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CLINICAL CASE

COVID-19 associated transverse myelitis: case report

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Abstract

Background: *Transverse myelitis (TM) is a demyelinating inflammatory disease that presents with motor, sensory, and autonomic dysfunction, which may be acute or subacute. COVID-19-associated TM has been described in a scarce number of patients.* **Clinical case:** *A 15-year-old previously healthy male patient with respiratory disease before his neurological deterioration presented to the emergency room after developing a complete medullary syndrome located at the cervical-dorsal level, with ascending and symmetric paraparesis that rapidly progressed to paraplegia, with sensory dysfunction from the T3 level, sphincter dysfunction and sudden ventilatory deterioration that required mechanical ventilation. Magnetic resonance imaging was compatible with acute TM. Inflammatory and non-inflammatory etiologies were discarded. In addition, a positive severe acute respiratory syndrome coronavirus 2 test was obtained. Treatment included steroid pulses and plasmapheresis, with an insidious evolution.* **Conclusion:** *COVID-19 is an infrequent cause of TM and should be suspected when other etiologies have been ruled out.*

Keywords: *Transverse myelitis. COVID-19. Myelopathy. Spinal cord disease.*

Mielitis transversa asociada a COVID-19: reporte de un caso

Resumen

Introducción: *La mielitis transversa (MT) es una enfermedad inflamatoria desmielinizante que se presenta con disfunción motora, sensitiva y autonómica, de forma aguda o subaguda. La MT asociada al COVID-19 se ha escrito en un escaso número de pacientes.* **Caso clínico:** *Se presenta el caso de un masculino de 15 años previamente sano, quien cursaba con un cuadro respiratorio y que desarrollo un deterioro neurológico súbito que involucro un síndrome medular completo localizado en el nivel cérvico dorsal, con paraparesia simétrica que progreso a la paraplejia, con disfunción sensitiva desde el nivel medular de T3, disfunción de esfínteres y deterioro ventilatorio que requirió manejo avanzado de la vía aérea. Su resonancia magnética fue compatible con mielitis transversa aguda. Se descartaron causas inflamatorias y no inflamatorias de la patología. Además, se obtuvo un resultado positivo de SARS-COV-2. Se inició tratamiento con pulsos de metilprednisolona y plasmaféresis, con una evolución insidiosa.* **Conclusión:** *El COVID-19 es una causa infrecuente de MT y debe sospecharse cuando otras causas han sido descartadas.*

Palabras clave: *Mielitis transversa. COVID-19. Mielopatía. Enfermedad de la medula espinal.*

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Introduction

Transverse myelitis (TM) is an inflammatory and immune-mediated demyelinating pathology with an acute or subacute onset and sensory, motor, and autonomic spinal dysfunction. TM might be partial, complete, longitudinally extensive, or central[1-4].

TM is infrequent in the pediatric population, with an estimated annual incidence of 1-4 cases/1,000,000 patients. It is more frequent in male patients during the pre-pubertal stage, while female patients have a predilection in the pubertal and adult stages. Presentation in children has both clinical and prognostic significance since it has been reported that children have a better prognosis with complete recovery at 2-year follow-up compared with adults. However, the latter might be age-related since younger patients have been reported to have the worst outcomes related to brain immaturity. The main differences in TM between children and adults include an initial presentation with back pain and fever in the pediatric population and a higher prevalence of sphincter dysfunction in adults[5-8].

Pathogenesis is diverse, and several factors have been related to its development, such as infectious, vascular, and autoimmune diseases[3]. Neurological impairment has increased since the onset of the COVID-19 pandemic, and neurological manifestations of the disease have been frequently reported, demonstrating its neurotropic capability. Mechanisms that explain the latter remain unclear[9].

Neurological involvement in COVID-19 has been reported as hyposmia/anosmia, dysgeusia/ageusia, headache, and other severe presentations such as stroke, meningitis, acute disseminated encephalitis, myasthenia gravis, Guillain-Barre syndrome, and acute TM[10].

COVID-19-related TM pathophysiology has been described as developing an immune response directed against the infectious agent that may target the central and peripheral nervous system, potentially, leading to neurological damage. Fuerthermore, it has been suggested that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can enter human cells through angiotensin-converting enzyme 2 (ACE2) receptors, which are also found on the membranes of spinal cord neurons[11].

