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MOGAD following anti-NMDAR encephalitis: A case report

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Abstract

Anti-N-methyl-D-aspartate receptor antibody and myelin oligodendrocyte glycoprotein antibody can coexist. Some patients have NMDAR encephalitis and MOG antibody disease successively. We report a rare case of MOGAD following anti-NMDAR encephalitis. Three years ago, a female of 44 years, our patient developed headache, mental disorder, and epilepsy. Cerebrospinal fluid was positive for NMDAR antibodies, and the patient's symptoms improved after immunomodulatory treatment. Three months ago, the patient had a sudden loss of vision in the left eye. Orbital magnetic resonance imaging was supportive of left optic neuritis. Cerebrospinal fluid was positive for NMDAR and MOG antibodies. She was then diagnosed with MOGAD with anti-NMDAR encephalitis. In conclusion, when patients with anti-NMDAR encephalitis have demyelinating symptoms such as decreased vision, numbness or weakness of the limbs, it is necessary to consider whether they are combined with MOGAD.

Keywords: Anti-NMDAR encephalitis, MOGAD, overlapping antibodies, immunomodulatory therapy, case report

INTRODUCTION

Anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis is a serious antibody-mediated neurological disease that can easily be misdiagnosed as psychosis, epilepsy or viral encephalitis. Myelin oligodendrocyte glycoprotein (MOG) antibody-associated disease (MOGAD) is an immune-mediated central nervous system inflammatory demyelinating disease identified in recent years, which has a disease spectrum that is different from that of multiple sclerosis (MS) and neuromyelitis optica spectrum disease (NMOSD). Most patients with MOGAD have a good prognosis, but some remain disabled.[1]

There were reported cases of overlapping autoimmune diseases of the central nervous system. NMDAR antibodies most commonly co-occur with aquaporin 4 (AQP4) or MOG antibodies. Patients with overlapping antibodies may have symptoms of autoimmune encephalitis and demyelination at the same time or successively.[2] Here, we present a rare case of overlapping anti-NMDAR encephalitis and MOGAD. The patient achieved a good outcome during the follow-up.

CASE REPORT

A 44-year-old female first visited the Department of Neurology in August 2018. She complained of headache for half a month and mental disorder for three days. The patient had intermittent headache with fever half a month prior. At that time, the patient denied cough, sputum, or mental abnormalities. When she went to the hospital, she was given oral antipyretic medication, and her temperature returned to normal. However, her headache persisted. Three days prior, the patient's headache severity increased and was accompanied by vomiting. The patient developed paroxysmal symptoms in speech and behavior. Sometimes, she did not understand the meaning of words. The patient's sleep time was significantly prolonged, and she slept for 16 hours a day. She was previously healthy and denied a smoking or drinking history. The patient had suffered from irregular menstrual cycles for nearly one year, ranging from 30 to 60 days. Her last menstruation was 28 days before admission. She denied being pregnant.

Physical examination showed that muscle strength in the extremities was normal. The

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meningeal irritation sign and the Babinski's sign were negative. Neuropsychological examination showed a slight decrease in cognition. The Mini-Mental State Examination (MMSE) score was 27 points, and the Montreal Cognitive Assessment (MoCA) score was 25 points. The results of routine hematological and biochemical investigations and thyroid function, autoantibody, and vasculitis antibody tests were normal. Two tumor indexes, CA125 (47.9 U/ml) and β-huma chorionic gonadotropin (β-HCG) (4556.7 U/L), were high. Transvaginal ultrasound examination indicated early intrauterine pregnancy and uterine fibroids. The patient and her family members decided to have her neurological disease treatment as priority, and to terminate the unexpected pregnancy. Cranial computed tomography (CT), magnetic resonance imaging (MRI) scan, chest and abdominal CT showed no abnormality.

