pISSN 1738-6586 / eISSN 2005-5013 / J Clin Neurol 2023;19(2):210-213 / https://doi.org/10.3988/jcn.2022.0307

Leptomeningeal Enhancement, a Phenotype of Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease With Caudate Nucleus Involvement: A Case Report and Literature Review

Seondeuk Kim[a]
Seoyeon Kim[a]
Yoonhyuk Jang[a]
Kon Chu[a,b]

[a]Department of Neurology, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea
[b]Laboratory for Neurotherapeutics, Center for Medical Innovation, Biomedical Research Institute, Seoul National University Hospital, Seoul, Korea

Received August 20, 2022
Revised November 29, 2022
Accepted December 7, 2022

Correspondence
Kon Chu, MD, PhD
Department of Neurology, Seoul National University Hospital, Seoul National University College of Medicine, 101 Daehak-ro, Jongno-gu, Seoul 03080, Korea
Tel +82-2-2072-1878
Fax +82-2-2072-7424
E-mail stemcell.snu@gmail.com

Dear Editor,

Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) produces various manifestations, including optic neuritis, transverse myelitis, acute disseminated encephalomyelitis, and brainstem demyelination.[1] However, brain magnetic resonance imaging (MRI) may also demonstrate leptomeningeal enhancement (LME) involving the brain cortex and other sites.[1] We present a case of MOGAD that presented not only with LME but also with a rare imaging feature that involved the caudate nucleus (CN). Furthermore, we systematically reviewed articles that reported similar phenotypes, and compared our case with the results of the literature review.

We present a 33 year-old female with a history of traveling to Finland and Las Vegas 2 weeks before the onset of the symptoms of fever (up to 38.5°C), headache, and nausea. She and her family denied any psychiatric or cognitive symptoms. A neurological examination revealed no focal neurological deficit except for neck stiffness with a positive Kernig's sign. To rule out meningitis, she underwent spinal tapping for cerebrospinal fluid (CSF) analysis that revealed pleocytosis (white blood cell [WBC] count=250/μL, 90% lymphocytes), elevated proteins (127.6 mg/dL), slightly decreased glucose levels (54 mg/dL; 120 mg/dL in serum), and increased immunoglobulin G index (0.71). Oligoclonal bands were absent. The cytology was negative for malignant cells. Brain MRI indicated LME that predominated in the left cerebral cortex and a T2-weighted hyperintense lesion with gadolinium enhancement that involved the head of the CN and the putamen (Supplementary Fig. 1A and B in the online-only Data Supplement). Regional slowing of the left frontotemporal area was confirmed on electroencephalography. Although intravenous (IV) acyclovir was administered before the CSF analysis, various CSF infection tests were subsequently found to be negative, including metagenomics for bacterial 16S and fungal internal transcribed spacer, cultures for bacteria, fungi, and tuberculosis (Tb), and polymerase chain reactions (PCRs) for several viruses and Tb. Nonetheless, flavivirus infections such as tick-borne encephalitis (TBE) could not be ruled out. She was therefore treated using IV immunoglobulin (IVIg, 2 g/kg for 5 days) for the two scenarios of autoimmunity and infection.

MOG antibody was subsequently confirmed as positive using fluorescence-activating cell sorting (ratio of positive cell=0.744 [positive >0.254], mean fluorescence intensity of fluorescein isothiocyanate channel=5.63 [positive >3.65]). She was negative for other autoimmune antibodies, including anti-aquaporin-4 antibody (Supplementary Materials in the online-only Data Supplement). Ophthalmological tests were performed using fundoscopy and optical coherence tomography, which indicated that both optic nerves were normal. The

Table 1. Demographics, clinical manifestations, and radiological findings of MOGAD patients with leptomeningeal enhancement in literature review and our case (*n*=35)

