

Autoimmune Encephalitis: Advances in Diagnosis and Immunotherapy

Yingbo Liu

*Beijing 101 High School, Beijing, China
alex.hello0alex@gmail.com*

Abstract. Autoimmune encephalitis (AE) is an inflammatory disorder of the central nervous system mediated by autoantibodies, with a significantly rising incidence in recent years. However, its diagnosis and treatment still face numerous challenges. Currently, AE diagnosis primarily relies on antibody testing and clinical evaluation, while immunotherapy follows a stepwise strategy. Nevertheless, some patients exhibit treatment resistance and risk of relapse. Although significant research progress has been made, the diagnosis of antibody-negative cases and personalized treatment strategies require further exploration. This article systematically analyzes AE diagnostic criteria, advances in immunotherapy, and pathogenesis research. Key findings demonstrate that novel biomarkers such as CSF sCD27 may enhance early diagnostic accuracy, stepwise therapeutic approaches can optimize clinical management, and mechanistic studies reveal the pathogenicity of anti-NMDAR antibodies along with the pivotal role of PV neuron injury. These findings provide critical insights for precision medicine in AE. Outstanding challenges persist in long-term outcome monitoring and refractory case management. Future directions should prioritize multi-omics diagnostic models, targeted therapy development, and multidisciplinary collaborative care systems to improve patient outcomes.

Keywords: Autoimmune encephalitis, immunotherapy, diagnosis.

1. Introduction

Autoimmune encephalitis (AE) represents a neuroinflammatory condition affecting the CNS that is antibody-driven, receiving growing research interest in neuroimmunology during the past decade. Although classified as a rare disease, epidemiological data demonstrate a marked upward trend in its incidence, establishing it as a key condition requiring multidisciplinary collaboration among neurology, psychiatry, and critical care medicine. AE occurs when autoantibodies produced within the body erroneously attack and damage neuronal surface or synaptic proteins, thereby triggering a range of neurological dysfunctions. The most clinically relevant autoantibodies target the N-methyl-D-aspartate receptor (NMDAR) and leucine-rich glioma-inactivated 1 (LGII) proteins, interfering with neuronal communication via different pathways and resulting in encephalitis symptoms [1].

Autoimmune encephalitis (AE) is a neuroinflammatory condition characterized by antibody-mediated attacks on the central nervous system. In recent years, AE has emerged as a focal point in neuroimmunology research due to its complex pathogenesis and clinical implications. While

officially categorized as rare, studies indicate a rising incidence, necessitating coordinated care across neurology, psychiatry, and intensive care disciplines. The disease arises when self-produced antibodies mistakenly target neuronal antigens—such as cell-surface or synaptic proteins—inducing functional impairments. Key pathogenic antibodies include those against NMDA receptors and LGI1, each interfering with synaptic transmission via unique pathways to produce encephalopathic features. [1]

The clinical significance of AE lies in its high incidence, diverse clinical presentations, and substantial impact on patients' quality of life. Despite being categorized as a rare disease, its diagnostic rate has risen sharply in recent years, now accounting for approximately 10%-20% of all encephalitis cases [1], with occurrences across all age groups and both sexes. The clinical manifestations of AE are highly variable, encompassing psychiatric abnormalities, cognitive impairment, and other symptoms that not only compromise daily functioning but may also cause long-term damage to mental health and social capabilities. Furthermore, AE patients often require prolonged treatment and rehabilitation, with some developing permanent neurological deficits, imposing significant economic burdens and profound impacts on familial and social relationships.

Although substantial progress has been made in AE research, clinical practice still faces multiple challenges, with diagnostic delays and treatment resistance representing two core issues [2,3]. As the primary concern, diagnostic delays stem from the disease's nonspecific and heterogeneous presentations, limitations in antibody testing, and insufficient physician awareness. Early AE symptoms are frequently atypical and easily confused with other neurological disorders, hindering accurate identification. While autoantibody detection serves as a critical diagnostic tool, results typically require days to weeks to obtain, and the sensitivity and specificity of testing are influenced by methodological and sample-related factors [2,3]. Additionally, some clinicians' limited familiarity with AE may delay its consideration in differential diagnoses.

Treatment resistance poses another major challenge. Although most patients respond well to first-line immunotherapy (e.g., corticosteroids, intravenous immunoglobulin), a subset exhibit refractory symptoms due to factors including disease severity, individual variability, and comorbidities: severe cases may involve widespread, irreversible neuronal damage; interpatient differences in treatment sensitivity can lead to drug insensitivity or resistance; and concurrent neurological or systemic diseases may further complicate therapeutic efficacy.