She was diagnosed to have encephalitis. Lumbar puncture was performed two days after admission. The pressure was 170 mmH2O. Cerebrospinal fluid (CSF) analysis revealed 110 cells/μL and a protein concentration of 0.371 g/L. The glucose and chloride were normal, bacterial and fungal cultures were negative. During hospitalization, the patient had seizures with limb convulsions and loss of consciousness. She was given levetiracetam, but the convulsion persisted. Electroencephalogram (EEG) showed diffuse slow wave without epileptiform discharge. Cell-based assay (CBA) was positive for NMDAR antibodies, the titer was 1:10 in CSF, 1:100 in serum. The CSF was negative for anti-dipeptidyl peptidase6 (DPPX) antibody, anti-gammaaminobutyric acid-B receptor (GABABR) antibody, anti-leucine-rich glioma-inactivated 1 (LGI1) antibody, anti-contactin-associated protein-like 2 (CASPR2) antibody, anti-α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid 1 (AMPA1) receptor antibody, anti-α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid 2 (AMPA2) receptor antibody, anti-IgLON family member-5 (IgLON5) antibody, and anti-glutamic acid decarboxylase 65-kilodalton isoform (GAD65) antibody. The NMDAR antibodies in CSF were repeated, and the titer was still 1:10. MOG antibody was not detected. The patient was thus diagnosed with anti-NMDAR encephalitis. The patient received high-dose intravenous methylprednisolone (IVMP, 1,000 mg/d for 3 days, then the dose was halved every 3 days) combined with intravenous immunoglobulin (IVIg, 400 mg/kg/d for 5 days). After the treatment, the patient's symptoms gradually improved. The patient requested termination of the pregnancy at the eighth week of pregnancy. She was then discharged with a modified Rankin scale (MRS) score of 1. Maintenance oral prednisone (60 mg/d) was given, which was reduced by 5 mg every 2 weeks to 5 mg/d and stopped at 6 months. At the eighth month after discharge, the patient had not had any more seizures. The EEG returned to normal. She stopped antiepileptic drugs. At the 13th month after discharge, the patient experienced pain in her right hip and felt weakness in the right lower limb. CT of the hip indicated necrosis of the right femoral head. The patient underwent right hip replacement at the local hospital. No mental problems or other neurological deficits were observed during the two-year follow-up.

The patient complained of blurred vision in her left eye for three days in December 2020, which progressed to total blindness left eye. She denied slurred speech or limb paralysis. Fundus fluoroscopy revealed edema in the left optic disc. The optic disc of the right eye had low fluorescence and slight atrophy. The diameter of both pupils was 0.3 cm, and the direct pupillary light reflex of the left eye was absent. There was no other abnormal sign, the muscle power of the limbs was normal.

After admission, further investigations showed fasting blood glucose of 7.2 mmol/L, and glycosylated hemoglobin was 6.4%. There was no abnormality in contrast enhanced cervical spinal magnetic resonance. Orbital MRI showed that the left optic nerve was swollen, and was gadolinium-enhanced. (Figure 1). The surrounding fat gap was blurred. No demyelinating lesions were found in cranial MRI. Because the patient complained of left hip pain, CT hip was performed, which showed avascular necrosis of the left femoral head. Lumbar puncture revealed normal cranial pressure. CSF analysis revealed 4 cells/μL and a protein concentration of 0.279 g/L. CSF was negative for oligoclonal bands (OBs) and AQP-4 antibodies. The MOG antibody titer was 1:10 in CSF, and 1:10 in serum. The NMDAR antibody titer was 1:1 in CSF, and 1:10 in serum (Table 1).

The diagnosis of coexistent anti-NMDAR encephalitis and MOGAD was made. The patient was treated with plasma exchange 4 times and vitamin B injection. The patient regained light perception after the first plasma exchange. After 14 days, the vision left eye improved further. and the patient could see hand-movement. Visual evoked potential showed delayed P100 latency in the left eye and normal in the right eye. The patient had abnormal liver function and was given