Acute TM presents with neurological manifestations depending on the affected medullary level. Motor impairment includes bilateral limb weakness or bilateral paraplegia, which may present with flaccidity or spasticity, while sensory involvement is represented as pain, dysesthesia, and paresthesia. The affected medullary level might be identified in 60% of cases[10,12,13,14]. Autonomic dysfunction presents as urinary retention, incontinence, constipation, and sexual dysfunction[15,16].

Regarding TM treatment, multiple courses of steroids, immunoglobulin, and plasma exchange have improved motor function. To date, no treatment specifically targeting COVID-19 infection has been described[17].

This report aims to present an acute inflammatory-mediated medullary disease in a pediatric patient in the context of a SARS-CoV-2 infection, in whom a broader diagnostic protocol discarded alternative etiologies, contributing to pediatric literature due to the low incidence of neurological impairment after COVID-19 infection. TM following COVID-19 infection in Mexico has been reported only in adult patients. This is the first report of this condition in a pediatric patient in the country[18].

Clinical case

A 15-year-old previously healthy male patient, with a complete immunization scheme for his age and a single dose of Pfizer-BioNTech vaccine (BNT162b2), administered 3 months before the disease onset, presented with upper respiratory symptomatology that partially improved with symptomatic ambulatory medication. Twenty-four hours later, he presented to the emergency room after experiencing thoracic oppressive pain at rest, radiating to both shoulders and bilateral palmar hypoesthesia. He further developed ascending symmetric paraparesis, which rapidly progressed to paraplegia and urinary incontinence.

During the neurological examination, upper cognitive function and cranial nerves were normal, with no signs of meningeal irritation. Sensory involvement affecting the T3 medullary level was documented. Deep tendon reflexes in upper limbs were reported as 2/4 and 0/4 in lower limbs on the Daniels scale, with non-pathologic Babinski reflex.

Forty-eight hours after admission, he developed a loss of ventilatory automatism that required advanced ventilatory support.

General laboratory tests were taken upon admission, with no pathological findings other than a positive SARS-CoV-2 real-time polymerase chain reaction by nasal swab. Head and spine computed tomography showed no alterations. Brain and spine magnetic resonance imaging (MRI) showed a hyperintense longitudinally extensive lesion from medullary levels C4 to T4 in the T2/STIR modality with discrete heterogeneous enhancement after the administration of contrast, with edema affecting the entire medullary cord in some regions and involvement of the gray matter at different levels, including anterior and posterior horns, mainly affecting the C7 medullary level, compatible with TM (Fig. 1).

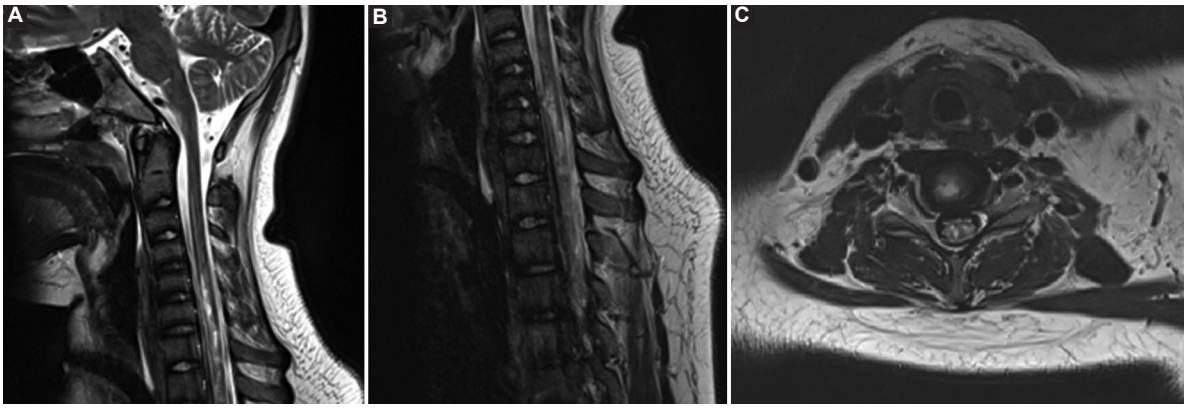

Figure 1. Cervical-thoracic magnetic resonance imaging. **A** and **B:** T2-weighted sagittal images demonstrate a longitudinally extensive hyperintense signal extending from the C4 to T4 vertebral levels, compatible with transverse myelitis. **C:** T2-weighted axial image at the cervical level reveals a central hyperintense signal within the spinal cord.

