

Acute Ascending Necrotizing Myelitis After COVID-19 Infection: A Clinicopathologic Report

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Abstract

Objectives

Neurologic manifestations of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2, COVID-19) infection are common and varied. The objective of this report was to describe clinicopathologic findings of rare acute ascending necrotizing myelitis (ANM) and briefly summarize similar COVID-19–associated longitudinally extended transverse myelitis cases.

Methods

We described the clinical presentation, disease course, diagnostic workup, therapeutic measures, and pathologic findings of ANM associated with COVID-19 infection.

Results

A 31-year-old previously healthy woman developed a longitudinally extensive lower thoracic myelopathy 3 weeks after COVID-19 infection. The thoracic spinal cord lesion extended to cervical level in 1 week and to the lower medullary level in 2 more weeks. Thoracic laminectomy at T5-T6 level and cord biopsy revealed necrobiotic changes without viral particles or microglial nodules. The clinical deficit stabilized after immunomodulatory and eculizumab therapies.

Discussion

COVID-19 infection can cause ANM. It adds to the spectrum of reported cases of COVID-19 – associated encephalitis and myelitis.

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2, COVID-19) infection frequently causes neurologic dysfunction involving the central and peripheral nervous system and skeletal muscle.^{1,2} We report clinicopathologic findings of a rare case of ascending necrotizing myelitis (ANM) and briefly summarize similar SARS-CoV-2–associated longitudinally extensive transverse myelitis (LETM) cases.

Case Report

A 31-year-old previously healthy woman presented to the emergency department with a 5-day history of acute ascending weakness, numbness, and autonomic symptoms. Three weeks before the onset of neurologic symptoms, she had a 4-day episode of fever, headache, malaise, and anosmia, and she, her husband, and their son were diagnosed SARS-CoV-2 positive by reverse transcription (RT)-PCR from nasopharyngeal samples. None of them were vaccinated against SARS-CoV-2. An MRI of the spine from an outside facility had shown a patchy enhancing T7-T9 spinal segmental lesion (Figure 1A).

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PRACTICAL IMPLICATIONS

Consider COVID-19–associated necrotizing myelitis in the differential diagnosis of longitudinally extensive transverse myelopathy. This case adds to the spectrum of necrotizing encephalitis reported in patients with SARS-CoV-2 infection.

Figure 1 MRI Spine



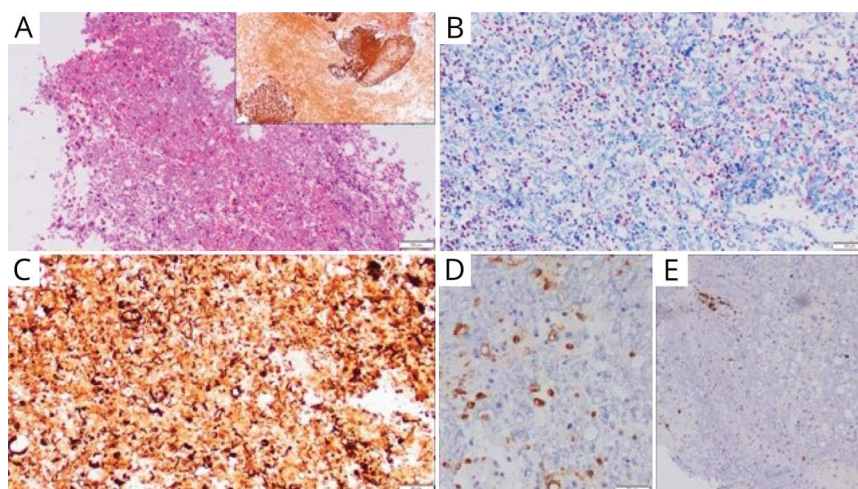
Sagittal T2-weighted images showing patchy intraspinal lesion at T7-T9 level on April 5, 2021 (A) and at T6-T9 level on April 10, 2021 (B). Sagittal T2-weighted images showing lesion extending to C7 cord on April 17, 2021 (C) and to lower medulla on May 4, 2021 (D)

A clinical examination at admission revealed incomplete transverse myelopathy with sensory level at the T10 cord, Medical Research Council (MRC) grades of 3 to -4 strength in her legs, and bladder and bowel dysfunction. An MRI of the spine showed an LETM involving the thoracic cord (Figure 1B). Lumbar puncture showed 19 white blood cells/mm³ (90% lymphocytes), 114 red blood cells/mm³, 124 mg/dL proteins, 56 mg/dL glucose, and negative microbial stains. CSF myelin basic proteins were elevated at 14.7, and oligoclonal bands were absent. CSF SARS-CoV-2 RT-PCR was not performed. Nasopharyngeal sample for SARS-CoV-2 RT-PCR was negative. Serum SARS-CoV-2 immunoglobulin (Ig) G antibodies (IgM and IgG) were positive. The following investigations were normal or unremarkable: CBC and differential, comprehensive metabolic panel, rheumatology panel, meningoenitis viral panel, ACE, and complement 3/4; serology of hepatitis B, hepatitis C, herpes

simplex virus-11, HIV-2, John Cunningham virus, varicella-zoster virus, aquaporin-4, and myelin oligodendrocyte glycoprotein; and whole-body PET scan, spinal MRA and selective spinal angiogram, brain MRI, and CT scans of the head, thorax, abdomen, and pelvis.