	Available		Unavailable
	Presence	Absence	
Sex			
Males	48.6 (17/35)	NA	0.0 (0/35)
Females	51.4 (18/35)	NA	0.0 (0/35)
Age, years	94.3 (33/35)	NA	5.7 (2/35)
	24.45±12.12 (2–55)	NA	NA
Precedent infection or vaccination	14.3 (5/35)	62.9 (22/35)	22.9 (8/35)
Detail	Covid-19 (2), vaginal herpes (1), ChAdOx1 vaccine (1), unknown (1)	NA	NA
History of traveling	5.7 (2/35)	71.4 (25/35)	22.9 (8/35)
Presence of tumor	5.7 (2/35)	88.6 (31/35)	5.7 (2/35)
Detail	Ovarian teratoma (1), ovarian borderline tumor (1)	NA	NA
Symptoms			
Fever	60.0 (21/35)	20.0 (7/35)	20.0 (7/35)
Headache	71.4 (25/35)	8.6 (3/35)	20.0 (7/35)
Seizure	54.3 (19/35)	42.9 (15/35)	2.9 (1/35)
Demyelination			
Optic neuritis	42.9 (15/35)	57.1 (20/35)	0.0 (0/35)
Myelitis	25.7 (9/35)	74.3 (26/35)	0.0 (0/35)
CSF study	77.1 (27/35)	0.0 (0/35)	22.9 (8/35)
Pleocytosis, among the presence of CSF study	Presence 96.3 (26/27) Absence 3.7 (1/27) Unavailable 0.0 (0/27)	NA	NA
WBC count among the presence of CSF study	115.38±124.91	NA	NA
Lympho-dominant pleocytosis	Presence 53.8 (14/26) Absence 11.5 (3/26) Unavailable 34.6 (9/26)	NA	NA
Elevated protein	Presence 66.7 (18/27) Absence 25.9 (7/27) Unavailable 7.4 (2/27)	NA	NA
Protein level (available only)	73.24±35.57	NA	NA
Decreased glucose	Presence 14.8 (4/27) Absence 25.9 (7/27) Unavailable 59.3 (16/27)	NA	NA
Glucose level (available only)	51.85±7.86	NA	NA
Oligoclonal band	14.3 (5/35)	54.3 (19/35)	31.4 (11/35)
MRI	100.0 (35/35)	0.0 (0/35)	0.0 (0/35)
Cortical/subcortical	85.7 (30/35)	14.3 (5/35)	0.0 (0/35)
Frontal	45.7 (16/35)	54.3 (19/35)	0.0 (0/35)
Insular	17.1 (6/35)	82.9 (29/35)	0.0 (0/35)
Cingulate	8.6 (3/35)	91.4 (32/35)	0.0 (0/35)
Parietal	40.0 (14/35)	60.0 (21/35)	0.0 (0/35)
Temporal	42.9 (15/35)	57.1 (20/35)	0.0 (0/35)
Occipital	17.1 (6/35)	82.9 (29/35)	0.0 (0/35)

Table 1. Demographics, clinical manifestations, and radiological findings of MOGAD patients with leptomeningeal enhancement in literature review and our case (*n*=35) (continued)

	Available		Unavailable
	Presence	Absence	
Midbrain	11.4 (4/35)	88.6 (31/35)	0.0 (0/35)
Pons	17.1 (6/35)	82.9 (29/35)	0.0 (0/35)
Medulla	8.6 (3/35)	91.4 (32/35)	0.0 (0/35)
Cerebellum	14.3 (5/35)	85.7 (30/35)	0.0 (0/35)
Corpus callosum	14.3 (5/35)	85.7 (30/35)	0.0 (0/35)
PVWM	8.6 (3/35)	91.4 (32/35)	0.0 (0/35)
Thalamus	17.1 (6/35)	82.9 (29/35)	0.0 (0/35)
Basal ganglia	20.0 (7/35)	80.0 (28/35)	0.0 (0/35)
Caudate	14.3 (5/35)	85.7 (30/35)	0.0 (0/35)
Globus pallidus	0.0 (0/35)	100.0 (35/35)	0.0 (0/35)
Putamen	11.4 (4/35)	88.6 (31/35)	0.0 (0/35)
Other autoantibodies	31.4 (11/35)	68.6 (24/35)	0.0 (0/35)
Detail	NMDAR (5), GFAP (2), NMDAR+GFAP (1), GAD (1), TPO (1), ANA (1)	NA	NA
Initial therapy			
Antiviral agents*	31.4 (11/35)	20.0 (2/35)	48.6 (22/35)
Antibiotics*	31.4 (11/35)	20.0 (2/35)	48.6 (22/35)

Data are % (*n*/*n*) or mean±SD values.
*Nine patients were treated with both antiviral and antibiotics.
CSF, cerebrospinal fluid; MOGAD, myelin oligodendrocyte glycoprotein antibody-associated disease; MRI, magnetic resonance imaging; NA, not applicable; PVWM, periventricular white matter; WBC, white blood cell.

findings of whole-spine MRI were also normal. PCR for the TBE virus and reverse transcriptase PCR for the Japanese encephalitis virus (JEV) were negative.

Agraphia developed in this patient despite receiving IVIg treatment. Under the assumption of MOGAD, we considered IV steroids because of concern about rapid deterioration. However, steroid administration can mask malignancies such as lymphoma, which could not be easily precluded by only one cytology assessment with a small sample volume. Rituximab and subsequently tocilizumab were therefore administered considering the delayed onset of response to rituximab. In the follow-up CSF analysis with an abundant sample volume of the cytology, pleocytosis and protein elevation improved but persisted (WBC=40/μL, 95% lymphocytes, proteins=89 mg/dL), and the cytology was negative for malignant cells. Her fever, headache, and agraphia improved after rituximab and tocilizumab therapy. Furthermore, the CN lesion and LME were found to have improved in the follow-up brain MRI performed 2 weeks after the initial MRI (Supplementary Fig. 1C and D in the online-only Data Supplement).

The literature review identified 34 patients with MOGAD and LME in 25 articles (The detailed data arrangement process is illustrated in the Supplementary Materials in the online-only Data Supplement). With our case added to the selected patient list, we investigated demographics, prevalence of clinical and laboratory manifestations, and the anatomical distribution of MRI lesions among these patients.

