Journal of Clinical and Nursing Research, 2024, Volume 8, Issue 8
http://ojs.bbwpublisher.com/index.php/JCNR
Online ISSN: 2208-3693
Print ISSN: 2208-3685

Two Cases of Autoimmune Encephalitis with Multiple Anti-neuronal Antibodies

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Abstract: Autoimmune encephalitis (AE) can arise from various etiologies and present with complex clinical manifestations, especially in cases involving multiple anti-neuronal antibodies. This report presents two cases of AE with multiple anti-neuronal antibodies admitted to Ningbo Medical Center Li Huili Hospital on October 9, 2020, and March 12, 2024. Case 1 is a 15-year-old boy with positive anti-N-methyl-D-aspartate receptor (NMDAR) and anti-metabotropic glutamate receptor 5 (mGluR5) antibodies in his serum and cerebrospinal fluid (CSF). Case 2 is a 14-year-old boy with positive NMDAR and myelin oligodendrocyte glycoprotein (MOG) antibodies in his CSF. Patients with AE who have multiple anti-neuronal antibodies present significant diagnostic and therapeutic challenges, warranting close clinical attention.

Keywords: Autoimmune encephalitis; Anti-neuronal antibody; Treatment

Online publication: September 9, 2024

1. Introduction

Autoimmune encephalitis (AE) is an inflammatory disease of the central nervous system mediated by autoimmune reactions that produce various specific antibodies. It accounts for 10%–20% of encephalitis cases and can occur at any age. The clinical manifestations are complex and diverse, presenting acutely or subacutely with symptoms such as psychiatric disorders, seizures, disturbances of consciousness, and memory deficits [1]. Compared to AE with a single antibody, AE with multiple anti-neuronal antibodies is more complex and requires special clinical attention. This report discusses two cases of AE with multiple anti-neuronal antibodies, analyzing their clinical characteristics and treatment processes to enhance clinical understanding and management strategies for this disease.

2. Case report

2.1. Case 1

A 15-year-old male patient was admitted to Ningbo Medical Center Li Huili Hospital on October 9, 2020, due to a “fever for 15 days and altered consciousness for 10 days.” The patient initially developed a high fever with

a temperature of 39.8°C 15 days prior and experienced altered consciousness, agitation, and limb convulsions 10 days prior to admission. Initially diagnosed with a "mental disorder" at a local psychiatric hospital, he was treated with olanzapine, but his symptoms worsened, prompting a transfer to our hospital.

Upon admission, his temperature was 38°C. He exhibited unclear consciousness, was uncooperative during examinations, and showed limb convulsions, increased muscle tone, and a questionable positive Babinski sign. Laboratory tests revealed leukocytes (WBC) at 13.1×10^9/L, neutrophils at 79.6%, lymphocytes at 12.0%, and creatine kinase (CK) at 3,277 U/L. CSF routine and biochemical examinations were normal, and cranial MRI showed no abnormalities. On the second day of admission, lumbar puncture pressure was 250 mmH_2O. A 24-hour video electroencephalogram (EEG) showed highly abnormal brain waves with widespread δ waves, δ brushes, and α rhythm, consistent with AE (**Figure 1**). Tests for anti-NMDAR and anti-mGluR5 antibodies were both positive twice, confirming a clinical diagnosis of AE.

Due to refractory status epilepticus, he was transferred to the Intensive Care Unit (ICU), where antiepileptic and sedative medications were adjusted based on continuous EEG monitoring. Immunotherapy improved his fever, but due to poor control of limb convulsions, rituximab was administered. The patient's consciousness cleared, and convulsions stopped with gradual recovery of activity. After one month, he developed a high fever (39.5°C) with multiple red skin rashes and mucosal bleeding, indicating immunodeficiency and a fungal infection, which were treated with caspofungin. Symptoms improved, and he was discharged on November 28, 2020.

