Case Report
Yonsei Med J 2023 Nov;64(11):692-695
https://doi.org/10.3349/ymj.2023.0202
Yonsei Medical Journal
YMJ
pISSN: 0513-5796 · eISSN: 1976-2437

Acute Necrotizing Myelitis Associated with COVID-19

Ji Eun Yoo[1], Hui Jin Shin[1], Hoon-Chul Kang[1], Joon Soo Lee[1], Heung Dong Kim[1], and Ha Neul Lee[2]

[1]Division of Pediatric Neurology, Department of Pediatrics, Epilepsy Research Institute, Severance Children's Hospital, Yonsei University College of Medicine, Seoul;
[2]Division of Pediatric Neurology, Department of Pediatrics, Yongin Severance Hospital, Yonsei University College of Medicine, Yongin, Korea.

Acute ascending hemorrhagic longitudinally extensive transverse myelitis is a rare inflammatory demyelinating disorder, which invades several vertebral segments and progresses rapidly and manifests severe symptoms. We present a case of acute necrotizing myelitis associated with COVID-19 infection. A 10-year-old female, with no previous medical history and no prior administration of COVID-19 vaccination, contracted COVID-19 in early April 2022. Two weeks later, she suffered from severe posterior neck pain and also presented with motor weakness and numbness in both lower extremities, making it difficult to walk independently and spontaneously void urine. Initial spinal cord MR showed longitudinally segmental extensive T2 hyperintensities. Cerebrospinal fluid (CSF) analysis revealed elevated red blood cell, normal white blood cell, and elevated protein levels and absence of oligoclonal bands. CSF culture and viral polymerase chain reaction were negative. Autoimmune work-up was negative. She was started on intravenous methylprednisolone 1g/day for 5 days and immunoglobulin (Ig) 2 g/kg for 5 days. She was also treated with six courses of therapeutic plasma exchange. Nevertheless, her pain and motor weakness persisted. She eventually developed respiratory failure. Follow-up MR presented a newly noted small hemorrhagic component. She was consequently treated with two additional courses of methylprednisolone and Ig. At 6-months follow-up, neurological examination showed improvement with normal sensory function and motor grade IV function in both upper extremities. We present the case of acute necrotizing myelitis associated with COVID-19 infection. Multiple courses of methylprednisolone and Ig showed mild improvement in motor and sensory function. However, poor prognosis was unavoidable due to rapid progression of the disease.

Key Words: Acute necrotizing myelitis, transverse myelitis, autoimmune, COVID-19

INTRODUCTION

Transverse myelitis is an inflammatory demyelinating disorder that can be associated with an autoimmune disorder or a multi systemic disease. Fulminant manifestation of transverse myelitis is rare. Acute ascending hemorrhagic longitudinally extensive transverse myelitis (LETM) invades three or more vertebral segments, progresses rapidly, and manifests with severe clinical symptoms. Acute ascending hemorrhagic LETM is often refractory to treatment and has poor prognosis. Recently, a few cases with acute ascending hemorrhagic LETM associated with COVID-19 have been reported in the literature.[1-4] We present the first case of a South Korean girl diagnosed with acute ascending hemorrhagic LETM associated with COVID-19.

Received: June 2, 2023 **Revised:** August 12, 2023
Accepted: August 15, 2023 **Published online:** October 17, 2023
Corresponding author: Ha Neul Lee, MD, PhD, Division of Pediatric Neurology, Department of Pediatrics, Yongin Severance Hospital, Yonsei University College of Medicine, 363 Dongbaekjukjeondae-ro, Giheung-gu, Yongin 16995, Korea.
E-mail: haneul_sky_lee@yuhs.ac

•The authors have no potential conflicts of interest to disclose.