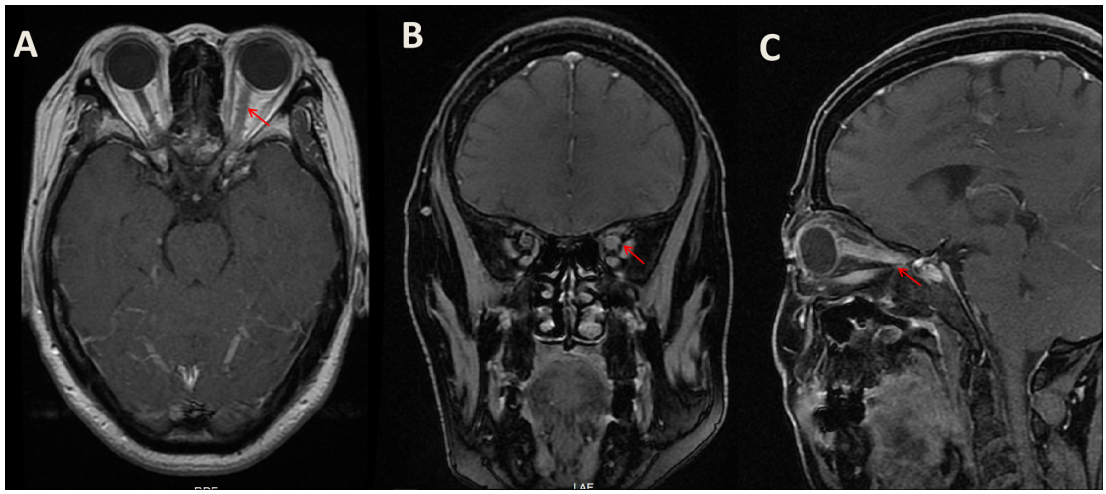

Figure 1. Contrast-enhanced T1-weighted images demonstrating enhancement and swelling of the left optic nerve (A,B,C).

oral diammonium glycyrrhizinate. She was given mycophenolate mofetil after her liver function returned to normal. At 4-month follow-up, the vision in her left eye recovered.

DISCUSSION

We report an unusual case of overlapping MOGAD and anti-NMDAR encephalitis. Our patient met the diagnostic criteria for both MOGAD and anti-NMDAR encephalitis. The patient responded well to immunomodulatory treatment.

Among the autoimmune encephalitides, anti-NMDAR encephalitis is the most common[3], accounting for approximately 80% of cases. Anti-NMDAR encephalitis is an autoimmune disease in which antibodies target the NR1 subunit of NMDAR.[4] The main manifestations are mental change, seizures, movement disorders, coma, and autonomic dysfunction. Anti-NMDAR encephalitis tends to occur in young women of childbearing age; with some patients occurring in pregnancy. Our patient had no immune abnormalities in the past, and no teratoma or lung tumors were found. Early pregnancy may have been a factor that induced the immune abnormalities. Joubert *et al*.[5] studied 11 pregnant women with anti-NMDAR encephalitis. Immunotherapy was used in most patients. Our patient had 2 previous births. According to her

Table 1: Timeline of the patient with two episodes of the disease

	First episode (August 2018)	**Second episode (December 2020)**
Symptoms	Headache, fever, speech and behavior abnormalities, seizure	Blurred vision of left eye
Enhanced MR	Normal	Left optic neuritis
CSF pressure (mmH2O)	170	180
CSF cells/μL	110	4
CSF protein (g/L)	0.371	0.279
CSF NMDAR titer	1:10	1:1
Serum NMDAR titer	1:100	1:10
CSF MOG titer	Not tested	1:10
Serum MOG titer	Not tested	1:10
EEG	Amplitude abnormalities	Normal
Therapy	IVMP, IVIg	Plasma exchange, mycophenolate mofetil

wishes, the pregnancy was terminated. The patient achieved a good prognosis, with an mRS score of 1 at discharge.

MOG is a protein that is expressed on the surface of myelin as well as on the cell bodies and processes of oligodendrocytes in the central nervous system.[6] MOGAD cause a wide spectrum of syndromes, mostly optic neuritis or myelitis in adults.[7,8] The disease course can be either monophasic or relapsing, with subsequent relapses most commonly involving the optic nerve. Acute attacks are usually treated with IVMP. Rituximab is recommended as second-line therapy if low-dose prednisone is not effective.[9,10] Our patient had elevated blood sugar and steroid-induced avascular necrosis of the femoral heads; therefore, steroid was not used in her second hospitalization. She responded to plasma exchange. After mycophenolate mofetil treatment, she had not experienced recurrence at four-month follow-up.

In the past few years, coexistence of antibodies related to autoimmune encephalitis have been reported.[11-13] Many cases of NMDAR antibodies combined with other autoimmune encephalitis antibodies, including GABABR antibody, CASPAR2 antibody, DPPX antibody and others have been reported. Some of these cases have concomitant demyelinating antibodies, such as AQP4, MOG, or glial fibrillary acidic protein (GFAP) antibodies. Some patients have two or three coexisting antibodies but do not have multiple clinical diseases. Some patients have mixed symptoms of different diseases at the same time or one after another. Pérez *et al*.[11] reported a patient with decreased binocular vision during the course of steroid reduction after the diagnosis of anti-NMDAR encephalitis. Therefore, the presence of MOG antibodies was evaluated. Some patients had relapses during the course of the disease, with a relapsing-remitting course.[14] If atypical symptoms occur during the course of anti-NMDAR encephalitis, such as decreased vision or limbs numbness or weakness, consideration should be given to the possibility of combined MOG-AD. Similarly, when patients with MOG-AD have symptoms such as seizures, prominent psychiatric manifestations, orofacial dyskinesias, or autonomic instability, it is necessary to consider whether they have anti-NMDAR encephalitis.