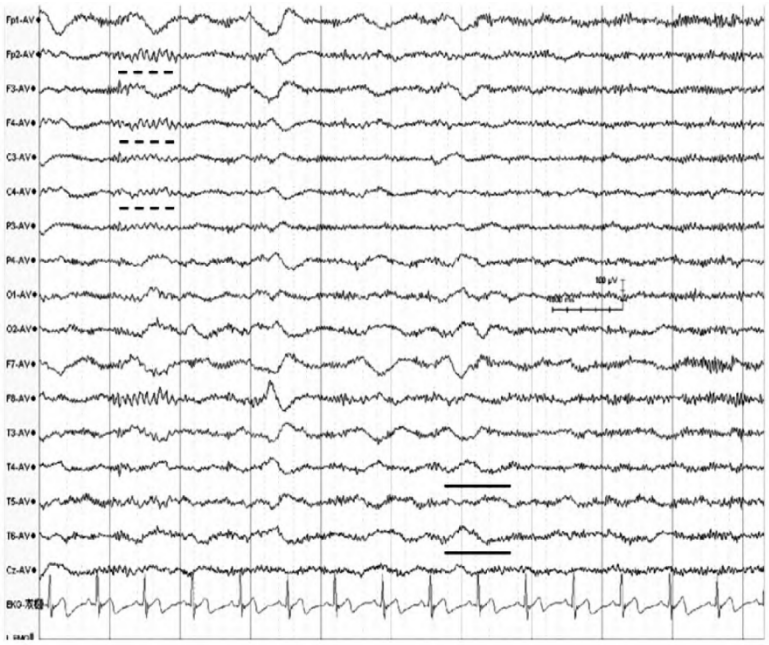

Figure 1. 24-hour video electroencephalogram examination of the patient showed abnormal brain wave height, extensive δ wave, δ brush (solid line segment), and α rhythm (dashed line segment)

2.2. Case 2

A 14-year-old male patient was admitted to Ningbo Medical Center Li Huili Hospital on March 12, 2024, due to "uncontrolled limb tremors for 3 days, worsening with mental abnormalities for 1 day." He had experienced persistent headaches 20 days prior and developed a fever with a maximum temperature of 39°C, chills, dizziness, and nausea 9 days prior. Treated with antipyretics and symptomatic therapy at a local hospital, his symptoms persisted, and left limb tremors began 3 days prior to admission.

Upon admission, his temperature was 37.8°C, and he had clear consciousness but was uncooperative

during examination, with normal limb muscle tone and a negative Babinski sign. Head CT was normal. Laboratory tests showed WBC at 10.4×10^9/L, neutrophils at 80.7%, lymphocytes at 11.7%, and CK at 934 U/L. Lumbar puncture pressure was 280 mmH_2O on the first day. CSF biochemistry showed elevated microprotein (46.3 mg/dL), with other parameters normal. There was no obvious abnormality in the electroencephalogram of the patient (**Figure 2**). Tests for anti-NMDAR and anti-MOG antibodies were positive, confirming a clinical diagnosis of AE.

Treatment included methylprednisolone pulses, followed by ICU admission for plasma exchange and continued antiviral and antiepileptic therapy. Although symptoms improved, recurrent psychiatric symptoms persisted, prompting treatment with ofatumumab, leading to further improvement. The patient was discharged on April 1, 2024.

