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A case of unilateral recurrent cerebral cortical encephalitis with anti-myelin oligodendrocyte glycoprotein antibodies

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Abstract:

Myelin oligodendrocyte glycoprotein (MOG)-antibody-associated disease (MOGAD) is an independent inflammatory demyelinating disease. A rare phenotype of MOGAD is cerebral cortical encephalitis (CCE). This case report presents unilateral recurrent cerebral cortical encephalitis (CCE) with positive anti-MOG antibodies from a 55 year old man who was admitted with headache, fever and aphasia. This case highlights the findings of hyperintense lesions in the cortex of the right temporal gyrus with slight swelling on T2 FLAIR and anti MOG antibodies in serum (1:20) and CSF (1:80) when the patient presented again to hospital after the initial improvement with IVIG and glucocorticoids. In addition, the patient was found to have atrophy of the whole brain, especially the right temporal lobe, after becoming symptom-free with glucocorticoids. In summary, anti-MOG-associated CCE can be diagnosed with headache, fever, and seizures associated with the presence of anti-MOG antibodies. Unilateral CCE is a special clinical feature of MOGAD and cerebral atrophy can be found. Steroid therapy remains to be the standard treatment.

Keywords:

Atrophy, cerebral cortical encephalitis, myelin oligodendrocyte glycoprotein, recurrent

Introduction

Myelin oligodendrocyte glycoprotein (MOG) is a protein specifically expressed on the surface of myelin sheaths and oligodendrocytes in the central nervous system, which distinguishes from the classic multiple sclerosis and AQP4-immunoglobulin G (IgG)-positive neuromyelitis optica spectrum disorders.^[1] MOG antibody (MOG-ab)-associated disease (MOGAD) has a range of various clinical phenotypes and radiological features, including optic neuritis, transverse myelitis, acute disseminated encephalomyelitis (ADEM), and brainstem syndrome.^[2] In addition,

encephalitis is an important phenotype with cortical lesions most frequently observed.^[3] Unilateral cerebral cortical encephalitis (CCE) is a rare phenotype of MOGAD which was first described by Ogawa *et al.*^[4] Previous studies show that patients with MOGAD are highly sensitive to corticosteroids and can achieve complete symptom remission.^[4-6] This case report presents ipsilateral recurrent unilateral CCE with positive anti-MOG antibodies.

Case Report

A 55-year-old man presented with headache and aphasia. His headache suddenly occurred 2 days in prior in the right temporal, parietal, and occipital lobes and persisted with no regression. The headache was associated with a fever of 37.5°C (99.5°F) that was controlled with oral

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medications. His aphasia occurred 1 day in prior and lasted for an hour with complete recovery subsequently. His aphasia recurred 3 h before his presentation to the hospital without remission. On admission, his vital signs were a temperature of 36.8°C, a heart rate of 66 beats per minute, and a blood pressure of 126/84 mmHg. He had anomia, hypoesthesia in the left limb, and positive Babinski sign on the left. There was no meningeal irritation sign, and the patient was alert. Complete blood count and other serum values were normal. Lumbar puncture revealed an opening pressure of 19 cm H₂O, white blood cell (WBC) of 2/cmm, elevated protein (0.48 g/L), and the absence of oligoclonal bands. Intrathecal IgG synthesis rate of 24 h was normal. Serum and cerebrospinal fluid (CSF) for anti-Hu, Yo, Ri, N-methyl-D-aspartate receptor (NMDAR), glutamic acid decarboxylase (GAD), voltage-gated potassium channel (VGKC), and anti-aquaporin-4 antibodies were negative as well as herpes virus antibodies. Brain magnetic resonance imaging (MRI) showed T2-fluid-attenuated inversion recovery (FLAIR) hyperintensity and swelling of the right temporal and occipital cortex and adjacent sulci [Figure 1a-d] without obvious contrast enhancement [Figure 1e and f]. Routine electroencephalogram showed persistently slow waves in the right hemisphere but showed epileptic discharge during the interictal state.