In conclusion, we report a rare case of overlapping anti-NMDAR encephalitis and MOGAD. Our patient is currently using immunomodulatory therapy, and the progress is good.

DISCLOSURE

Ethics: Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

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Conflict of interest: None

REFERENCES

1. Wynford-Thomas R, Jacob A, Tomassini V. Neurological update: MOG antibody disease. *J Neurol* 2019;266(5):1280-6. doi: 10.1007/s00415-018-9122-2.
2. Titulaer MJ, Höftberger R, Iizuka T, Leypoldt F, *et al*. Overlapping demyelinating syndromes and anti–N-methyl-D-aspartate receptor encephalitis. *Ann Neurol* 2014;75(3):411-28. doi: 10.3389/fimmu.2022.857443.
3. Dutra LA, Abrantes F, Toso FF, *et al*. Autoimmune encephalitis: a review of diagnosis and treatment. *Arq Neuropsiquiatr* 2018;76(1):41-9. doi: 10.1590/0004-282X20170176.
4. Dalmau J, Armangué T, Planagumà J, *et al*. An update on anti-NMDA receptor encephalitis for neurologists and psychiatrists: mechanisms and models. *Lancet Neurol* 2019;18(11):1045-57. doi: 10.1016/S1474-4422(19)30244-3.
5. Joubert B, García-Serra A, Planagumà J, *et al*. Pregnancy outcomes in anti-NMDA receptor encephalitis: Case series. *Neurol Neuroimmunol Neuroinflamm* 2020;7(3):e668. doi: 10.1212/NXI.0000000000000668.
6. Vourc'h P, Andres C. Oligodendrocyte myelin glycoprotein (OMgp): evolution, structure and function. *Brain Res Brain Res Rev* 2004; 45:115-24. doi: 10.1016/j.brainresrev.2004.01.003.
7. Borisow N, Mori M, Kuwabara S, *et al*. Diagnosis and treatment of NMO spectrum disorder and MOG-encephalomyelitis. *Front Neurol* 2018;9:888. doi: 10.3389/fneur.2018.00888.
8. Wynford-Thomas R, Jacob A, Tomassini V. Neurological update: MOG antibody disease. *J Neurol* 2019;266(5):1280-6. doi: 10.1007/s00415-018-9122-2.
9. Hegen H, Reindl M. Recent developments in MOG-IgG associated neurological disorders. *Ther Adv Neurol Disord* 2020;13:1756286420945135. doi: 10.1177/1756286420945135.
10. Salama S, Khan M, Pardo S, *et al*. MOG antibody-associated encephalomyelitis/encephalitis. *Mult Scler* 2019;25(11):1427-33. doi: 10.1177/1352458519837705.
11. Pérez CA, Agyei P, Gogia B, *et al*. Overlapping autoimmune syndrome: A case of concomitant anti-NMDAR encephalitis and myelin oligodendrocyte glycoprotein (MOG) antibody disease. *J Neuroimmunol* 2020;339:577124. doi: 10.1016/j.jneuroim.2019.577124.
12. Zhou J, Tan W, Tan SE, *et al*. An unusual case of anti-MOG CNS demyelination with

concomitant mild anti-NMDAR encephalitis. *J Neuroimmunol* 2018;320:107-10. doi:: 10.1016/j.jneuroim.2018.03.019

13. Cao L, Ren L, Huang X. Clinical analysis of a patient simultaneously positive for antibodies of myelin oligodendrocyte glycoprotein and anti-N-methyl-D-aspartate receptor: A case report. *Medicine* (Baltimore) 2021;100(1):e24234. doi: 10.1097/MD.0000000000024234.
14. Fujimori J, Takahashi T, Kaneko K, *et al*. Anti-NMDAR encephalitis may develop concurrently with anti-MOG antibody-associated bilateral medial frontal cerebral cortical encephalitis and relapse with elevated CSF IL-6 and CXCL13. *Mult Scler Relat Disord* 2021;47:102611. doi: 10.1016/j.msard.2020.102611.