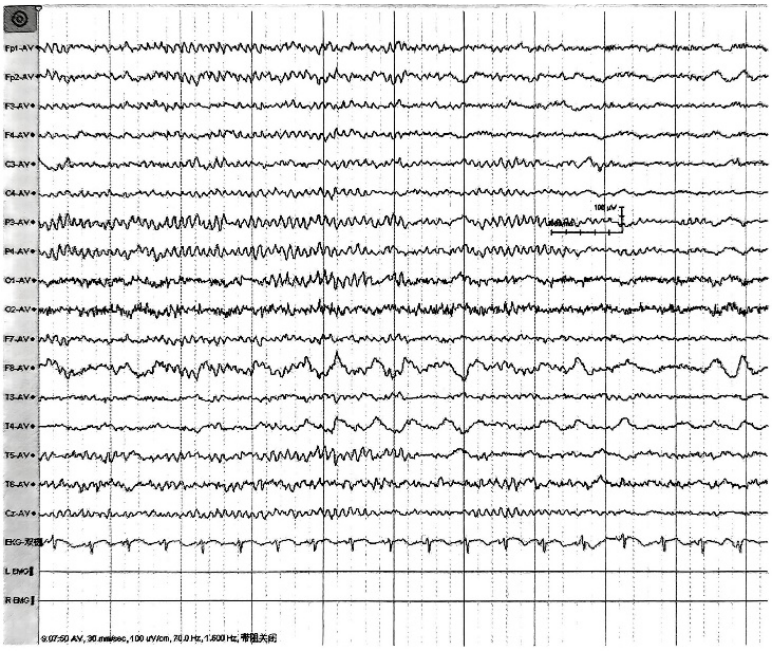

Figure 2. The EEG showed a rhythm as low as 50 μV, 9–10 Hz, with the two sides roughly symmetrical, good amplitude modulation, and a visible visual response. A small amount of low amplitude fast wave dispersion is visible. A small amount of compound slow wave dispersion as low as 20 μV, 2–5 Hz is distributed. There was no obvious abnormality in EEG and no obvious epileptic activity

3. Discussion

Autoimmune encephalitis (AE) is an autoimmune disease of the central nervous system associated with specific antibodies, presenting with a wide range of neuropsychiatric symptoms such as consciousness disturbances, seizures, and behavioral abnormalities [2-6]. The two cases reported here reflect the clinical complexity and challenges of AE with multiple anti-neuronal antibodies.

In Case 1, the patient's symptoms of altered consciousness and limb convulsions were initially misdiagnosed as a psychiatric disorder, leading to a delay in the diagnosis and treatment of AE. Studies indicate that early diagnosis and treatment are crucial for improving patient outcomes [7-9]. Clinicians should maintain a high index of suspicion for AE and promptly perform neurological examinations and antibody testing to ensure accurate and timely diagnosis and treatment [7,10-14].

In Case 2, the patient presented with limb tremors and psychiatric symptoms, which improved with methylprednisolone pulses and plasma exchange. However, psychiatric symptoms recurred, necessitating

treatment with ofatumumab. This case highlights the need for prolonged immunotherapy and monitoring in similar cases.

For AE patients with multiple anti-neuronal antibodies, individualized and comprehensive treatment strategies should be employed, including immunotherapy, antiepileptic therapy, and possibly antineoplastic treatment [15-19]. Studies have shown that immunotherapies like rituximab and ofatumumab are effective in controlling disease progression and improving outcomes [2,20,21]. These treatments not only suppress immune responses but also protect and restore neurological function [22-27]. Additionally, patients may experience disease relapse or related complications during follow-up, necessitating continuous monitoring of immune function and neurological symptoms to adjust treatment plans as needed [20,24]. Therefore, during the treatment process, it is necessary to continuously monitor the patient's immune function and neurological symptoms. Timely adjustments to the treatment plan should be made to improve therapeutic efficacy [20,28].

4. Conclusion

In conclusion, the diagnosis and treatment of AE with multiple anti-neuronal antibodies are challenging, requiring clinicians to have a high level of awareness and competence. Comprehensive treatment strategies should be employed to control disease progression, improve patient outcomes, and enhance the quality of life [29,30].

Ethics statement

This case report was prepared in accordance with the ethical guidelines of Ningbo Medical Center Li Huili Hospital. Written informed consent was obtained from the patent.

Author contributions

Writing – original draft: Guomin Xie, Wen Zhao
Writing – review & editing: Guomin Xie, Xiping Wu

Disclosure statement

The authors declare no conflict of interests.

Funding

(1) Zhejiang Health Science and Technology Project (Project No. 2021KY1034)
(2) Ningbo Leading Medical & Health Discipline Project Grant (Grant No. 2022-F05)

References

[1] Granerod J, Ambrose HE, Davies NW, et al., 2010, Causes of Encephalitis and Differences in Their Clinical Presentations in England: A Multicentre, Population-Based Prospective Study. Lancet Infect Dis, 10(12): 835–844. https://doi.org/10.1016/S1473-3099(10)70222-X

[2] Wang JD, Xie L, Fang X, et al., 2022, [Clinical Validation of the 2020 Diagnostic Approach for Pediatric Autoimmune Encephalitis in a Single Center]. Zhonghua Er Ke Za Zhi, 60(8): 786–791. https://doi.org/10.3760/cma.

