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Case Report
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MOG-Ab Titter-Guided Approach for Steroid Tapering to Prevent Relapse in Patient with Anti-MOG Antibody-Associated Unilateral Cortical Encephalitis: A Case Report

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Abstract

Myelin-resistant oligodendrocyte glycoprotein (MOG)-associated encephalitis with seizures (FLAMES) with unilateral cortical fluid attenuation inversion recovery sequence (FLAIR) high-signal lesions are a recently proposed rare clinic-radiological subset of anti-MOG antibody-associated disease characterized by unilateral cortical FLAIR high signal lesions. Intravenous glucocorticoids are considered the first-line treatment for anti-MOG antibody-associated encephalitis. Although steroids are the treatment of choice, MOG-positive encephalitis has a high recurrence rate and there are no evidence-based rules to assist in steroid tapering, with steroid doses adjusted only based on clinical experience and fixed hormone durations. This report emphasizes the value of MOG antibody titers as an indicator for adjusting steroid doses to prevent recurrence in some cases, and, as a side note, a unique clinic-radiological syndrome to aid the timely diagnosis of this disease.

Keywords

Anti-Myelin Oligodendrocyte Glycoprotein Antibody (MOG-Ab); Anti-MOG Antibody-Associated Unilateral Cortical Encephalitis; Steroid Hormones; Immunotherapy

Introduction

Myelin Oligodendrocyte Glycoprotein (MOG) Antibody-Associated Disease (MOGAD) is a subtype of inflammatory demyelinating disease that is immunopathologically distinct from classical multiple sclerosis and AQP4-IgG-positive optic neuromyelitis optica spectrum diseases, with the clinical phenotype of optic neuritis, myelitis optica, or acute disseminated encephalomyelitis optica being the most common [1,2]. On the other hand, Unilateral Cortical Encephalitis (UCCE) associated with anti-MOG antibodies, on the other hand, is a rare phenotype that was first reported back in 2007 by Ogawa et al. [3] and found to have seizures, headaches, fever, and cortical symptoms as common clinical manifestations after pooling the cases of several patients. Imaging is characterized by unilateral cortical high signal on a T2-weighted liquid attenuated inversion recovery (T2 FLAIR) sequence. A new term “flame”, was introduced by Budhram et al. [4] in 2009 to describe the clinical and radiological syndrome of anti-MOG-associated encephalitis with seizures in unilateral cortical FLAIR high signal lesions. A review of previous literature shows few, if

any, reports addressing this diagnosis. In this context, we report a case of anti-MOG-associated encephalitis with a unilateral cortical FLAIR high-signalled lesion with epilepsy as an idiopathic symptom, and we recommend monitoring the MOG antibody titers to prevent the recurrence by adjusting the steroid dose, thus expanding the clinician's knowledge and understanding of the diagnosis and management of this disease.

Case Presentation

The patient, a 40-year-old female, presented to our hospital with a 2-month aggravation of severe right-sided headache with episodic convulsions for 1 day. During the course of the disease, the patient had taken oral cephalosporin and azithromycin, but the symptoms did not improve significantly. One day before admission, the patient began to have convulsions, which manifested as a right-sided deviation of the corners of the mouth with salivation, loss of consciousness, and clenching of the hands in the fist which lasted for 3-5 minutes to resolve. On admission, her vital signs were at a temperature of 36.6 degrees Celsius, her blood pressure was 113/76 mmHg and her heart rate of 76 beats/minute. Neurological and laboratory examinations showed no irregularities. Laboratory examinations including whole blood cells, biochemistry, thyroid hormones and tumor markers did not reveal any oddity. Magnetic resonance imaging showed slightly reduced medullary signal in the right frontotemporoparietal lobe, high signal in T2-FLAIR in the cortical region, no diffusion restriction on the Diffusion-Weighted Imaging (DWI) and no intensification on enhancement scan and speckled tiny long T1 and inappreciable high signal on FLAIR were seen in the right radiological crown **(Figures 1A-D).** The EEG during the intractable period suggested the issuance of sharp and slow waves in the right frontotemporal region. After admission, the patient was considered to have infectious encephalitis based on the MRI and clinical manifestations and was given anti-infective and antiviral treatment for the 6th day, but the patient did not develop. The results of a lumbar puncture performed on the 7th day suggested an intracranial pressure of 200 mmHg, a total leukocyte count of 22*10^6/L in the cerebrospinal fluid, an immunoglobulin IgG of 37.24 mg/L, normal protein, sugar, and chloride. The CBA-based assay was positive for MOG and antibodies within the cerebrospinal fluid and serum (1:1000). Autoantibody tests associated with autoimmune encephalitis were negative. The following day, a high dose of glucocorticoid shock therapy (methylprednisolone 1 g/d for 3 days) was given, after which the hormone dose was started to be reduced (0.5 g/d). The following day, the patient started to have convulsions, manifested by staring with both eyes to the right, straightening of the limbs and loss of consciousness, which lasted for about 3 minutes and resolved for a total of 3 episodes in one day. The titer of MOG antibody in the serum was 1:100 by CBA, so the hormone reduction was suspended and the dose of 1g/d was maintained for 1 week, and the titer of MOG antibody in the serum was weakly positive (1:10) by CBA, the steroid dose was then slowly reduced again, and when the dose was reduced to 120 mg/d, we retested the intrasera MOG antibody titre as negative and changed the hormone to oral prednisolone (**Figure 2** for the procedure). The patient recovered rapidly and was discharged by day 30 with only a mild headache remaining, with no associated symptoms or significant discomfort during the follow-up period.

