Case report

COVID-19–associated acute transverse myelitis: a rare entity

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SUMMARY
SARS-CoV-2 has wreaked havoc globally and has claimed innumerable lives all over the world. Apart from the characteristic respiratory illness, this disease has been associated with florid extrapulmonary manifestations and complications. A 59-year-old female healthcare worker presented with features of acute-onset non-compressive myelopathy with a sensory level at T10 segment along with high-grade fever for 4 days. MRI of dorsal spine was suggestive of myelitis at T7 vertebral level. She was initiated on injectable steroids and did show some initial signs of recovery. A day later, she developed an acute-onset respiratory failure but could not be revived despite our best efforts. Her nasopharyngeal and oropharyngeal swab turned out to be positive for SARS-CoV-2 reverse transcriptase polymerase chain reaction (RT-PCR). We hereby report a case of acute transverse myelitis with COVID-19 as a probable aetiology.

BACKGROUND
COVID-19 emerged in Wuhan city of China in December 2019 and did spread rapidly claiming innumerable lives as a global health pandemic. SARS-CoV-2 infection classically presents with fever and respiratory illness. However, neurological manifestations are also being reported in the literature. The neurological features of this infection include headache, dizziness, anosmia, taste disturbances, cerebrovascular accident, Guillain-Barré syndrome, acute encephalitis and acute transverse myelitis (ATM). We report a case of ATM associated with COVID-19 infection in a 59-year-old female healthcare worker which is most probably the first reported case from India.

CASE PRESENTATION
A 59-year-old non-diabetic and non-hypertensive obese female healthcare worker was admitted under our care with complaints of acute-onset progressive ascending flaccid paraplegia of both lower limbs along with retention of urine and constipation and high-grade fever for 4 days. The fever was not associated with any shortness of breath, expectoration, haemoptysis, chest pain, orthopnoea, and loss of smell or taste sensation. There was no history of trauma, preceding diarrhoea or recent vaccination. The patient was neither on chloroquine or hydroxychloroquine for chemoprophylaxis against COVID-19 nor was she on any regular medications. On admission, she was febrile (temperature 102°F) with tachycardia (pulse rate 116/min). Her blood pressure was 114/64 mm Hg and respiratory rate was 18 breaths/min. Pulse oximetry revealed oxygen saturation of 97% on room air. On neurological examination, she had paraplegia (weakness of Medical Research Council Muscle Scale 0/5 in both proximal and distal lower limbs) with profound hypotonia of both lower limbs. Her deep tendon reflexes of lower limbs were absent with bilateral mute plantar response. All modalities of sensation were diminished below the T10 segmental level. Higher function tests and cranial nerve examination revealed no abnormality and neurological examination including the deep tendon reflexes of the upper limbs were within normal limits. Other systemic examinations were unremarkable.

INVESTIGATIONS
Her complete haemogram was within normal limits. Viral serology for hepatitis B, hepatitis C, HIV I and II were negative. Her renal and liver function tests were unaltered. Her chest X-ray did not reveal any abnormality.

Her initial nasopharyngeal and oropharyngeal swab for RT-PCR to detect SARS-CoV-2 was negative. MRI T2-weighted imaging of dorsal spine revealed hyperintensity in the spinal cord at T6–T7 vertebral level, suggestive of myelitis (figure 1). A cerebrospinal fluid (CSF) study was done and the results are tabulated in table 1.

A nerve conduction study of both lower limbs was planned but had to be aborted due to some technical malfunction.

DIFFERENTIAL DIAGNOSIS
In a background of acute-onset ascending symmetric flaccid paraplegia, a differential of acute inflammatory demyelinating polyradiculopathy (Guillain-Barré syndrome), para/post-infectious myelitis, traumatic spinal injury, epidural haematoma/abscess, post-diptheric polyneuropathy, acute intermittent porphyria, periodic paralysis, neurotoxic snake envenomation and paralytic poliomyelitis may be considered. Our patient had non-selective symmetric long tract involvement leading to bilateral lower extremity weakness, symmetric sensory deficits below a definite segmental level along with bladder and bowel involvement. These features of a non-compressive myelopathy along with evidence of myelitis on MRI dorsal spine is characteristic of ATM.
The patient was started on injection methyl-prednisolone at a dose of 1 g/day and did show some signs of initial recovery and was able to move her toes. She was also given antipyretics and supportive care.

OUTCOME AND FOLLOW-UP

However, a day later, she developed a sudden-onset respiratory distress with rapid desaturation to 72% oxygen saturation on room air and extreme air hunger. She was tachypnoeic (32/min) but was haemodynamically stable. On auscultation, there were bibasal coarse crepitations with poor air entry in both lungs. An arterial blood gas revealed type 1 respiratory failure. Immediately, she was shifted to isolation ward with high-flow oxygen support (8 L/min) with non-rebreathing mask, which improved her oxygen saturation to 90%. Her nasopharyngeal and oropharyngeal swab was sent for a repeat SARS-CoV-2 RT-PCR. In a very short span of time, she had a sudden cardiac arrest and we initiated resuscitation as per ACLS (advanced cardiac life support) protocol. Unfortunately, we lost the patient despite our best efforts to resuscitate her and subsequently her swab report for SARS-CoV-2 RT-PCR came out to be positive.

