

MOG-antibody Related Unilateral Cerebral Cortical Encephalitis With Refractory Cephalalgia: a Case Report

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Case report

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Abstract

Background: Myelin oligodendrocyte glycoprotein (MOG) antibody positive unilateral cerebral cortical encephalitis (UCCE) comprises a new entity with heterogeneity which usually present as epilepsy. Cases with cephalalgia as the only clinical feature were rare reported. Here, We report a case with MOG antibody positive UCCE who only presented with refractory cephalalgia and had a good response to glucocorticoid. MOG antibody-related UCCE should be identified when patients present with refractory headache and it may represent benign cortical encephalitis.

Case Presentation: The case of a 41-year-old woman with MOG antibody positive UCCE presented with refractory cephalalgia. Neurological examination is normal, and fundus examination suggested bilateral optic nerve head edema. Brain MRI discovered Flair hyperintense lesions in the sulci of right temporoparietal occipital cortex. MOG antibody was positive both in the serum and cerebrospinal fluid. When the patient was treated with intravenous methylprednisolone, her headache completely disappeared and brain MRI showed partly recovery. At the follow-up of 6 months after discharge, she had no relapse, serum MOG antibody was negative and the high signal intensity on Flair had completely disappeared.

Conclusions: MOG antibody-positive UCCE with headache as the single clinical symptom may represent benign cortical encephalitis.

1. Background

MOG associated disorder (MOGAD) refers to a spectrum of acquired demyelinating diseases in the central nervous system, with optic neuritis (ON)–transverse myelitis (TM) and acute disseminated encephalomyelitis (ADEM) as common clinical manifestations^[1-2]. In recent years, cases with MOG antibody related UCCE were reported and characterized mostly by epileptic seizures^[3]. However, we encountered an adult patient with MOG antibody related UCCE who presented with refractory cephalalgia and initially was misdiagnosed as viral encephalitis. Her symptoms improved completely after glucocorticoid therapy.

2. Case Presentation

A 41-years-old woman was admitted to our department with refractory headache lasting for more than one month. The headache was persistent and initially centered on the medial side of her forehead, following in the back of the right orbit. At the beginning, she took two tablets of somedon everyday which were effective in relieving the pain, however, the intensity of headche worsened before admission. During the course of her illness, she had no nausea, vomit, convulsions, disturbance of consciousness, and fever. There were no remakable findings in her past and family history.

On admission her vital signs were stable: the body temperature:36.8°C,pulse: 77/min and blood pressure:138/73mmHg.Both medical and neurological physical examinations were normal. Complete

blood cell counts showed leukocytosis (12,650 cells/ul, normal < 9,100),C-reactive protein slightly elevated (8mg/l,normal < 5),Serum procalcitonin and biochemical index were normal. The GAD antibody, antinuclear antibody, thyroidperoxidase antibody and thyroglobulin antibody tests were negative in the serum. The cerebrospinal fluid (CSF) pressure from lumbar puncture was 30 cm of H₂O,CSF analysis showed pleocytosis (260cells/ul, white blood cell 80cells/ul, proportion of monocytes:75%),protein concentration was mildly elevated (71mg/dl, normal < 45) and glucose was normal. CSF smear showed: numerous lymphocytes and sporadic monocytes and erythrocytes. Immunoglobulin in CSF was raised (6.25mg/dl,normal < 3.4) and oligoclonal bands (type II) was positive. CSF etiology detection had no indication of bacterial, viral or fungal infection. Autoimmune encephalitis antibodies including N-methyl-D-aspartate-receptor antibodies (NMDAR-Abs), contactin associated protein2 (CASPR2) antibodies, leucine-rich glioma inactivated1 (LGI1), α -amino-3-hydroxy-5-methyl-isoxazolepropionic acid receptor (AMPA) antibodies, and gamma-aminobutyric acid(GABA) receptor antibodies in both serum and CSF were negative. Initial brain magnetic resonance imaging (MRI) without enhancement showed fluid attenuated inversion recovery (FLAIR) and diffusion weighted images (DWI) hyperintense lesions in the sulci of the right fronto-parietal-occipital cortex, arterial spin labeling (ASL) brain perfusion image revealed focal hyper-perfused areas in the right cerebral hemisphere, including the mean cerebral blood flow (mCBF) was 36.45% higher and the arterial cerebral blood volume (aCBV) 44.95% higher than that in the left.MR angiography (MRA) showed no intracranial vascular dilatation (Fig. 1A-J).Fundus examination revealed bilateral papillary edema and her visual evoked potential results were normal. No epileptic discharge was observed in her electroencephalogram.