CASE REPORT

A 10-year-old female patient with no medical history and no prior administration of COVID-19 vaccination developed sudden unilateral motor weakness and paresthesia at 2 weeks after diagnosis of COVID-19. During COVID-19 infection, she had a mild fever less than 38 degrees for several days with mild rhinorrhea. She was eventually unable to walk independently or spontaneously void urine. Upon admission, neurological examination revealed paralysis of both lower extremities. Magnetic resonance imaging (MRI) of the brain was normal, whereas initial MRI of the spinal cord showed longitudinally

segmental extensive T2 hyperintensities involving C6–T10 and marked swelling with cord extension in T4–6 (Fig. 1). Cerebrospinal fluid (CSF) analysis showed elevated red blood cell (8340/μL; normal range 0–6), normal white blood cell (WBC) (5/μL > corrected WBC < 0; normal range < 5), elevated protein (430 mg/dL; normal range 15–45), elevated albumin (306 mg/dL; normal range 10–30), and normal glucose (44 g/dL; normal range 40–70) levels, as well as the absence of oligoclonal bands (Table 1). We performed infection work-up-related tests, such as CSF panel for common viruses and bacteria that cause meningoencephalitis and blood tests that included inflammatory markers, including erythrocyte sedimentation rate, and C-reactive protein. We also performed CSF polymerase chain reaction with serum antibodies for several possible virus infections, such as cytomegalovirus, herpes simplex virus, varicella zoster virus, rubella, and Epstein-Barr virus. The infection work-up was all negative except for the serology of SARS-COV-2, which showed signs of recent infection (SARS-CoV-2 Ab Nucleocapsid 106.0, Spike 3.62). Autoimmune work-up was negative, which included serum antinuclear antibodies, myelin oligodendrocyte glycoprotein antibodies, aquaporin 4 antibodies, and rheumatoid factor (Table 2).

Initial treatment consisted of intravenous methylprednisolone (1 g/day for 5 days) and intravenous immunoglobulin (IVIG) (2 g/kg for 5 days), followed by six courses of therapeutic plasma exchange (TPE). After treatment, her symptoms did not worsen in the upper extremities, yet we did not see improvement with lower extremity paralysis, apart from horizontal, wriggling movement of her legs with no antigravity strength. The symptoms began to worsen as fever began to develop. We performed further blood tests and employed a respiratory virus panel, which were negative for new viral or bacterial infection. We concluded that the fever was temporarily caused by TPE. She developed new-onset paresthesia of the lower extremities and motor weakness (grades I–II) in the upper extremities associated with the progression of acute LETM. She eventually developed acute respiratory failure due to insufficient respiratory muscle function, making intubation, tracheostomy, and intensive care unavoidable. A spinal cord biopsy at the T3–4 and thoracolumbar levels was performed to exclude malignancy. During biopsy, a remnant cord structure was barely observed, presenting as a grayish pinkish yellowish mush-like material with barely any CSF. Pathology showed near-total necrosis. Follow-up MRI of the spinal cord also presented with a newly noted, small hemorrhagic component at the C4–5 and T8–9 levels (Fig. 2). Subsequent treatment consisted of two additional courses of intravenous methylprednisolone (1 g/day for 5 days) and IVIG (2 g/kg for 5 days). Subsequently, oral steroids were administered for 2 months. IVIG was administered monthly. At 5-months, she was able to decannulate her tracheostomy tube and to eat food orally with substantial help (ADL-MBI). At 6-months follow-up, neurological examination showed improvement, with normal sensory function and motor grade IV function in both upper extremities only.

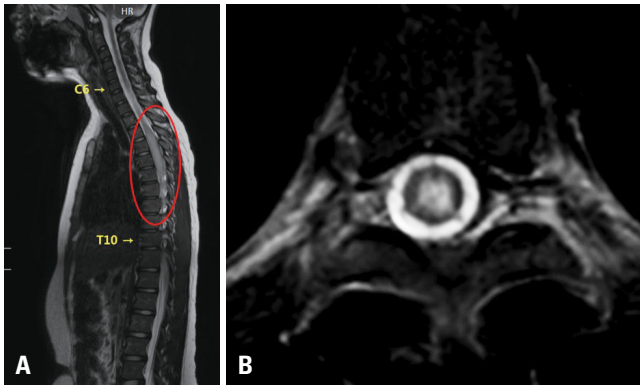

Fig. 1. T2 (A) sagittal and (B) transverse initial spinal MRI shows longitudinally segmental extensive T2 hyperintensities involving spinal cord levels C6–T10 and marked swelling with cord extension at T4–6.