On hospital day 3, he developed involuntary movement of the left hand and generalized tonic seizure for several

minutes with unconsciousness, limb jerking, and left eye gaze. Diazepam was added for seizure control, and the patient was found to have a mild left hemiparesis subsequently. On hospital day 5, he developed an involuntary twitch of the right corner of the mouth. Intravenous immunoglobulin (0.4g/kg-d for 5 days) was started for possible autoimmune encephalitis and his left hemiparesis was improved slightly. In addition, high-dose glucocorticoid was given (methylprednisolone 1 g/day for 5 days), followed by a gradual reduction to oral prednisolone. The patient improved rapidly and was able to be discharged without residual symptoms. His prednisone was gradually reduced and stopped over 3 months. A repeat MRI revealed full resolution from the initial abnormalities.

The patient presented 4 months later to the hospital with paroxysmal dizziness for a week. The patient had gradual memory impairment and slow responsiveness ever since her discharge from the previous hospital admission. Lumbar puncture showed an opening pressure of 13.5 cm H₂O and WBC of 16/cmm. Serum and CSF showed negative results for anti-CV2/CRMP5,-PNMA2,-Ri,-Yo,-Hu,-Amphiphysin, NMDA-R-IgG, CASPR2-IgG, AMPA1-R-IgG, AMPA2-R-IgG, LGI1-IgG, and GABAB-R-IgG antibodies. Anti-MOG antibodies were positive both in serum (1:20) and in the CSF (1:80). Visually evoked potentials demonstrated impaired optic pathway conduction bilaterally, as manifested by a prolonged latency of

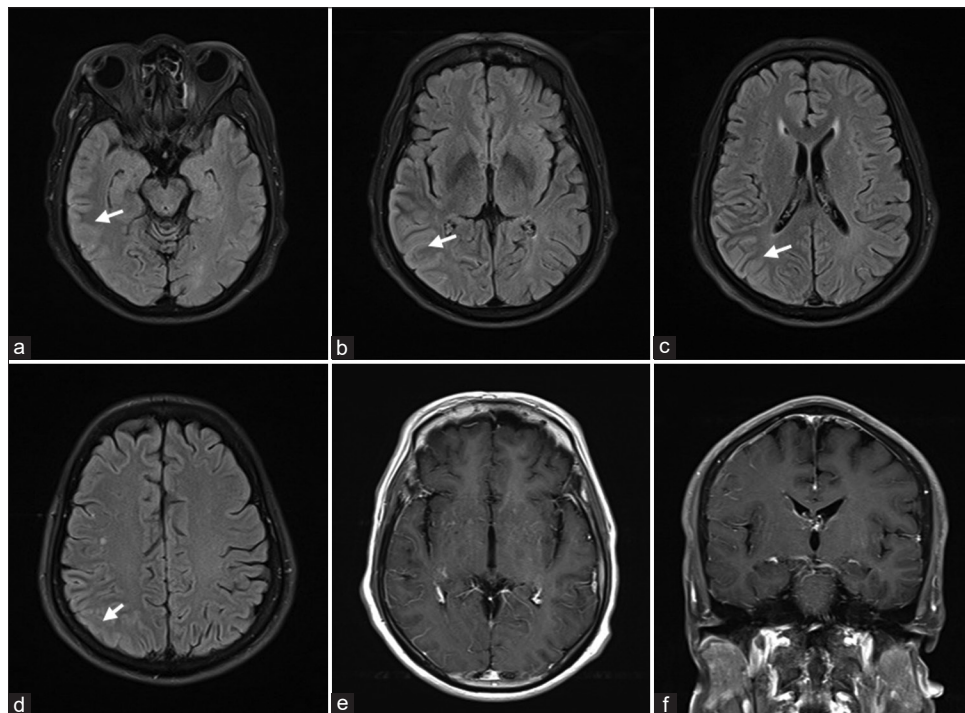


Figure 1: Brain MRI with anti-MOG-associated cerebral cortical encephalitis after the first. Axial T2-FLAIR images showed hyperintensity and swelling of the cortex in the right temporal, parietal, and occipital lobes (a-d) without gadolinium contrast enhancement (e and f). Lesions indicated by white arrowheads. MRI: Magnetic resonance imaging, T2-FLAIR: T2-weighted fluid-attenuated inversion recovery, MOG: Myelin oligodendrocyte glycoprotein