The sex ratio was 0.94 males per 1 female. The mean age was 24.45 years, encompassing both children and adult patients. Most patients reported fever, headache, and seizure as the presenting symptoms. Antecedent or subsequent optic neuritis and myelitis were present in 42.9% and 25.7% of patients, respectively. The CSF profile indicated pleocytosis in 96.3%, and the WBC was 115.38±124.91/μL (mean±standard deviation). Protein levels were elevate in 66.7% (73.24±35.57 mg/dL). Oligoclonal bands were present in only 14.3%. Cortical/subcortical lesions were most common (85.7%) on brain MRI, but infiltration of the basal ganglia was also observed in 20.0%. Among them, five patients (14.3%), including ours, had LME with CN lesions (Table 1).

Multiple differential diagnoses should be considered in cases of LME with a CN lesion. Among infectious meningoencephalitis, TBE virus, West Nile virus, and JEV can be suspected.[2] Finck et al.[2] recently suggested that the Borna disease virus initially prefers CN invasion. Various autoimmune diseases may also present with a CN lesion.[3] MRI findings of Rasmussen encephalitis can present with involvement of the unilateral CN head and cortex with or without atrophy, which was similar to the condition of our patient.

While LME may be an important feature of MOGAD, pre-

vious cohort studies have paid little attention to LME.[4-8] A systematic analysis by Ineichen et al.[9] of LME in various neurological disorders indicated that the prevalence of LME was lower in neuromyelitis optica spectrum disorder, and LME was associated with some manifestations of multiple sclerosis. Still, LME in MOGAD has not been demonstrated accurately, which calls for further research in this area.

In conclusion, MOGAD should be considered when in presentations of LME with CN lesions.

Supplementary Materials

The online-only Data Supplement is available with this article at https://doi.org/10.3988/jcn.2022.0307.

Ethics Statement

This study followed the tenets of the Declaration of Helsinki. Written informed consent was obtained from the patient.

Availability of Data and Material

The datasets generated or analyzed during the study are available from the corresponding author on reasonable request.

ORCID iDs

Seondeuk Kim	https://orcid.org/0000-0003-1791-1815
Seoyeon Kim	https://orcid.org/0000-0002-2983-8697
Yoonhyuk Jang	https://orcid.org/0000-0002-3346-3357
Kon Chu	https://orcid.org/0000-0001-5863-0302

Author Contributions

Conceptualization: Kon Chu. Data curation: Seondeuk Kim, Seoyeon Kim. Formal analysis: Seondeuk Kim, Seoyeon Kim. Supervision: Yoonhyuk Jang, Kon Chu. Writing—original draft: Seondeuk Kim. Writing—review & editing: Yoonhyuk Jang, Kon Chu.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

Funding Statement

None

REFERENCES

1. Marignier R, Hacohen Y, Cobo-Calvo A, Pröbstel AK, Aktas O, Alexopoulos H, et al. Myelin-oligodendrocyte glycoprotein antibody-associated disease. *Lancet Neurol* 2021;20:762-772.
2. Finck T, Liesche-Starnecker F, Probst M, Bette S, Ruf V, Wendl C, et al. Bornavirus encephalitis shows a characteristic magnetic resonance phenotype in humans. *Ann Neurol* 2020;88:723-735.
3. Bekiesinska-Figatowska M, Mierzewska H, Jurkiewicz E. Basal ganglia lesions in children and adults. *Eur J Radiol* 2013;82:837-849.
4. Gadde JA, Wolf DS, Keller S, Gombolay GY. Rate of leptomeningeal enhancement in pediatric myelin oligodendrocyte glycoprotein antibody-associated encephalomyelitis. *J Child Neurol* 2021;36:1042-1046.
5. Salama S, Khan M, Shanechi A, Levy M, Izbudak I. MRI differences between MOG antibody disease and AQP4 NMOSD. *Mult Scler* 2020;26:1854-1865.
6. Li H, Yang L, Wu Z, Zhou L, Bao Y, Geng D, et al. Brain MRI features of Chinese Han patients with MOG-antibody disease. *Mult Scler Relat Disord* 2020;43:102167.
7. Hou C, Wu W, Tian Y, Zhang Y, Zhu H, Zeng Y, et al. Clinical analysis of anti-NMDAR encephalitis combined with MOG antibody in children. *Mult Scler Relat Disord* 2020;42:102018.
8. Cobo-Calvo A, Ruiz A, Maillart E, Audoin B, Zephir H, Bourre B, et al. Clinical spectrum and prognostic value of CNS MOG autoimmunity in adults: the MOGADOR study. *Neurology* 2018;90:e1858-e1869.
9. Ineichen BV, Tsagkas C, Absinta M, Reich DS. Leptomeningeal enhancement in multiple sclerosis and other neurological diseases: a systematic review and meta-analysis. *Neuroimage Clin* 2022;33:102939.