Anti-MOG antibody-positive meningoencephalitis without demyelinating lesions

Yamane, Tetsuya ; Ueda, Takuya ; Nishiyama, Masahiro ; Hongo, Hiroto ; Ishida, Yusuke ; Maruyama, Azusa

(Citation)
Pediatrics International,65(1):e15612

(Issue Date)
2023-08-17

(Resource Type)
journal article

(Version)
Accepted Manuscript

Clinical Note

Title: Anti-MOG antibody-positive meningoencephalitis without demyelinating lesions

Running title: MOGAD without demyelinating lesions

Tetsuya Yamane, M.D.[1)], Takuya Ueda, M.D.[1)], Masahiro Nishiyama, M.D., Ph.D[1,2*)], Hiroto Hongo, M.D.[1)],Yusuke Ishida, M.D., Ph.D[1)], Azusa Maruyama, M.D.[1)]

[1)] Department of Neurology, Hyogo Prefectural Kobe Children's Hospital, Kobe, Japan

[2)] Department of Pediatrics, Kobe University Graduate School of Medicine, Kobe, Japan

***Corresponding author:**

Masahiro Nishiyama, M.D., Ph.D

Department of Neurology, Hyogo Prefectural Kobe Children's Hospital, Kobe, Japan

1-6-7 Minamimachi, Minatojima, Chuo-ku, Kobe, Hyogo, 650-0047, Japan

Tel: +81-78-945-7300, Fax: +81-78-302-1023

E-mail: nishiyan0203@yahoo.co.jp

Text pages: 2

Words: 725

Reference pages: 1

Tables: 0

Figures and legends to figures: 1

Key words: autoimmune, infant, meningoencephalitis, myelin-oligodendrocyte glycoprotein, white matter

The basic diagnostic criterion for myelin oligodendrocyte glycoprotein associated disease (MOGAD) is a positive anti-myelin oligodendrocyte glycoprotein (MOG) antibody test.[1] MOGAD is characterized as acquired demyelinating syndromes, such as optic neuritis, transverse myelitis, and acute disseminated encephalomyelitis.[1] Recently, cortical encephalitis with high signal, mainly in the cerebral cortex, is also reported.[2] Few cases of aseptic meningitis with white matter or cortical involvement are reported.[3] We experienced a case of anti-MOG antibody-positive meningoencephalitis with leptomeningeal enhancement without white matter or cortical lesions in a 4-year-old child. Informed consent for this case report was obtained from the patient's parents.

A 4-year-old boy, without prior medical history, was admitted to the initial hospital with fever lasted for five days and headache. He had neck rigidity, and examination of the cerebrospinal fluid (CSF) revealed a slightly increased cell count (8/μL) and protein level (48 mg/dL). However, because the CSF culture, CSF polymerase chain reaction using the BioFire FilmArray meningitis/encephalitis panel, and magnetic resonance imaging (MRI) did not reveal any abnormal finding, he was diagnosed with idiopathic aseptic meningitis and followed up without specific treatment. On day 4, he experienced a cluster of convulsive seizures. At first, he experienced a left facial spasm and weakness of the extremities, which improved after 5 minutes. He had left facial spasm and eye deviation, which improved with midazolam (0.15 mg/kg) after 3 minutes at the second episode. He presented with prolonged unconsciousness and was transferred to our hospital. On admission, his consciousness level tended to improve; however, he experienced drowsiness and irritability, and the Glasgow Coma Scale (GCS) was 14 (E4V4M6). On day 5, re-examination of the CSF revealed an increased cell count (248/μL) and protein level (132 mg/dL). Electroencephalogram showed intermittent generalized slow waves of 2-3 Hz. Suspecting immune encephalitis, the patient was treated with intravenous methylprednisolone (30 mg/kg/day) for three days. On day 6, fever resolved, and on day 8, level of consciousness and headache improved. On day 10, MRI showed a contrasting effect in the meninges, but no lesions in the white matter (Figure 1). Live cell-based assays revealed seropositivity for anti-MOG antibodies on day 4, and the patient was diagnosed with anti-MOG antibody-positive meningoencephalitis. He did not have any symptoms of optic neuritis or myelitis. Oligoclonal band was negative and the IgG index was 0.54; however, we could not measure the myelin basic protein due to lack of test reagents. Serum anti-nuclear, anti-DNA, and anti-cardiolipin β2-glycoprotein I antibodies were negative. Steroids were tapered off over a month, and an MRI scan one month later showed that the contrast effect on the meninges had disappeared. At nine months after the disease onset, the patient had no recurrence, although the serum

remained positive for anti-MOG antibodies.