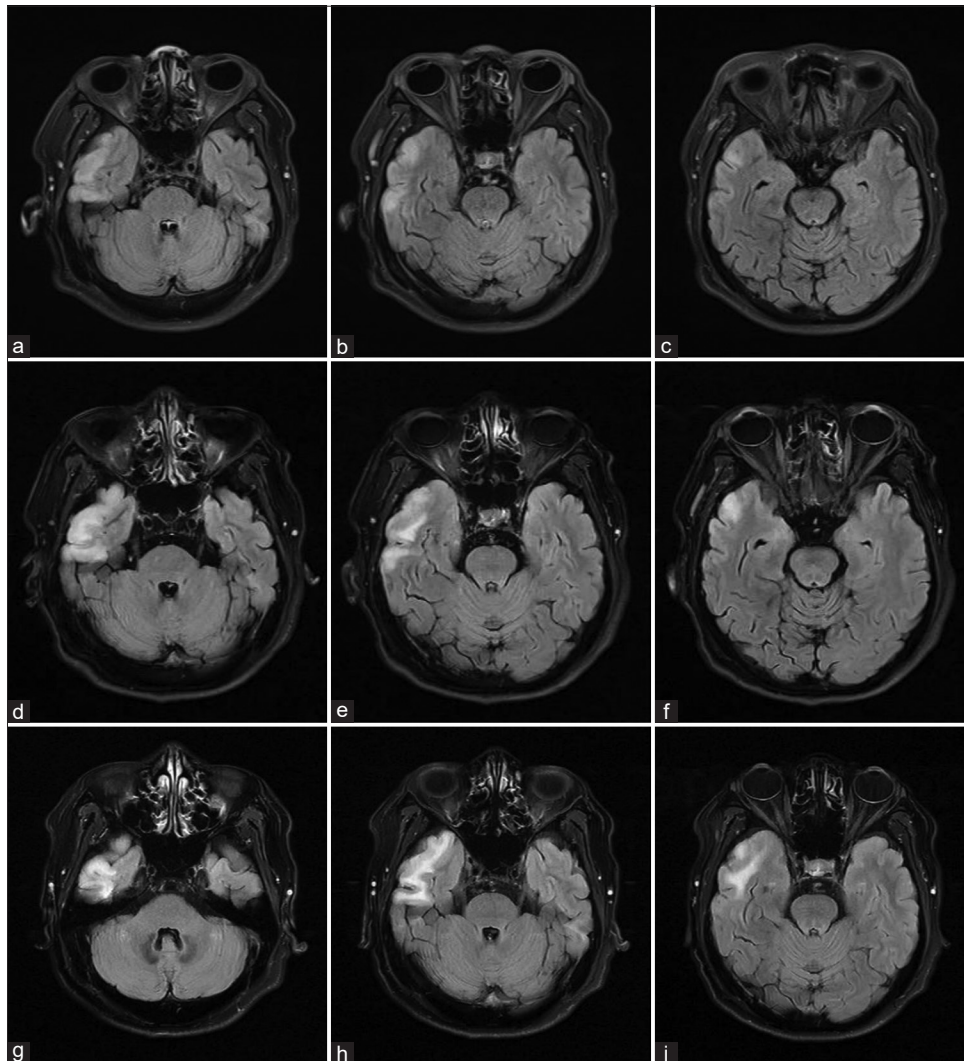


Figure 2: Brain MRI after the second admission showed hyperintense lesions in the right temporal gyrus with slight swelling on T2-FLAIR (a-c). The lesions became larger 5 days later (d-f). The patient was discharged 17 days later with improved symptoms; MRI still showed abnormal signals in the right temporal gyrus on T2-FLAIR (g-i). MRI: Magnetic resonance imaging, T2-FLAIR: T2-weighted fluid-attenuated inversion recovery

bilateral P100 wave. Brain MRI showed hyperintense lesions in the cortex of the right temporal gyrus with slight swelling on T2-FLAIR [Figure 2a-c], and the lesions became larger 5 days later [Figure 2d-f]. Furthermore, there was slight partial marginal enhancement with contrast. There was no abnormality from optic MRI.