She received a 3-day course of IV methylprednisolone (IVMP) (1 g/d). Over the following 3 days, her deficit progressed to complete paraplegia with sensory level to the T6 cord segment. Plasmapheresis (5 sessions at 40 mL/kg/d on alternate days) was started. During the second week of her hospital stay, weakness and numbness progressed to the left hand and forearm with MRI lesions extending to the C7 cord (Figure 1C). A 3-day course of cyclophosphamide therapy (1 g/d) was added. Given the aggressive course and possibly impending respiratory compromise, she underwent a T5-T6-level laminectomy and spinal cord biopsy. Pathology

Figure 2 Pathology Showed Numerous Areas of Necrotic Spinal Cord Tissue Surrounded by Reactive Gliotic Parenchyma



(A) Hematoxylin-eosin stain shows a focus of necrosis with granular, vacuolated background. Inset shows a glial fibrillary acidic protein stain with patches of dark brown gliotic viable areas in the background of amorphous necrotic zones that label light brown. (B) Luxol fast blue stain shows loss of myelin. (C) Neurofilament immunohistochemical study shows fragmentation and loss of axons. (D) CD68 immunohistochemical study shows numerous macrophages in the necrotic areas. (E) CD3 immunohistochemical study shows rare perivascular and parenchymal mature T cell.

Table Summary of Reported Cases of Para SARS-CoV-2 or Post-SARS-CoV-2 Infectious Longitudinally Extensive Transverse Myelitis

Study	Sex/ age, y	Latency, d	Lesion level				CSF			SARS-CoV-2	Treatment	Outcome	Remarks	
			M	Cx	Tx	L	WBC	RBC	Pr					
Reference 7	M/52	NM			+	+			+	-ve	CS, acyclovir	Death	Acute flaccid myelitis	
Reference 8	M/60	14		+	+							Unchanged	Diabetes mellitus	
Reference 9	F/28	NM			+			NP			CS, PE, IVIg	Improved	—	
Reference 10	F/69	8	+	+	+	+	+	+	+	-ve	CS, PE	Stabilized	ANM, SARS-CoV-2 +ve nasopharynx	
Reference 11	M/44	NM					+	+	+	-ve	CS	Improved	ADEM	
Reference 12	M/54	Several days		+	+	+	+		+	-ve	CS, IVIg	Improved	ADEM	
Reference 13	F/61	4		+	+				+	-ve	CS	Stabilized	—	
Reference 14	M/32	NM		+	+	+					CS, PE	Improved	—	
Reference 15	M/21	17		+	+	+			+	-ve	CS, acyclovir	Recovered	—	
Reference 16	M/24	Concurrent			+	+				NP	PE, acyclovir	Improved	Fever, pneumonia, SARS-CoV-2 +ve nasopharynx	
Reference 17	M/60	10			+	+			+	-ve	CS	Improved	—	
Reference 18	F/3	21	+	+	+	+	+	+	+	-ve	CS		SARS-CoV-2 +ve nasopharynx	
Reference 19	M/27	NM		+	+	+			+	-ve	CS, IVIg, PE, Rituximab	Improved	—	
Reference 20	M/63	NM		+	+			Normal		NM	CS, PE	In hospital	HIV+ve	
Reference 21	F/14	NM		+	+			NP				NM	SARS-CoV-2 +ve nasopharynx	
Reference 22	M/26	NM		+	+	+				NM	NM	In hospital	MOG IgG+ve	
Reference 23	M/52	Concurrent			+	+			+	NM	CS, IVIg	Improved	SARS-CoV-2 +ve nasopharynx, ADEM	
Reference 24	M/47	10		+	+	+			+	NM	CS, IVIg	Unchanged	—	
	F/67	NM		+				Normal		NM	Antibiotics, acyclovir, PE	Improved	—	
Reference 25	F/11	NM		+				Normal		NM	CS, PE	Stabilized	SARS-CoV-2 +ve nasopharynx	
Reference 26	F/38	14		+	+	+	+			-ve	CS, IVIg, PE	Improved	—	
Reference 2	M/72	NM		+	+	+	+			-ve	CS	Improved	—	
Reference 27	F/7 mo	7			+	+			+		CS, IVIG	Improved	SARS-CoV-2 +ve nasopharynx	
Reference 28	M/31	21		+	+			Normal		-ve	CS, IVIg	Resolved	—	
Reference 29	F/9	NM		+				Normal		NM	CS, IVIg, infliximab	Improved	SARS-CoV-2 +ve nasopharynx, multisystem inflammation	
Reference 30	F/11	3			+	+	+	+	+	NM	CS, IVIg, PE	Improved	ADEM, GBS	
Reference 31	F/53	14			+	+				NM	PE	Improved	Diabetes mellitus	
Reference 32	F/35	5			+			Not done			CS	Improved	SARS-CoV-2 +ve nasopharynx	
Reference 33	M/73	21			+	+			+	NM	CS	Improved	Diabetes mellitus	
	M/44	28			+			Normal		NM	PE	Improved	—	
Reference 34	F/20	13		+	+			NP			CS, IVIg	Recovered	—	
Reference 35	F/61	7		+					+	+	-ve	PE	Improved	AMAN