This case study provided two important insights into the spectrum of MOGAD and its treatment. First, our case suggests that anti-MOG antibodies may be involved, even in young children with meningoencephalitis without imaging lesions in the brain parenchyma. MOGAD is often associated with demyelinating lesions as imaging findings because demyelination with inflammation is thought to be the main feature.[1] Additionally, cases of cortical encephalitis and aseptic meningitis are reported; however, the patients often show lesions in the brain parenchyma.[2, 3] In addition, most reported cases are in school children and adults, and cases in preschool children are rarely reported.[3] We speculate that undiagnosed MOGAD may be present in aseptic meningitis of unknown cause in young children because, currently, anti-MOG antibodies are not widely examined in these patients.

Second, our case highlights the need for specific treatments in children with aseptic meningitis. Among young patients with aseptic meningitis, which is often experienced in pediatric practice, anti-MOG antibodies may be present in some patients, and steroid therapy might be effective in some of these patients. Steroids are known to be effective against MOGAD.[4] However, whether our case could be diagnosed as MOGAD by the laboratory finding of positive anti-MOG antibody alone remains unclear. Anti-MOG antibody was positive in our patient; however, it was unrelated to pathology and may have been detected incidentally. Therefore, the need for treatment is inconclusive. It is also known that the disease can relapse and progress to other anti-MOG-related diseases,[5] indicating the requirement of adequate treatment and careful follow-up. Taken together, the measurement of anti-MOG antibodies is useful, even in cases with equivocal imaging findings, for additional treatment options and prevention of relapse.

Author contributions

T.Y. collected the data and drafted the manuscript. T.U. collected the data and critically reviewed the manuscript. M.N. designed the study and revised the manuscript. H.H. and Y.I. reviewed and revised the manuscript. A.M. reviewed and supervised the study. All authors read and approved the final manuscript.

Acknowledgements

This work was partly supported by JSPS KAKENHI [grant number JP22K09119] and a Grant-in-Aid [grant number 2020C02] from the Japan Intractable Diseases (Nanbyo) Research Foundation to MN.

1

2 Disclosure

3 The authors declare no conflict of interest.

4

5

6

References

1. Banwell B, Bennett JL, Marignier R, et al. Diagnosis of myelin oligodendrocyte glycoprotein antibody-associated disease: International MOGAD Panel proposed criteria. *Lancet. Neurol.* 2023; 22: 268-82.

2. Ogawa R, Nakashima I, Takahashi T, et al. MOG antibody-positive, benign, unilateral, cerebral cortical encephalitis with epilepsy. *Neurol. Neuroimmunol. Neuroinflamm.* 2017; 4: e322.

3. Gombolay GY, Gadde JA. Aseptic meningitis and leptomeningeal enhancement associated with anti-MOG antibodies: A review. *J. Neuroimmunol.* 2021; 358: 577653.