The patient was diagnosed with MOG antibody-positive CCE. High-dose glucocorticoids (1,000 mg/d) were administered. A repeat MRI study noted abnormal signals in the right temporal lobe on T2-FLAIR [Figure 2g-i]. After 12 days of treatment, the patient became free from the symptoms, and glucocorticoids were gradually tapered; he was subsequently discharged from the hospital. Oral prednisolone (60 mg/d) was started 11 days after and eventually tapered to 5 mg/d. Brain MRI was repeated 5 months after and showed atrophy of the whole brain, especially the right temporal lobe, and no residual hyperintense lesion [Figure 3]. Oral

prednisone was continued for another 8 months, and the patient reported no new complaints. Repeated brain MRI has no significant change compared to the previous ones during follow-up period.

Discussion

MOGAD has heterogeneous clinical and imaging presentations, and encephalitis is an important phenotype.^[3] Unilateral CCE is a rare finding of anti-MOG, which was first reported by Ogawa *et al.*^[4] The authors described four cases who had seizures, MOG-IgG positivity, and unilateral cortical hyperintensities on T2-FLAIR sequences of MRI. Its incidence is extremely low compared to stroke.^[7] The imaging features of anti-MOG-associated encephalitis with seizures were named as FLAIR-hyperintense Lesions in Anti-MOG-associated Encephalitis with Seizures (FLAMES) by Budhram *et al.*;^[8] the common

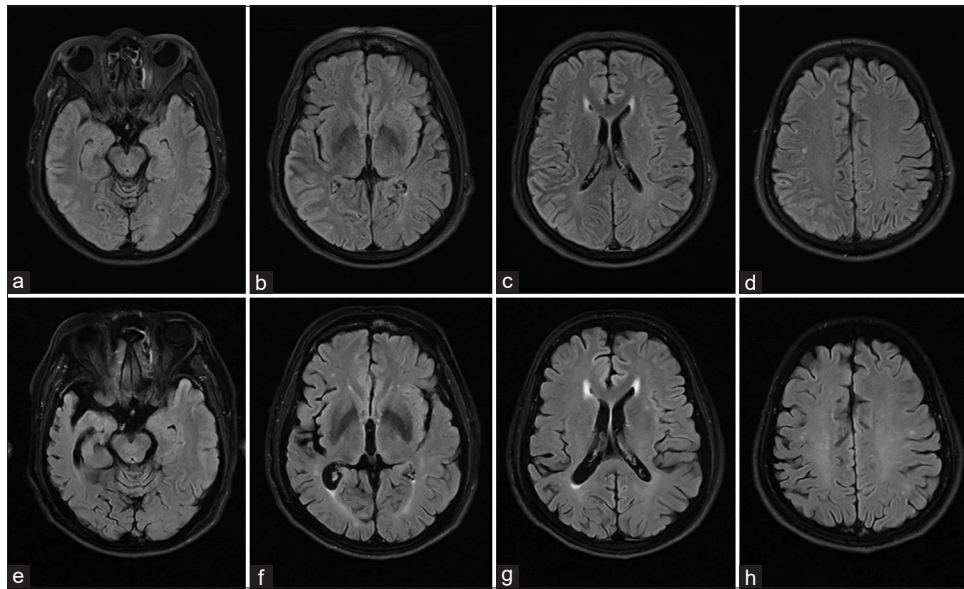


Figure 3: Compared to the initial brain MRI during the first admission (a-d), MRI performed 14 months later during follow-up (e-h) showed cortical atrophy, especially in the right temporal lobe, and dilation of the right temporal horn. MRI: Magnetic resonance imaging

clinical manifestations were seizures, headache, fever, and cortical symptoms in the “FLAMES” location.^[8]