Despite the negative etiological testing, the patient was diagnosed with central nervous system infection based on her symptom and cerebrospinal fluid characteristics, and was treated with intravenous ganciclovir (600mg daily for 2 weeks) and ceftriaxone sodium (2-3g daily for 10 days).At the same time, mannitol dehydration was administered to reduce cranial pressure. Her headache partly relieved. The second brain MRI (the fifth day after admission) displayed decreased in intensity and range in FLAIR hyperintense lesions which were not enhanced with gadolinium contrast. Despite improvement in symptom and imaging, her headache was still existing, we realized that MOGAD had a possibility. We tested anti-MOG antibodies both in serum and CSF with a cell-based assay (CBA) and showed positive results for serum anti-MOG antibodies (1:100) (Fig. 2A-C) and CSF anti-MOG antibodies (1:3.2) (Fig. 2D-F).Therefore, the final diagnosis of the case was MOG antibody-associated unilateral cerebral cortical encephalitis.

On the ninth day after admission, intravenous methylprednisolone (80mg daily) was administered. Surprisingly, her headache absolutely disappeared immediately after the administration of methylprednisolone. On the 15th day, CSF results (the second times) showed pressure was 22 cm of H₂O,white blood cell 42cells/ul, and protein concentration was normal. CSF oligoclonal bands was negative. The MRI lesions improved (Fig. 1H-I) and the serum anti-MOG antibodies titer dropped (1:10) (Fig. 1).The patient was discharged with oral prednisolone (50mg/day, gradually tapered off) to prevent further relapses. Until now,the patient has been followed up for six months without relapse and she takes oral prednisolone (15mg/day).The FLAIR hyperintense lesions of right cerebral cortex had completely

disappeared at the first month and the sixth month follow-up after leaving the hospital (Fig. 1J), a perfusion image obtained by ASL technique showed no obvious differences in bilateral cerebral hemispheres at the sixth month follow-up (Fig. 1F). The MOG antibodies in serum were negative at both the fourth and sixth month follow-up and her fundus examination was normal.

3. Discussion And Conclusion

In the paper, we describe an adult case presented with refractory cephalalgia whose CSF suggested leukocytosis and inflammatory changes dominated by monocytes, the patient was first diagnosed as central nervous system infection and was treated with intravenous anti-infectious agents. Afterwards, existing headache and the lesions features in brain MRI reminded us to test anti-MOG antibodies both in serum and CSF. Finally, the patient was diagnosed with anti-MOG-antibody associated UCCE. When administrated with intravenous glucocorticoid, her symptom had a completely relief. At six months follow-up, her MOG antibodies in serum were quickly negative and her brain MR has the similar changes, and she has the better functional outcome.

MOGAD patients present great differences in brain MR^[4-5], and no highly specific radiological features has been identified to differentiate MOGAD from non-MOG antibody cases. Study found more than half of the patients had no evident lesions in brain routine MR^[6]. However, compared with the elderly, younger patients tended to have a higher proportion of abnormal brain MR^[7]. The abnormal features in brain MR are as follows: larger size lesions which commonly located in the cerebellum, pons, midbrain, gray matter and juxtacortical areas^[8]. AEDM is commonly found in child cases^[9], while MOGAD with unilateral cortical lesions is relatively seldom. When searching literatures, we found 10 reported cases of MOG antibody-positive UCCE, the majority was adult onset except for one case of childhood onset. In these cases^[3,10-13], the most common clinical presentations were epileptic seizures (9/10), headache (7/10), fever (3/10), optic neuritis (3/10), however, headache as the single feature of MOG antibody-associated UCCE was reported in only one case with chronic pulsatile headache, whose MRA showed vasodilatation of the left middle cerebral artery branches^[12], and the authors assumed that meningeal irritation or vasodilatation of vessels along the cortical sulcus were the possible causes of migraine. Unlike this case, patient of our case had a non-pulsatile headache, and MRA did not find vascular dilatation, we speculate that it may be caused by increased intracranial pressure and focal inflammatory irritation. CSF results identified that 8 of 10 cases showed leukocytosis and elevated protein was common in 4 of 10 cases, therefore, it is often easily misdiagnosed as infectious diseases in central nervous system, in the 10 cases mentioned above, 5 were initially misdiagnosed and were treated with antiviral drugs, until patients had recurrences, visual disturbance or typical features of brain MR, MOG antibodies with a cell-based assay were tested, and patients were eventually diagnosed as MOGAD. In therapeutic aspects, almost all cases (9/10) were administrated with immunotherapy, 7 cases were treated with high-dose IV methylprednisolone (HIMP), 1 with dexamethasone (33mg everyday), 1 with methylprednisolone (40mg/day), and all the patients had good response to immunotherapy, six cases had no recurrence after corticosteroid therapy. Only one patient who manifested recurrent convulsive seizures followed by fever