A diagnostic protocol for demyelinating disease was performed, including cerebrospinal fluid (CSF) analysis, which showed a protein level of 51.9 mg/dL, a CSF glucose level of 61 mg/dL, and no pleocytosis. A viral panel with negative results for enterovirus, herpesvirus, and cytomegalovirus (CMV) in multiplex modality was also obtained. Mycobacterium tuberculosis complex, a highly prevalent pathogen in our setting, was discarded.

Myelin basic protein (MBP) and aquaporin-4 antibodies were requested, with a positive result for MBP. The CSF oligoclonal banding test was reported as negative. Cerebral and spinal angiography discarded a vascular malformation.

Methylprednisolone pulses of 1 g/day were initiated in the context of a demyelinating pathology. Due to the disease's refractoriness, plasma exchange was initiated 72 h after hospitalization, completing five sessions.

The patient presented with a complex neurological impairment that required neurological and pulmonary rehabilitation, as well as the placement of a gastrostomy tube and tracheostomy cannula.

He was discharged after 2 months of hospital stay, with complete improvement of upper limb mobility and residual paraplegia in lower limbs, with fine and gross sensitivity affected. At present, he is dependent on a urinary catheter due to urinary incontinence.

Discussion

Defining TM etiology might be challenging, and it is not uncommon for an infectious disease to precede TM cases. Herpes simplex virus 2, Varicella zoster virus, Epstein-Barr virus, CMV, flavivirus, and enterovirus, all of which were discarded in our patient, have been related to the pathology. Moreover, only SARS-CoV-2 infection was confirmed. The exact pathophysiology of TM remains unknown, while four mechanisms have been proposed to develop the disease: the direct effect, molecular mimicry, microbe superantigen-mediated inflammation, and the humoral response[19-21].

SARS-CoV-2 has a great neurotropic and neuroinvasive capacity related to its affinity for ACE2, which is present not only in respiratory system cells but also in neurons and glial cells[7].

Higher levels of Interleukin 6, a pro-inflammatory cytokine, lead to greater production of acute phase reactants, like C-reactive protein and fibrinogen, which were elevated in our patient[20,21].

The presence of MBP antibodies in our patient demonstrates a genetic and immunologic host predisposition[22].

Neurological deficits due to SARS-CoV-2 have been increasingly reported, and their relation must be suspected when other causes have been discarded. The latency period has yet to be established since reports vary from 15 h to 5-day post-respiratory disease to 10-day to 6-week post-COVID-19 confirmation[19-23].

Our patient presented with a complete acute medullary syndrome, typical of TM, due to its immune-mediated mechanism, which meets the criteria of the TM Consortium Working Group[1].

Symptom progression tends to be rapidly progressive, with a nadir between 4 h and 21 days. It is vital to discard an extra-axial compression etiology[24,25].

We describe imaging results consistent with TM on MRI, including a hyperintense lesion in T2/STIR modality, longitudinally extensive, well-defined, and homogeneous from C4 to T4 medullary levels[26].

The differential diagnosis includes Guillain-Barre syndrome, which also presents in its acute form with weakness and areflexia. However, a defined sensory level and urinary retention allow differentiation from TM[26]. The differential diagnosis should also include myelin oligodendrocyte glycoprotein antibody-associated disease, although no radiological findings in the optic nerve or visual impairment were reported[27].

High doses of methylprednisolone have been described as a first-line treatment for TM. Plasmapheresis has been described as an appropriate therapeutic approach in severe or steroid-refractory cases, as our patient received five sessions of this therapy[25].

Close observation of children with COVID-19 should be considered if any neurological involvement is present due to the gravity and risk of sequelae.

Conclusion

COVID-19 is an infrequent cause of Transverse Myelitis and should be suspected when other etiologies have been carried out. Due to the gravity and sequelae risk, close observation of children with COVID-19 should be considered if any neurological involvement is present. MRI plays a crucial role in differential diagnosis with other neuropathies and should not be delayed.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

Protection of people and animals. The authors declare that the procedures followed conformed to the ethical standards of the responsible human experimentation committee and following the World Medical Association and the Declaration of Helsinki.

Data confidentiality. The authors declare that they have followed their work center's protocols for publishing patient data.

Right to privacy and informed consent. The authors have obtained the approval of the Ethics Committee for the analysis and publication of routinely obtained clinical data. Informed patient consent was not required as it was a retrospective observational study.

Use of artificial intelligence to generate texts. The authors declare that they have not used any generative artificial intelligence in the writing of this manuscript or for the creation of figures, graphs, tables, or their corresponding captions or legends.

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