DISCUSSION

Transverse myelitis (TM), a heterogeneous non-compressive myelopathy, is characterised by acute-onset or subacute-onset spinal cord dysfunction due to inflammation. It clinically manifests as neurological deficits with varying degree of involvement of sensory, motor and autonomic modalities. The common aetiologies of ATM can be broadly classified as para-infectious/post-inflammatory, toxin/drug-induced, paraneoplastic, autoimmune disorders and acquired demyelinating diseases such as multiple sclerosis or neuromyelitis optica spectrum disorders.

The most common neurological complaints reported in COVID-19 to date are headache, dizziness, hypoguesia and anosmia. Other complex neurological manifestations such as Guillain-Barré syndrome, large-vessel strokes and acute encephalitis have also been reported in literature.

The primary target of SARS-CoV-2 virus is respiratory epithelium via the angiotensin-converting enzyme-2 (ACE 2) receptor. ACE 2 receptors are also present in glial cells of brain and spinal neurons, and this could be a probable mechanism for dissemination of SARS-CoV-2 into the central nervous system. It is also hypothesised that dissemination of the virus into the nervous system can occur through olfactory bulb in which the sensory neurons connect the central nervous system to the nasal cavity, terminate in the olfactory bulb and pass through the cribriform plate. Hypoxic damage and metabolic abnormalities, direct invasion by the virus or an exaggerated immune response to the virus are proposed to cause neurological dysfunction.

Immune-mediated damage mainly occurs due to activation of inflammatory cells such as T lymphocytes and macrophages and subsequent overproduction of inflammatory cytokines, resulting in ‘cytokine storm’. Interleukin 6 (IL-6) causes further damage by causing endothelial dysfunction, activation of coagulation and complement cascade and ultimately results in organ dysfunction. The exact pathogenesis of ATM remains obscure and an exaggerated inflammatory response (‘cytokine storm’) related to a viral infection has been proposed as a possible cause.

The first reported case of COVID-19–associated ATM was reported from Wuhan in a 66-year-old man who developed paraparesis 1 week after the onset of fever. The second case was reported in a 28-year-old female patient who presented with features of ATM after a confirmed COVID-19 infection and she had hypoxic damage and metabolic abnormalities, direct invasion by the virus or an exaggerated immune response to the virus are proposed to cause neurological dysfunction.

Table 1

<table>
<thead>
<tr>
<th>Table 1</th>
<th>CSF examination</th>
<th>Reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cell count</td>
<td>White blood cell count</td>
<td>0.005×10⁹ /L</td>
</tr>
<tr>
<td></td>
<td>All are lymphocytes</td>
<td></td>
</tr>
<tr>
<td>Glucose</td>
<td>75 mg/dL</td>
<td>44–100 mg/dL</td>
</tr>
<tr>
<td>Protein</td>
<td>71.4 mg/dL</td>
<td>15–45 mg/dL</td>
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<tr>
<td>Chloride</td>
<td>134 mmol/L</td>
<td>120–135 mmol/L</td>
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<tr>
<td>Adenosine deaminase</td>
<td>4.5 µ/L</td>
<td>0–9 µ/L</td>
</tr>
<tr>
<td>Ziehl-Neelsen stain</td>
<td>No acid-fast Bacillus</td>
<td></td>
</tr>
<tr>
<td>Gram stain</td>
<td>No organism</td>
<td></td>
</tr>
<tr>
<td>RT-PCR for SARS-CoV-2</td>
<td>Not detected</td>
<td></td>
</tr>
</tbody>
</table>

Figure 1 MRI (T2WI) dorsal spine showing hyperintensity in spinal cord corresponding to T6–T7 vertebra, suggestive of acute myelitis.

Learning points

- As the number of persons infected with SARS-CoV-2 continues to rise globally, healthcare workers on the front lines bear witness to the varied clinical course and outcomes. Physicians should remain cognisant and aware of the less prevalent and atypical sequelae of novel coronavirus–related symptoms and complications.
- The neurological features of COVID-19 include headache, dizziness, anosmia, taste disturbances, cerebrovascular accident, Guillain-Barré syndrome, acute encephalitis and acute transverse myelitis (ATM).
- ATM may be considered as a potential rare but serious neurological complication associated with COVID-19 infection. It has severe consequences and early identification is very important to initiate appropriate treatment.
- Nasopharyngeal swab for SARS-CoV-2 RT-PCR does not have 100% sensitivity. It is affected by factors like specimen collection and viral load. In case of high clinical suspicion, a swab can be repeated after an initial negative nasopharyngeal swab.
had significant improvement in symptoms after receiving intravenous corticosteroids and plasma exchange.\textsuperscript{10} A few cases from different parts of the world has also been reported.\textsuperscript{11,12} 

Our patient presented with non-selective symmetric long tract involvement leading to bilateral lower extremity weakness and symmetric sensory deficits below a definite segmental level. These features are compatible with a non-compressive myelopathy, which along with early bladder and bowel dysfunction and evidence of myelitis on MRI dorsal spine is characteristic of ATM.

Considering the onset of these symptoms in the background of a confirmed COVID-19 test and initial improvement with steroids, ATM may be considered as an immune-mediated response to the virus. Therefore, in the current pandemic scenario, COVID-19 may be considered as a differential diagnosis in patients presenting with neurological symptoms like ataxia, loss of consciousness, status epilepticus, convulsion, encephalitis, neuritis or myelitis.

**Contributors** AC contributed to conception, initial drafting of manuscript, critical revision of content and final approval of manuscript. UC, AKR and PB contributed to patient management, conception, critical revision of content and final approval of manuscript. All authors are in agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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REFERENCES