Table 1. Results of Initial CSF Studies

CSF studies	Value	Normal range
Color	Pale xanthochromia	
Turbidity	Hazy	
RBC (/μL)	8340	0–6
TNC (Total nucleated cells) (/μL)	5	
WBC (/μL)	TNC	0–30
SG	1.007	
pH	7.800	
Albumin (mg/dL)	306.0	10–30
Protein, total (mg/dL)	430.7	430.7
Glucose (mg/dL)	44	44

CSF, cerebrospinal fluid; RBC, red blood cell; TNC, total nucleated cells; WBC, white blood cell; SG, specific gravity.

Table 2. Results of Initial Laboratory Tests

Lab findings	Value	Normal range
Blood sugar (mg/dL)	83	70–100
BUN (mg/dL)	21.7	7–17
Creatinine (mg/dL)	0.69	0.37–0.72
White blood cells (10^3/μL)	12120	4.0–10.8
Hemoglobin (g/dL)	14.2	14.0–18.0
Platelets (10^3/μL)	358	150.0–400.0
Aspartate aminotransferase (IU/L)	29	13.0–34.0
Alanine aminotransferase (IU/L)	14	5.0–46.0
Na (mmol/L)	139	135.0–145.0
K (mmol/L)	4.1	3.5–5.5
Cl (mmol/L)	99	98–110
Albumin (g/dL)	5.0	3.8–5.4
Total protein (g/dL)	8.3	6.0–8.0
CRP (mg/L)	<0.6	0–8
ESR (mm/hr)	38	0.0–20.0

BUN, blood urea nitrogen; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.

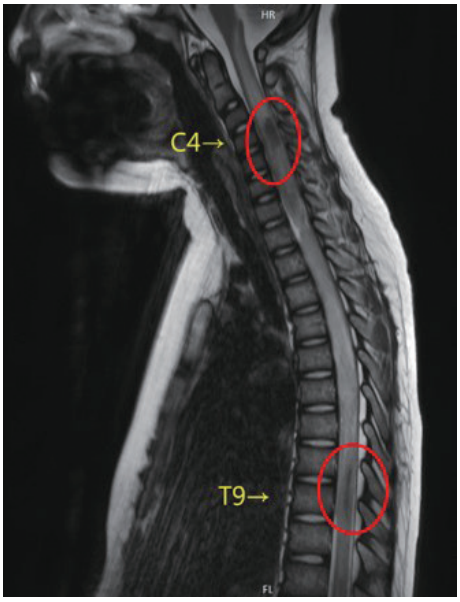

Fig. 2. Follow-up MRI of the spinal cord presents a newly noted small hemorrhagic component at levels C4–5 and T8–9.

DISCUSSION

During the ongoing COVID-19 pandemic, several cases of neurological complications related to SARS-CoV-2 have been reported.[5] As in other countries, many neurological symptoms related to COVID-19 have been reported in Korea. The most common complications are brain fog and headache, followed by dizziness, memory impairment, myalgia, anosmia/ageusia, and acute stroke.[6,7] In contrast, our case had focal neurological deficits and motor and sensory weakness. To our knowledge, this is the first case of a Korean pediatric patient diagnosed with LETM associated with COVID-19.