j.cn112140-20220111-00039

[3] Yeshokumar AK, Coughlin A, Fastman J, et al., 2021, Seizures in Autoimmune Encephalitis – A Systematic Review and Quantitative Synthesis. Epilepsia, 62(2): 397–407. https://doi.org/10.1111/epi.16807

[4] Petit-Pedrol M, Armangue T, Peng X, et al., 2014, Encephalitis with Refractory Seizures, Status Epilepticus, and Antibodies to the GABAA Receptor: A Case Series, Characterisation of the Antigen, and Analysis of the Effects of Antibodies, Lancet Neurol, 13(3): 276–286. https://doi.org/10.1016/s1474-4422(13)70299-0

[5] Lin Z, Zhou F, Ni L, et al., 2024, Case Report: Successful Treatment of An Anti-D2R and DPPX Antibody-Associated Autoimmune Encephalitis Patient with High-Dose Methylprednisolone and Intravenous Immunoglobulin. Front Immunol, 15: 1338714. https://doi.org/10.3389/fimmu.2024.1338714

[6] Zhao J, Wang C, Xu X, et al., 2019, Coexistence of Autoimmune Encephalitis and Other Systemic Autoimmune Diseases. Front Neurol, 10: 1142. https://doi.org/10.3389/fneur.2019.01142

[7] Nissen MS, Ryding M, Meyer M, et al., 2020, Autoimmune Encephalitis: Current Knowledge on Subtypes, Disease Mechanisms and Treatment. CNS Neurol Disord Drug Targets, 19(8): 584–598. https://doi.org/10.2174/1871527319666200708133103

[8] Alexopoulos H, Dalakas MC, 2019, The Immunobiology of Autoimmune Encephalitides. J Autoimmun, 104: 102339. https://doi.org/10.1016/j.jaut.2019.102339

[9] Zhu S, Yu J, Wu Y, et al., 2022, Pathophysiology and Clinical Management of Autoimmune Encephalitis-Associated Seizures. Neuroimmunomodulation, 29(4): 282–295. https://doi.org/10.1159/000524783

[10] Al-Diwani A, Pollak TA, Langford AE, et al., 2017, Synaptic and Neuronal Autoantibody-Associated Psychiatric Syndromes: Controversies and Hypotheses. Front Psychiatry, 8: 13. https://doi.org/10.3389/fpsyt.2017.00013

[11] Titulaer MJ, McCracken L, Gabilondo I, et al., 2013, Treatment and Prognostic Factors for Long-Term Outcome in Patients with Anti-NMDA Receptor Encephalitis: An Observational Cohort Study. Lancet Neurol, 12(2): 157–165. https://doi.org/10.1016/S1474-4422(12)70310-1

[12] Yan W, Mengke W, Zhiqiang S, et al., 2024, Clinical Features, Cerebrospinal Fluid Changes, and Prognosis in Chinese Patients with Autoimmune Encephalitis. Acta Neurol Belg, preprint. https://doi.org/10.1007/s13760-024-02537-6

[13] Hayden Z, Bóné B, Orsi G, et al., 2021, Clinical Characteristics and Outcome of Neuronal Surface Antibody-Mediated Autoimmune Encephalitis Patients in a National Cohort. Front Neurol, 12: 611597. https://doi.org/10.3389/fneur.2021.611597

[14] Masciocchi S, Businaro P, Scaranzin S, et al., 2024, General Features, Pathogenesis, and Laboratory Diagnostics of Autoimmune Encephalitis. Crit Rev Clin Lab Sci, 61(1): 45–69. https://doi.org/10.1080/10408363.2023.2247482

[15] Baumgartner A, Rauer S, Hottenrott T, et al., 2019, Admission Diagnoses of Patients Later Diagnosed with Autoimmune Encephalitis. J Neurol, 266(1): 124–132. https://doi.org/10.1007/s00415-018-9105-3

[16] Endres D, Maier V, Leypoldt F, et al., 2022, Autoantibody-Associated Psychiatric Syndromes: A Systematic Literature Review Resulting in 145 Cases. Psychol Med, 52(6): 1135–1146. https://doi.org/10.1017/S0033291720002895