The patient of this case was presented with the typical clinical manifestations of anti-MOG-associated CCE, including headache, fever, and seizure. In addition, diagnosis of anti-MOG-associated CCE could be confirmed with hyperintense cortical lesions on T2-FLAIR and a high titer of anti-MOG antibody from serum and CSF. However, some unique clinical features were noted in this case, compared to those in the past. In previously reported cases, most patients responded well to high-dose glucocorticoids and recovered completely with no relapse.^[4,8-15] A few cases with relapse^[3,16-19] typically presented with optic neuritis, ADEM, longitudinally extensive transverse myelitis, or brainstem syndromes. Interestingly, there was a relapse after a high-dose glucocorticoid therapy in this case and lesions were found in the ipsilateral cerebral cortex. Based on previous studies, a few possibilities responsible for these unique clinical features were considered: (1) a rapid tapering or withdrawal of high-dose steroids,^[6] (2) high antibody levels, and (3) and/or persistent seropositivity.^[20,21] In fact, studies had shown that a long-term immunotherapy was associated with a reduction of relapse rate in patients with MOGAD, which advocated the need of immunosuppressants.^[22,23] Unfortunately, the patient of this case did not agree with MOG antibody titer again. The treatment was guided symptomatically and mainly based on the imaging study changes, which was the limitation of this case study.

In the past reports, abnormal signals on brain MRI disappeared without residual lesions in most treated

patients. The patient of this case, on the other hand, developed cognitive impairment associated with global cerebral atrophy after two episodes of unilateral cortical encephalitis, which had rarely occurred from adult patients with anti-MOG-associated CCE. Armangue *et al.*^[24] conducted a multicenter observational study and described a 9-year-old boy with a clinical presentation of cortical encephalitis. His MRI initially became normal after treatment. However, he developed a relapse with clinical and radiographic features similar to the initial episode. Severe cortical atrophy was noted from a follow-up MRI 6 months later, and this was associated with poor recovery. In a retrospective study, Wang *et al.*^[3] described 18 patients with anti-MOG-associated encephalitis. Two of these patients had temporal lobe atrophy and another patient with faint residual white matter lesions. The rest showed complete clinical resolution after being treated. It seems to be reasonable to speculate that the pathogenesis of anti-MOG-associated encephalitis is immune mediated or autoantibody mediated based on the fact that persistent anti-MOG antibodies are associated with chronic damage to the cerebral cortical cells. Moreover, the patient of this was relatively older than other reported patients with anti-MOG-associated encephalitis.

The relationship between CCE and MOG antibodies is not well understood. Brain biopsy is hardly performed to assess anti-MOG-associated CCE. Lymphocytic infiltration has been observed in the subarachnoid space, brain parenchyma, and perivascular regions, and demyelination is largely absent.^[25] Oligodendrocytes are notably present in the subcortical white matter, and myelinated oligodendrocytes are also found in the cortical gray matter for axonal conduction. These

histological findings may be associated with the cortical symptoms in MOGAD.^[26] When the white matter is damaged, oligodendrocytes and other cells in the neurovascular unit can mend damage to the white matter and restore brain function ensuing neural injury.^[27] Finally, it is possible that MOG antibody may not be directly involved in the unilateral CCE. A separate autoimmune entity, such as NMO/D coexisting with MOG antibody, may be responsible for the encephalitis.

Conclusion

MOGAD is often presented with CCE. When anti-MOG-associated CCE is suspected, especially with headaches, fever, and seizures, serum should be analyzed for the presence of MOG-ab at the earliest for a timely treatment. Anti-MOG-associated CCE can cause global cerebral atrophy after treatment and can relapse as other MOGADs. The standard steroid therapy is required for MOGAD with unilateral cortical encephalitis; immunosuppressants may be necessary with gradual tapering to prevent recurrence. Finally, MOGAD is a newly discovered brain disease, and cortex encephalitis is one of the subtypes. There appear to be various subtypes to be discovered, and the unknown pathogenesis needs a lot of laboratory work.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

Dr. Yuchuan Ding is an Associate Editor, Dr. Xiaokun Geng is an Editorial Board member of *Brain Circulation*. The article was subject to the journal's standard procedures, with peer review handled independently of them and their research groups.

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