LETM shows invasion of longer segments than acute transverse myelitis; thus, its prognosis is worse. Hemorrhagic transformation and necrosis have only been observed in LETM.[8] Similar to previously reported cases, our diagnosis was based on clinical manifestations, imaging, laboratory studies, and biopsy.[5,8-10] The majority of LETM cases in the literature received more than one form of immune therapy. Our patient was treated with intravenous methylprednisolone, IVIG, and TPE, as in previous reports. Some patients were additionally treated with rituximab, infliximab, or eculizumab. Notably, although our patient did not undergo these immunotherapies, her prognosis was not significantly different from that of previously reported cases. Despite a lack of supporting evidence, we treated our patient with repeated steroids, IVIG, and TPE. We expected this treatment to be effective as similar diseases in the same demyelinating disease spectrum as acute LETM, such as Guillain-Barré Syndrome, use repeated steroid therapy, IVIG, and TPE.[11-16]

There are two possible mechanisms of pathogenesis related to the occurrence of acute LETM via infection with SARS-CoV-2. First, direct invasion and replication in spinal cord neurons of the SARS-CoV-2 virus itself is possible. The virus disseminates to the central nervous system (CNS) through angiotensin-converting enzyme 2. Second, severe systemic disease or cytokine storm syndrome may have caused indirect injury to myelin. Post-viral immunological reaction to SAR-CoV-2 results in hyperactivity of innate immunity, with activation of inflammatory cells and overproduction of inflammatory cytokines, including interleukin 2, 6, 7, and 10, and tumor necrotizing factor-α, causing damage to myelin. Similar to most previously reported cases, our patient also displayed a delay in clinical symptoms, which occurred 2 weeks after COVID-19 infection.[5,8] This suggests that the second mechanism was more likely in our case.

Although our patient showed negative results for autoimmune work-up, treatment with steroids and plasma exchange was effective. This indicated that the etiology may have been post-infectious as a secondary immunogenic overreaction in our case. Autoimmunity, mediated by excessive cytokine release and cross-reactivity between CNS components and viral particles, may lead to CNS damage. Moreover, autoimmunity mediated by the cross-reaction between viral particles and demyelination can result in acquired atypical demyelination.[17]

There is an increasing number of reported cases of LETM related to COVID-19 across the globe. Most cases have been reported in adults.[9] This type of myelitis often progresses rapidly and involves poor prognosis. Untreated central or peripheral nervous system inflammation at a very young age can lead to long-term sequelae in many ways.[18] Therefore, early diagnosis and treatment initiation are important. In addition, after the acute phase, rehabilitation treatment will help improve a patient's quality of life.[17]

In conclusion, we present the case of acute ascending hemorrhagic LETM associated with COVID-19 infection. Multiple courses of intravenous methylprednisolone and IVIG helped to improve motor and sensory function. However, residual neurological sequelae were unavoidable because of rapid and severe progression of the disease.

AUTHOR CONTRIBUTIONS

Conceptualization: Ha Neul Lee. Data curation: Ji Eun Yoo, Hoon-Chul Kang, Joon Soo Lee, and Heung Dong Kim. Formal analysis: Ji Eun Yoo. Investigation: Ji Eun Yoo. Methodology: Ji Eun Yoo. Project administration: Ha Neul Lee. Supervision: Hui Jin Shin and Ha Neul Lee. Validation: Ji Eun Yoo. Visualization: Ji Eun Yoo. Writing—original draft: Ji Eun Yoo. Writing—review & editing: Hui Jin Shin and Ha Neul Lee. Approval of final manuscript: Ha Neul Lee.

ORCID iDs

Ji Eun Yoo https://orcid.org/0009-0009-7801-4625
Hui Jin Shin https://orcid.org/0000-0002-1541-2564
Hoon-Chul Kang https://orcid.org/0000-0002-3659-8847
Joon Soo Lee https://orcid.org/0000-0001-9036-9343
Heung Dong Kim https://orcid.org/0000-0002-8031-7336
Ha Neul Lee https://orcid.org/0000-0002-3562-9402