[17] Chekanova EO, Shabalina AA, Zakharova MN, 2023, Klinicheskie Kharakteristiki i Kratkosrochnye Iskhody Autoimmunnogo Entsefalita u Vzroslykh [Clinical Characteristics and Short-Term Outcomes of Autoimmune Encephalitis in Adults]. Zh Nevrol Psikhiatr Im S S Korsakova, 123(7. Vyp. 2): 103–115. https://doi.org/10.17116/jnevro2023123072103

[18] Liao D, Zhong L, Yang L, et al., 2023, Clinical and Radiological Features, Treatment Responses and Prognosis in Pediatric Patients with Co-Existing Anti-N-Methyl-D-Aspartate Receptor and Myelin Oligodendrocyte Glycoprotein Antibody-Associated Encephalitis: A Single Center Study. Mult Scler Relat Disord, 81: 105133. https://doi.org/10.1016/j.msard.2023.105133

[19] Wu Q, Xie Q, Liu L, et al., 2023, Factors Influencing Prognosis and Relapse in Patients with Anti-N-Methyl-D-Aspartate Receptor Encephalitis. Mult Scler Relat Disord, 74: 104697. https://doi.org/10.1016/j.msard.2023.104697

[20] Zhou Y, Chen H, Zhu M, et al., 2024, Clinical Characteristics of Autoimmune Encephalitis with Co-Existence of Multiple Anti-Neuronal Antibodies. BMC Neurol, 24(1): 1. https://doi.org/10.1186/s12883-023-03514-x

[21] Cafalli C, Amorim E, Silva F, et al., 2020, Autoimmune Encephalitis (AIE). Rev Assoc Med Bras (1992), 66(9): 1172–1178. https://doi.org/10.1590/1806-9282.66.7.1172

[22] Thaler FS, Zimmermann L, Kammermeier S, et al., 2021, Rituximab Treatment and Long-term Outcome of Patients with Autoimmune Encephalitis: Real-world Evidence from the GENERATE Registry. Neurol Neuroimmunol Neuroinflamm, 8(6): e1088. https://doi.org/10.1212/NXI.000000000000108

[23] Zhou Q, Yin D, Ma J, et al., 2023, The Therapeutic Effect of Ofatumumab in Autoimmune Encephalitis: A Case Series. J Neuroimmunol, 377: 578062. https://doi.org/10.1016/j.jneuroim.2023.578062

[24] Kang Q, Liao H, Yang L, et al., 2022, Clinical Characteristics and Short-Term Prognosis of Children with Antibody-Mediated Autoimmune Encephalitis: A Single-Center Cohort Study. Front Pediatr, 10: 880693. https://doi.org/10.3389/fped.2022.880693

[25] Wang B, Wang C, Feng J, et al., 2022, Clinical Features, Treatment, and Prognostic Factors in Neuronal Surface Antibody-Mediated Severe Autoimmune Encephalitis. Front Immunol, 13: 890656. https://doi.org/10.3389/fimmu.2022.890656

[26] Nepal G, Shing YK, Yadav JK, et al., 2020, Efficacy and Safety of Rituximab in Autoimmune Encephalitis: A Meta-Analysis. Acta Neurol Scand, 142(5): 449–459. https://doi.org/10.1111/ane.13291

[27] Shang H, Shen X, Yu X, et al., 2024, B-cell Targeted Therapies in Autoimmune Encephalitis: Mechanisms, Clinical Applications, and Therapeutic Potential. Front Immunol, 15: 1368275. https://doi.org/10.3389/fimmu.2024.1368275

[28] Qiao S, Zhang SC, Wang ZH, et al., 2022, Coexistence of Multiple Anti-Neuronal Antibodies in Autoimmune Encephalitis in China: A Multi-Center Study. Front Immunol, 13: 858766. https://doi.org/10.3389/fimmu.2022.858766

[29] Dalmau J, Geis C, Graus F, 2017, Autoantibodies to Synaptic Receptors and Neuronal Cell Surface Proteins in Autoimmune Diseases of the Central Nervous System. Physiol Rev, 97(2): 839–887. https://doi.org/10.1152/physrev.00010.2016

[30] Ryding M, Mikkelsen AW, Nissen MS, et al., 2023, Pathophysiological Effects of Autoantibodies in Autoimmune Encephalitides. Cells, 13(1): 15. https://doi.org/10.3390/cells13010015