Although there are a limited number of reports of para/postinfectious hemorrhagic myelitis dating back to 1915, this disease was reported in patients infected with herpes viruses and in those with immunocompromised conditions. A few noninfectious cases were associated with systemic lupus erythematosus and vaccination against papillomavirus or influenza viruses. In this case series, the authors from the United States presented three female patients who developed hemorrhagic myelitis within four weeks after being infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In contrast to typical inflammatory or demyelinating myelitis, their clinical recovery was poor. The disease responded poorly to immunosuppressive therapies and resulted in residual quadriplegia or paraplegia.

Numerous factors contribute to hemorrhagic myelitis, such as direct neuroinvasion of viruses, para/postinfectious inflammatory cascades, complement activation, vasculopathy, and coagulopathy. Histopathological examinations demonstrated hemorrhagic changes involving gray matter, early necrotizing features, and perivascular lymphocytic infiltration.

The main differences between hemorrhagic myelitis and inflammatory or demyelinating myelitis are the severity of the neurologic deficit, low clinical response to immunosuppressive therapy, and long-term disability.

### *Case series*

The researchers presented three women aged 26, 43, and 44 years who developed hemorrhagic myelitis within 4 weeks after being infected with SARS-CoV-2.

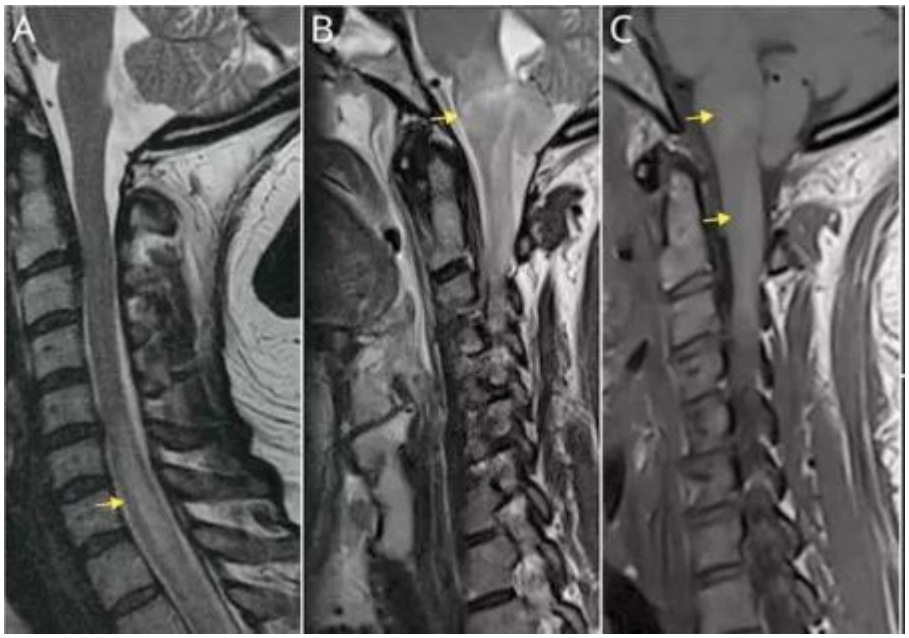
*Case 1*

A 43-year-old woman ten days after developing symptoms of upper respiratory tract infection, was admitted to the hospital for acute bilateral weakness of the lower extremities, urinary retention, and ascending sensory loss. She tested positive on reverse transcription polymerase chain reaction (rt-PCR) for SARS-CoV-2. Neurologic examination showed flaccid paraplegia and sensory level at T4. The spine magnetic resonance imaging (MRI) 24 hours after the onset of neurologic symptoms showed contrast enhancement and central T2-weighted hyperintensity at level C5-T12.

The cerebrospinal fluid (CSF) examination demonstrated pleocytosis (949 leukocytes/μL, 93% neutrophils), elevated protein level (210 mg/dL), elevated immunoglobulin (Ig) G index (0.82), and increase of erythrocytes (226/μL). Other CSF tests, including the meningoencephalitis panel and viral tests for herpes simplex virus (HSV), varicella-zoster

virus, and SARS-CoV-2 were all negative. Serum antinuclear antibodies, antibody panel for autoimmune myelopathy, aquaporin–4 IgG, HIV serology, and myelin oligodendrocyte glycoprotein (MOG) antibodies were all negative. Platelets, prothrombin time, and activated partial thromboplastin time were normal.