https://doi.org/10.3349/ymj.2023.0202

REFERENCES

1. Preziosa P, Moiola L, Baldoli C, Longo D, Sangalli F, Radaelli M, et al. Necrotic-hemorrhagic myelitis: a rare malignant variant of parainfectious acute disseminated encephalomyelitis in childhood. J Neurol Sci 2018;384:58-60.
2. Sotoca J, Rodríguez-Álvarez Y. COVID-19-associated acute necrotizing myelitis. Neurol Neuroimmunol Neuroinflamm 2020;7:e803.
3. Arslan D, Acar-Ozen P, Gocmen R, Elibol B, Karabudak R, Tuncer A. Post-COVID-19 longitudinally extensive transverse myelitis: is it a new entity? Neurol Sci 2022;43:1569-73.
4. Moreno-Escobar MC, Kataria S, Khan E, Subedi R, Tandon M, Peshwe K, et al. Acute transverse myelitis with dysautonomia following SARS-CoV-2 infection: a case report and review of literature. J Neuroimmunol 2021;353:577523.
5. Fumery T, Baudar C, Ossemann M, London F. Longitudinally extensive transverse myelitis following acute COVID-19 infection. Mult Scler Relat Disord 2021;48:102723.
6. Kim HK, Cho YJ, Lee SY. Neurological manifestations in patients with COVID-19: experiences from the central infectious diseases hospital in South Korea. J Clin Neurol 2021;17:435-42.
7. Jung YH, Ha EH, Park J, Choe KW, Lee WJ, Jo DH. Neurological and psychiatric manifestations of post-COVID-19 conditions. J Korean Med Sci 2023;38:e83.
8. Schulte EC, Hauer L, Kunz AB, Sellner J. Systematic review of cases of acute myelitis in individuals with COVID-19. Eur J Neurol 2021;28:3230-44.
9. Howard CW, Racosta JM, Robinson DB. Acute hemorrhagic longitudinally extensive transverse myelitis – A case report and review of the literature. Neuroimmunol Rep 2022;2:100051.
10. Guada L, Cabrero FR, Baldwin NL, Levi AD, Gultekin SH, Verma A. Acute ascending necrotizing myelitis after COVID-19 infection: a clinicopathologic report. Neurol Clin Pract 2022;12:e28-32.
11. French Cooperative Group on Plasma Exchange in Guillain-Barrk Syndrome. Efficiency of plasma exchange in Guillain-Barré syndrome: role of replacement fluids. Ann Neurol 1987;22:753-61.
12. Algahtani H, Shirah B, Alrefaei K, Albassam M, Abdelghaffar N. Are repeated cycles of intravenous immunoglobulin justified in patients with poorly responsive Guillain-Barré syndrome? Neurohospitalist 2020;10:224-8.
13. Arsura EL, Bick A, Brunner NG, Grob D. Effects of repeated doses of intravenous immunoglobulin in myasthenia gravis. Am J Med Sci 1988;295:438-43.
14. Griffiths TD, Newman PK. Steroids in multiple sclerosis. J Clin Pharm Ther 1994;19:219-22.
15. Shaygannejad V, Ashtari F, Alinaghian M, Norouzi R, Salari M, Fatehi F. Short-term safety of pulse steroid therapy in multiple sclerosis relapses. Clin Neuropharmacol 2013;36:1-3.
16. van Doorn PA. Diagnosis, treatment and prognosis of Guillain-Barré syndrome (GBS). Presse Med 2013;42(6 Pt 2):e193-201.
17. Fonseca JP, Coelho A, Lourenço AC, Pires C, Margalho P. Longitudinally extensive transverse myelitis (LETM) secondary to SARS-CoV-2 infection: a recent reality in spinal cord injury rehabilitation. Clin Case Rep 2022;10:e05876.
18. Brisca G, Sotgiu S, Pirlo D, Tubino B, Siri L, Chianucci B, et al. Longitudinally extensive transverse myelitis (LETM) and myopericarditis in a 7-month-old child with SARs-CoV-2 infection. Neuropediatrics 2022;53:61-4.