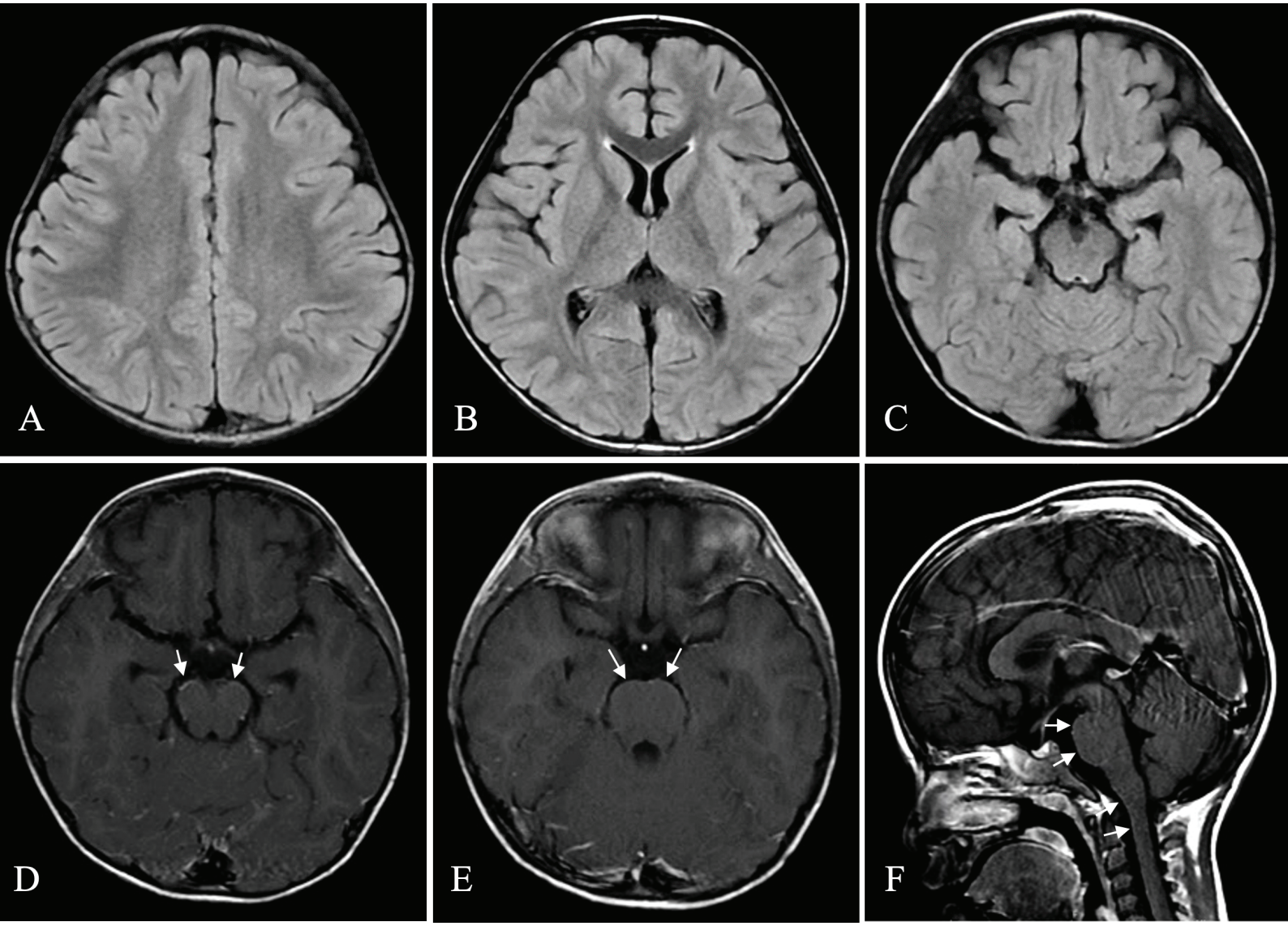
4. Ramanathan S, Mohammad S, Tantsis E, et al. Clinical course, therapeutic responses and outcomes in relapsing MOG antibody-associated demyelination. *J. Neurol. Neurosurg. Psychiatry* 2018; 89: 127-37.

5. Lin S, Long W, Wen J, Su Q, Liao J, Hu Z. Myelin oligodendrocyte glycoprotein antibody-associated aseptic meningitis without neurological parenchymal lesions: A novel phenotype. *Mult. Scler. Relat. Disord.* 2022; 68: 104126.

Figure legends

Figure 1. Magnetic resonance images of the brain

After 10 days of onset, no abnormalities were seen on axial T2-weighted fluid-attenuated inversion recovery (T2-FLAIR) imaging pre-gadolinium (A–C). On axial (D, E) and sagittal (F) T1-weighted imaging post-gadolinium, leptomeningeal enhancement is observed (arrow).


A
B
C
D
E
F