and headache was treated only with intravenous acyclovir, but she did not suffer from relapse for 2 years, hence, MOG antibody-positive UCCE may represent corticosteroid-responsive encephalitis and benign phenotype, but there is no agreement on the dose of the hormone. In addition, study indicated that MOG-Ab dynamics and their faster negativity would be an implication for good prognosis^[14], besides a research from childhood encephalitis showed that cases with brain hypoperfusion had poor neurological outcome and those with local hypertransfusion were more likely to have seizure^[15], which imply that cerebral perfusion may be associated with prognosis.

Our case of young adult female patient has two features. Firstly, as far as we know, this is the second case who presented headache as the single clinical symptom. Secondly, her symptom was completely relieved although the case was not treated with HIMP, and six months after discharge, she had no relapse, and her serum MOG antibodies and brain MR, including structural MR and ASL, turned to normal results, that may imply the better outcome and lower rate of relapse^[14, 16].

In conclusion, headache can be the single symptom of MOG antibody-related UCCE and it had a good response to glucocorticoid. The main differential diseases include central nervous system infections and autoimmune encephalitis. When brain MR shows FLAIR hyperintense lesions in unilateral cerebral cortical, we should be reminded of MOG-antibody-positive UCCE. Moreover, further analysis is needed to develop a reasonable immunotherapy and methods for assessing recurrence.

Abbreviations

MOGAD = Myelin oligodendrocyte glycoprotein associated disorder; UCCE = unilateral cerebral cortical encephalitis; ON = optic neuritis; TM = transverse myelitis; ADEM = acute disseminated encephalomyelitis; CSF = cerebrospinal fluid; NMDAR = N-methyl-D-aspartate-receptor; CASPR = contactin associated protein; LGI = leucine-rich glioma inactivated; AMPAR = α -amino-3-hydroxy-5-methyl-isoxazolepropionic acid receptor; GABA = gamma-aminobutyric acid; MRI = magnetic resonance imaging; DWI = diffusion weighted images; FLAIR = fluid attenuated inversion recovery; MRA = MR angiography; ASL = arterial spin labeling; mCBF = mean cerebral blood flow; aCBV = arterial cerebral blood volume; CBA = cell-based assay.

Declarations

Ethics approval and consent to participate

Written informed consent was obtained from the patient.

Consent for publication

All authors agree with the publication of this article.

Availability of data and materials

The datasets generated during the current study period are not publicly available (due to data non-disclosure), but are available on reasonable request from the corresponding authors.

Competing interests

None

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Authors' contributions

Ning Ren was the guarantor of integrity of the entire study and contributed to study concepts; Jing Lei contributed to case imaging studies; Haibao Zhu and Xiujie Liu contributed to literature research; Jie Qin and Zilong Zhu contributed to data acquisition; Cuihong Ma was the drafter and reviewer of the submission.

