case report showed us that there may be severe spinal cord injury following COVID-19 infection that is not reversible. According to the last MRI performed 9 months later, there is downward regression of cervical progression but still patchy enhancement was seen in the thoracic spine.

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**Ethical code**

The study was approved by the Iranian Ethics Committee under the code IR.RUMS.REC.1399.246 in accordance with Helsinki Criteria.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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