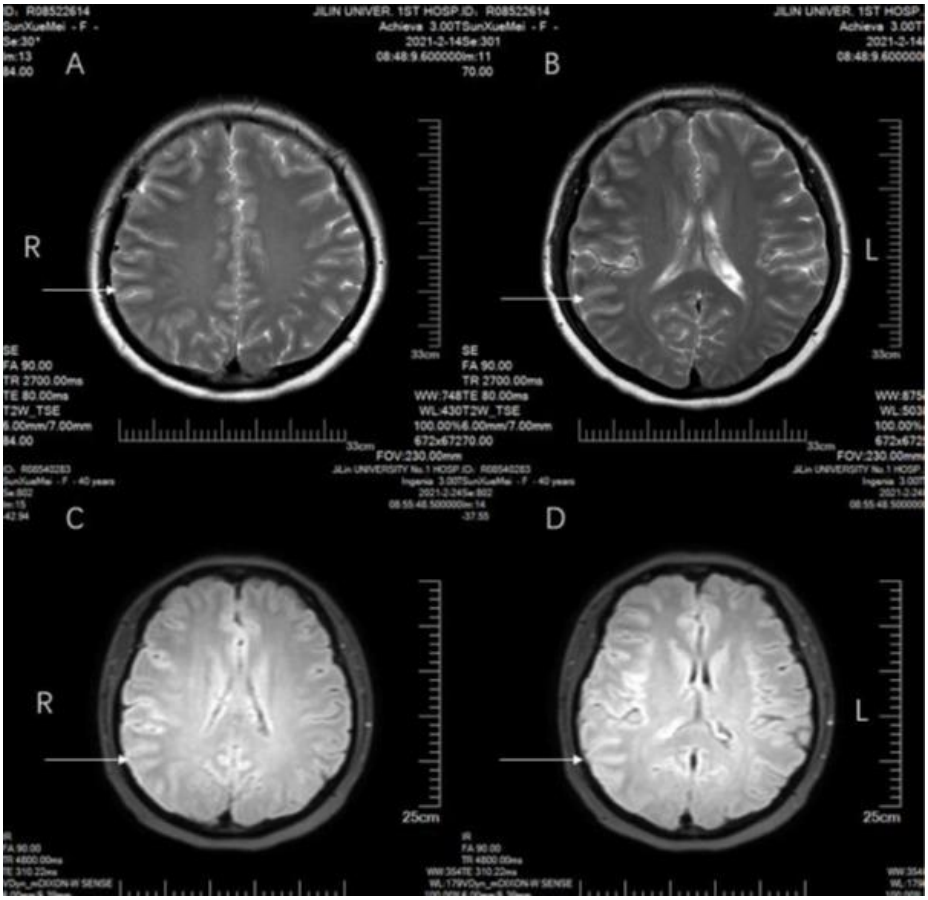

Figure 1: Abnormal signal in the frontotemporoparietal cortical area. T2 weighted (A-D) images showed high signal in the left frontotemporoparietal cortical area.