Continued

Table Summary of Reported Cases of Para SARS-CoV-2 or Post-SARS-CoV-2 Infectious Longitudinally Extensive Transverse Myelitis (continued)

Study	Sex/ age, y	Latency, d	Lesion level				CSF			SARS-CoV-2	Treatment	Outcome	Remarks
			M	Cx	Tx	L	WBC	RBC	Pr				
Current report (Guada et al.)	F/31	21	+	+	+	+	+	+	+	NP	CS, PE, IVIg, eculizumab	Stabilized	ANM

Abbreviations: ADEM = acute disseminated encephalomyelitis; AMAN = acute motor axonal neuropathy; ANM = acute necrotizing myelopathy; CS = corticosteroids; Cx = cervical; GBS = Guillain-Barre syndrome; Ig = immunoglobulin; L = lumbar; Me = medulla; MOG-IgG = myelin oligodendrocyte glycoprotein antibody-immunoglobulin G; NP = not performed; NM = not mentioned; PE = plasma exchange; Pr = protein; RBC = red blood cell; SARS-CoV-2 = severe acute respiratory syndrome coronavirus-2 RT-PCR; Tx = thoracic; WBC = white blood cell.

showed necrobiotic parenchyma with neutrophil, T lymphocyte, and macrophage infiltrates; no microorganisms or microglial nodules were seen (Figure 2). During the fourth week, a repeat MRI showed the cord lesion extending to the caudal medulla (Figure 1D). She received a repeat 5-day course of IVMP and IVIg. In addition, given the progressive lesion despite immunosuppressive therapies and necrobiotic cord histopathology, an empirical trial with weekly IV anticomplement5 (eculizumab) at 600 mg/d for 4 weeks was started. She showed improvement in arm strength and was discharged in a clinically stable state 34 days after hospital admission.

At 5-month postdischarge clinic follow-up, her arm strength has improved to MRC grade 5, leg strength to trace at ankles and 2 at hips, and sensory impairment at T7 cord level, and she remained incontinent.

Discussion

Acute ANM is a rare spinal cord disorder. There are a few descriptive cases of ANM associated with neuromyelitis optica, vasculitis, paraneoplastic syndrome, and post-radiation myelopathy and as an adverse reaction to immune checkpoint inhibitors in oncologic treatment.³⁻⁵

COVID-19 infection frequently causes neurologic manifestations.^{1,2} In our case, the recovery from initial COVID-19 infection, a 3-week interval between infectious illness and ANM, and the lack of pathologic detection of viral particles suggest postinfectious immune-mediated rather than SARS-CoV-2 infectious myelitis. In a recent review of 43 patients with COVID-19-associated acute transverse myelitis (ATM) reported from 21 countries,² 13 cases (31%) experienced localized segmental acute transverse myelitis and 28 cases (69%) showed LETM on MRI scans. Most cases (68%) had a latency of 10 days to 6 weeks, indicating postinfectious complications after COVID-19 infection.² In another review of 20 cases of ATM,⁶ the neurologic symptoms followed a mean of 10.3 days of SARS-CoV-2 infection, and the spinal cord lesions spanned a mean of 9.8 vertebral segments, with necrotic-hemorrhagic transformation in 3 cases. CSF PCR for SARS-CoV-2 was negative in all 14 cases examined.⁶ Outside the neuromyelitis optica spectrum disorder,

postinfectious LETM is less common than segmental ATM, and the preponderance of LETM in these series is noteworthy.

A brief review of literature shows 33 reported cases of LETM involving ≥ 4 spinal cord segments on MRI scans in association with SARS-CoV-2, ranging in age from 7 months to 73 years^{4,7-35} (Table). Two cases were contemporaneous to infective illness^{16,23} and 18 cases 3–29 days after the infection^{8,10,12,13,15,17,18,24-29,31-35} (Table). SARS-CoV-2 RT-PCR was positive in CSF sample in only 1 case¹⁸ and in nasopharyngeal swabs in 9 cases.^{10,16,18,21,23,25,27,29,32} Most patients were treated with immunomodulatory therapies, but prognosis for neurologic recovery was poor (Table).

Acute encephalitis, including necrotizing encephalitis, has been described with COVID-19 infection.^{1,36} This is a case of COVID-19-associated ANM with histopathologic confirmation. It adds to the spectrum of encephalomyelitis in COVID-19 infection.

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Appendix (continued)

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Allan D. Levi, MD, PhD	Department of Neurosurgery, University of Miami Miller School of Medicine, FL	Drafting/revision of the article for content, including medical writing for content; and major role in the acquisition of data
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Ashok Verma, MD, DM, MBA	Department of Neurology, University of Miami Miller School of Medicine, FL	Drafting/revision of the article for content, including medical writing for content; study concept or design; analysis or interpretation of data; and additional contributions: revision of the manuscript

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