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Figures

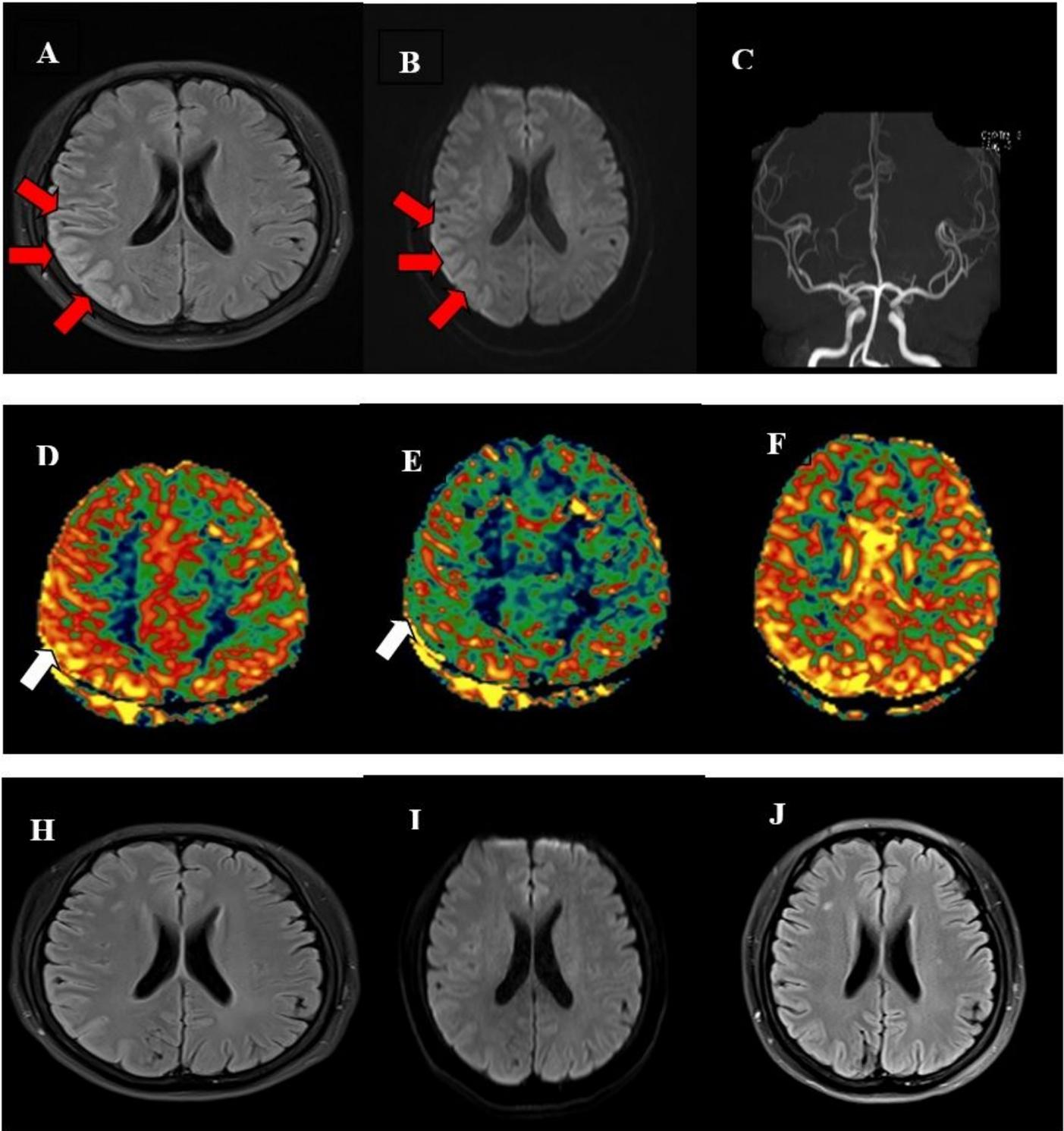


Figure 1

Axial images of brain MRI (Siemens Prisma, Germany, 1.5 T) scan at admission showed right cerebral cortical lesions on FLAIR (A, red arrows) and DWI imaging (B, red arrows), MRA indicated no intracranial vascular dilatation (C). ASL revealed hyper-perfusion in right cerebral hemisphere (D-F: mean cerebral brain flow, E: arterial cerebral blood volume, white arrows indicate abnormality); MRI FLAIR lesions

improved on discharging from hospital (H) and DWI high signals disappeared (I). Follow-up at 1 month after discharge FLAIR showed the hyperintensity of the right cortex completely disappeared (J).