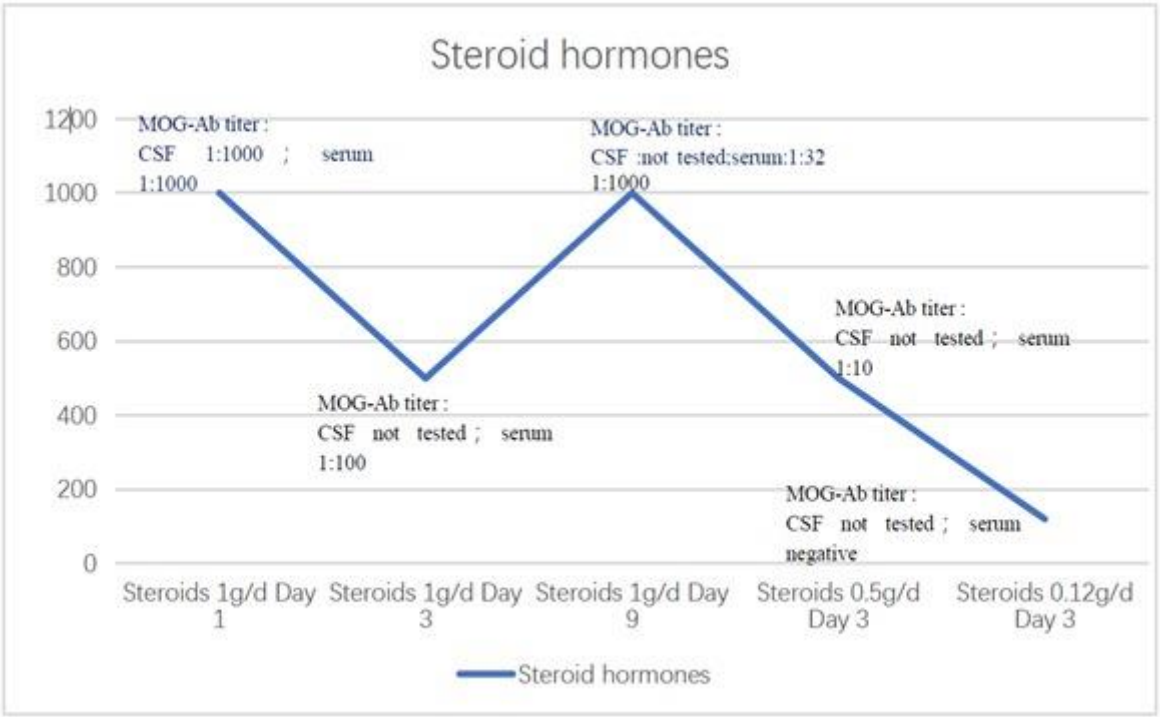

Figure 2: Clinical Course Patients experienced a total of five steroid shocks during their first episode, the first steroid 1g/d for 3 days; The second steroid 1 g/d was reduced to 0.5 g/d on the third day, when the patient's convulsions were

worse than before, so the steroid 1 g/d course was extended; the third time, when the steroid 1g/d had been applied for 9 days, the patient's serum MOG-Ab titer 1:32, the steroid was reduced to 0.5 g/d; On the fourth occasion, steroid 0.5 g/d had been applied for 3 days, serum MOG-Ab titer 1:10 was checked and the steroid was reduced to 0.12 g/d; on the fifth occasion, steroid 0.12g/d had been applied for 3 days, serum MOG-Ab titer negative was checked and the hormone was switched to oral administration.