The patient was treated with intravenous methylprednisolone (IVMP) for five days, but her condition deteriorated to quadriplegia and respiratory failure, so therapeutic plasma exchange was initiated. A control spine and brain MRI after 11 days showed an extension of T2-weighted hyperintensity upward into the brainstem and a new hemorrhage. A control CSF analysis after 12 days showed 5 erythrocytes/µL, 5 leukocytes/µL (51% lymphocytes), 31 mg/dL of protein, and an elevated IgG index (1.09). The patient was treated with intravenous immunoglobulin (IVIG), and another five-day course of IVMP, followed by oral prednisone. Despite all therapies, the patient remained quadriplegic and mechanically ventilated.




*Case 2*

A 44-year-old woman with a history of right lower extremity weakness developed new ascending bilateral paresthesia in the lower extremities three weeks after symptomatic SARS-CoV-2 infection. The neurologic examination showed normal muscle strength, hyperreflexia, and sensory level at T8. After 30 days, the spine MRI demonstrated an extension of T2-weighted hyperintensities at levels T6-8 and T9-10, with contrast

enhancement. The brain MRI showed multiple periventricular and pericallosal non-enhancing T2-weighted lesions.

The CSF examination demonstrated 94 erythrocytes/µL, 7 leukocytes/µL (94% lymphocytes), 32 mg/dL of protein, elevated IgG index (1.77), and serum-unmatched oligoclonal bands. The bacterial stain, culture of CSF, and tests for cytomegalovirus, HSV, and varicella zoster virus were all negative. Serum antinuclear antibodies, HIV serology, aquaporin-4–4 IgG, and MOG antibodies were all negative. Platelets, PT, and APTT were normal.

She received IVMP for three days. However, after 15 days she developed paraplegia and urinary retention. A control spine MRI after 9 weeks demonstrated progression of T2-weighted hyperintensity at C2-L1 with patchy contrast enhancement. She received another five-day course of IVMP, followed by plasmapheresis and oral prednisone. A control spine MRI after four months showed an evolution to chronic hemorrhage at T6-T7. She remained paraplegic at approximately eight months. A control spine MRI after one year showed myelomalacia at T5-T9.

***Case 3***

A woman aged 26 years was hospitalized for COVID-19 myocarditis, cardiogenic shock, and multiorgan failure. Five months before she developed the symptoms of SARS-CoV-2 infection. She was vaccinated with the adenovirus-vectored COVID-19 vaccine (Janssen Biotech).

The patient was treated with dexamethasone for 10 days, but after four weeks she developed acute ascending sensory loss, followed by flaccid paraplegia and areflexia. The CSF examination performed three days after the onset of neurologic symptoms showed 23 erythrocytes/µL, 3 leukocytes/µL (75% neutrophils), 36 mg/dL of protein, and matched oligoclonal bands.

Nine days after the onset of neurologic symptoms, a spine MRI showed expansile T2-weighted hyperintensity with precontrast T1 hyperintensity and microhemorrhage on T2-weighted sequences. After 19 days, CSF analysis showed 2 erythrocytes/µL, 1 leukocyte/µL (55% lymphocytes), 36 mg/dL of protein, and a slightly elevated IgG index (0.67). The viral tests of CSF for the cytomegalovirus, HSV, varicella-zoster virus, and Epstein-Barr virus were negative. Serum HIV and antinuclear antibodies were also negative. Platelets, PT, and

APTT were normal.

The patient was treated with IVMP followed by oral prednisone. However, the control neuroimaging after two months showed persistent hemorrhage. At five months, she remained paraplegic.

*Conclusion*

This study presented three female patients aged 26, 43, and 44 years who developed hemorrhagic myelitis within four weeks after being infected with SARS-CoV-2. They all had a poor clinical recovery. The authors stated that previous studies reported five other cases of hemorrhagic myelitis following SARS-CoV-2 infection. The MRI findings and clinical outcomes in these studies were similar to those reported in this study. The treatment included steroids, plasmapheresis, and rituximab, but minimal or no improvement was also observed during follow-up.

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***Journal Reference***

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