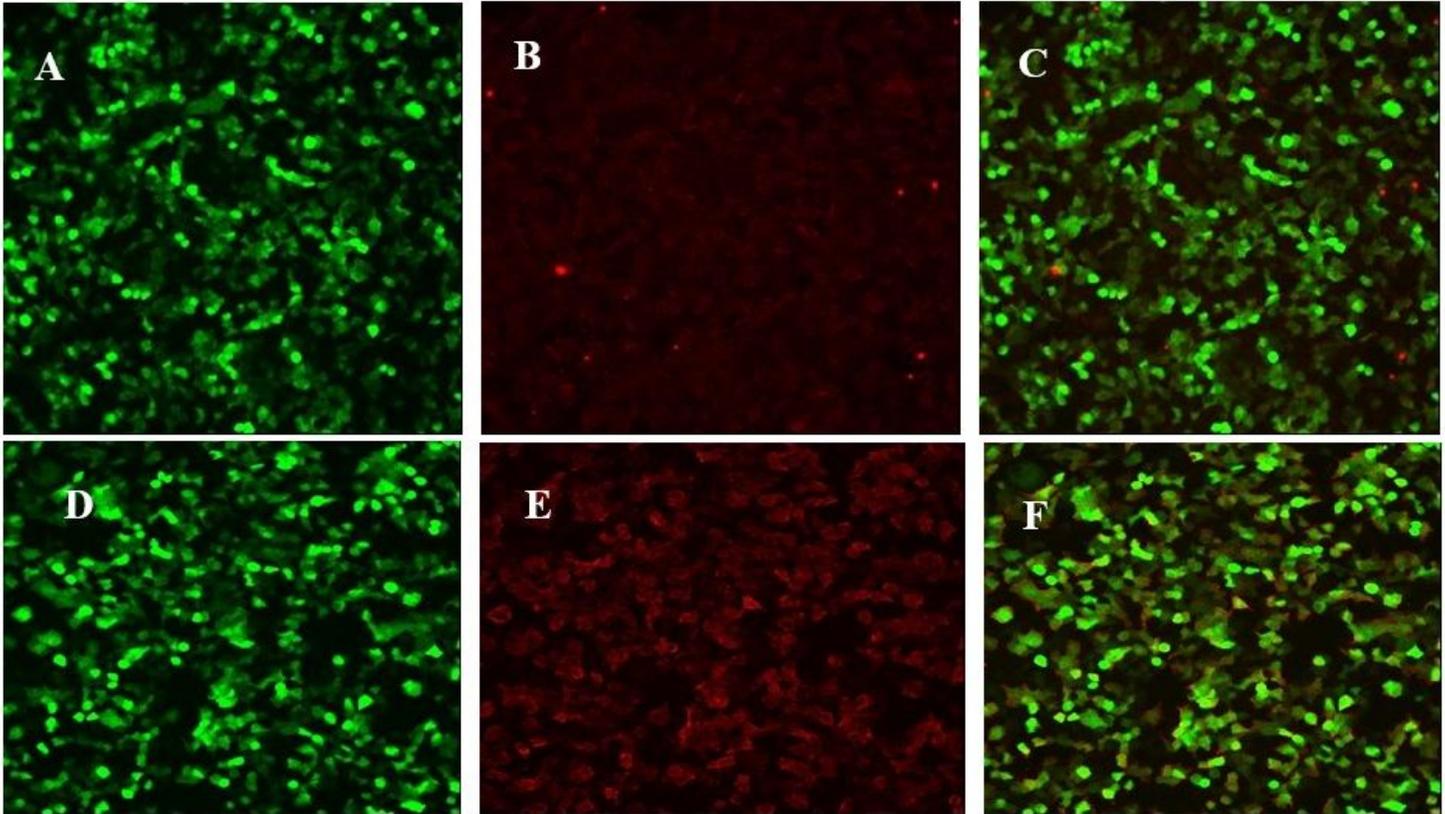


Figure 2

Anti-MOG antibodies test with a cell-based assay (CBA) showed serum positive (A: MOG-G, B: MOG-R, C: MOG-M) and CSF positive (D: MOG-G, E: MOG-R, F: MOG-M) in the first time.