Discussion

FLAMES is a unique clinical imaging feature manifested in anti-MOG-associated encephalitis, which is characterized by unilateral cortical T2-FLAIR high signal on head MRI without involvement of the adjacent paracortical white matter, combined with epilepsy, headache, fever, or cortical symptoms associated with the location of T2-FLAIR high signal (e.g., aphasia, psychosis, hallucinations, hallucinations, etc.), while positive cerebrospinal fluid and serological tests for MOG-IgG can be used as a diagnosis of exclusion [5,6]. In this case, the patient initially presented with severe headache followed by progressive exacerbation of epileptic symptoms, mildly elevated intracranial pressure, cerebrospinal fluid protein, positive serum, cerebrospinal fluid MOG antibodies, and combined with MRI cortical T2-FLAIR high-signal lesions. The clinical and neuroradiological features of this case were considered consistent with the diagnosis of anti-MOG-associated UCCE. MOG is a member of the immunoglobulin (Ig) superfamily, which is only expressed in the Central Nervous System (CNS), an immune area. Therefore, the mechanism of MOG-Ab production is unknown. However, as a candidate for CNS autoantigen, it is speculated that MOG antigen may be leaked into the periphery to be recognized by the immune system during increased blood-brain barrier permeability [7,8]. A study by Berer K et al. [9] found that mammalian intestinal flora aided MOG-specific CD4+ T cell and B cell production and activation and promoted MOG-Ab production. When the blood-brain barrier is damaged again, the long latent MOG-Ab enters the CNS and causes neurological damage by activating the cytotoxic effect received by the antibody complement. The inflammatory response of the lesion also recruits more lymphocytes and macrophages into the CNS to secrete a large number of cytokines to induce a further inflammatory cascade leading to demyelination and oligodendrocyte degradation. Steroid hormones inhibit the protein kinase scr by binding to the T cell membrane surface receptor (TCR), which sheds it from the TCR and in turn inhibits the phosphorylation of some important molecules downstream of the TCR signalling pathway, such as MAPK, JNK, PKB, PKC, and P38, thereby rapidly exerting an inhibitory effect on the TCR-mediated signalling pathway [10,11] In addition, steroid hormones have an inhibitory effect on B cells, mainly by reducing the number of B cells in the spleen and lymph nodes, inhibiting the value-added of early B cells, thereby reducing IgG and increasing IgE production, while high doses of hormone shock can promote immunoglobulin catabolism and reduce synthesis, ultimately reducing circulating antibody levels [12,13]. Therefore, steroid hormones are still the mainstay of treatment for this disease, but this has been challenged by recent reports of patients recovering without immunotherapy [14]. In combination with the majority of case reports, patients usually respond rapidly and effectively to immunotherapy (e.g., corticosteroids), when considering that seizures may last for days or weeks before complete remission in the absence of immunotherapy, severe headaches caused by cranial hypertension, and to ease the recurrence of the condition. Early steroid hormone therapy is recommended even if milder unilateral cortical encephalitis occurs or even if the disease is eventually cured, but a single episode may adversely affect the patient and the instability of self-limitation of this disease [14,15]. Meanwhile, the uncertainty of the disease recurrence during the application of hormones specifically the fluctuating progression of the disease that appears during steroid tapering, greatly consumes the patience of clinicians and patients during the treatment. The relationship between MOG-Ab titres and relapse has been mentioned in several retrospective studies, including Di Pauli et al. [11] in a study of MOG antibody-associated disease (MOGAD), who found that in some cases, even when the MOG-Ab potency was below

1:640, cases had a high risk of relapse and that when the threshold for MOG-Ab was set at 1:1280, the sensitivity and specificity for non-multiple sclerosing disease with a sensitivity and specificity of 46% and 86%, respectively. Similarly, our case relapsed at antibody titres greater than 1:100, in line with recent findings, and in response to the relapse-prone nature of the treatment, we broke away from the conventional thinking of using only fixed-duration adjustments of hormone doses and used a negative MOG-Ab potency as one of the indicators for reducing the steroid dose. The patient recovered and was followed up for a period of 1 year with hormone withdrawal and no relapse.

Conclusion

The prognosis for anti-MOG antibody-associated CCE with epilepsy as the first symptom is usually good with early hormonal shock therapy. However, there is significant scope for improvement in the progression of relapses during steroid dose reduction, so this report proposes the use of negative MOG-Ab potency as an indicator of change in MOG antibody titres to assist in steroid dose reduction to prevent relapses. However, large clinical trials are still needed to confirm this approach, whereby negative titres guarantee a gradual reduction in steroids associated with anti-MOG antibodies to CCE.

Author Contributions

Zong Zhi Jiang, Qian Yu, Ruqing Qiu, Zhen Wei Ma, Wei Sun and Xue Fan Yu contributed to the writing and critical revision of the manuscript. All the authors gave important contributions to the final form of the manuscript.

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Ethical Conduct of Research

The study was approved by the Central Institutional Review Board of the First Hospital of Jilin University. Written informed consent was obtained from the patients to publish the case report and accompanying images.

Data Sharing Statement

Written consent for the publication of the case was obtained from the patient. Copies of the consent forms were approved by all authors and are available for review by the editor-in-chief of the journal.

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