Diagnostic delays and treatment resistance remain pivotal challenges in contemporary AE management. Future research must focus on optimizing early diagnostic strategies and developing more effective therapies to improve patient outcomes and quality of life.

2. Disease classification and clinical features

AE can be further subdivided into various subtypes based on different antibody types, each with its unique clinical characteristics (Table 1).

2.1. Antibody types and symptoms

2.1.1. Anti-NMDAR encephalitis

Anti-NMDAR encephalitis is the most common type of autoimmune encephalitis, accounting for approximately 54%-80% of all AE cases [4]. Its clinical features include acute or subacute onset, with patients often exhibiting psychiatric abnormalities such as hallucinations, delusions, and agitation, accompanied by cognitive impairment manifested as memory loss and attention deficits.

Seizures are also common symptoms, presenting in various forms including generalized tonic-clonic seizures and focal seizures. Additionally, patients may experience speech disorders, movement disorders (e.g., orofacial dyskinesia, limb tremors), and decreased consciousness, potentially progressing to coma in severe cases. Autonomic dysfunctions such as sinus tachycardia and hypersalivation are frequently observed [5].

2.1.2. Anti-LGI1 encephalitis

Anti-LGI1 encephalitis primarily affects middle-aged and elderly individuals, with a slight male predominance. Its clinical characteristics include acute or subacute onset, with main symptoms comprising seizures (particularly temporal lobe epilepsy) often preceded by aura symptoms such as "goosebumps" sensations. Recent memory decline is another common manifestation, with patients showing difficulty recalling recent events. Psychiatric abnormalities like depression and anxiety are also frequently observed. Faciobrachial dystonic seizures (FBDS), characterized by frequent, brief dystonic movements of unilateral arms and face (sometimes extending to lower limbs), represent pathognomonic seizure symptoms with significant diagnostic value [6].

2.1.3. Anti-CASPR2 antibody-associated encephalitis

Anti-CASPR2 antibody-associated encephalitis is relatively rare among AE subtypes, with a median onset age around 60 years. Its clinical manifestations are diverse, primarily including various forms of epileptic seizures, psychiatric abnormalities (e.g., mood swings, personality changes), and recent memory impairment. Some patients may also present with peripheral nerve hyperexcitability symptoms such as myokymia and muscle stiffness [6].

2.1.4. Anti-GABA_B antibody-associated encephalitis

Anti-GABA_B antibody-associated encephalitis shows a predilection for middle-aged and older adults, demonstrating a male preponderance. It typically presents with acute onset, reaching peak severity within days to weeks. Primary symptoms include drug-resistant generalized tonic-clonic seizures that frequently progress to status epilepticus, along with psychiatric manifestations like irritability and delirium. Recent memory decline is another common feature. Brain MRI often reveals abnormal signals in medial temporal lobes and basal ganglia, while EEG typically shows temporal epileptiform discharges or slow-wave activity [4,6].

2.2. Pediatric AIE

Anti-NMDAR encephalitis represents the most common form of pediatric AE. While clinical manifestations resemble those in adults, some children may present with psychiatric symptoms or seizures as initial manifestations, which can be more insidious or atypical. Diagnosis requires comprehensive evaluation including clinical presentation, CSF antibody testing, and neuroimaging. Positive anti-NMDAR antibodies in CSF serve as crucial diagnostic evidence. Brain MRI may demonstrate nonspecific changes that nevertheless support diagnosis when combined with clinical and serological findings [7].

Differential diagnosis should distinguish acute disseminated encephalomyelitis (ADEM) from pediatric AE. ADEM, a common pediatric demyelinating disorder potentially related to autoimmune mechanisms (though not classified as direct AE), presents with acute multifocal neurological dysfunction including consciousness impairment, seizures, and movement disorders. Brain MRI

typically reveals extensive, multifocal white matter lesions, while CSF analysis may show mild pleocytosis and elevated protein. Although clinical presentations overlap somewhat, ADEM differs from typical AE in pathophysiological mechanisms and imaging characteristics - for instance, ADEM usually demonstrates more diffuse MRI abnormalities and potentially more pronounced CSF alterations [7].

Table 1. Major classifications and clinical characteristics of AE

Antibody Type / Encephalitis Subtype	Demographic Features	Onset Presentation	Psychiatric Manifestations	Memory Impairment	Seizure Characteristics
Anti-NMDAR	Most common (14-80% of AE cases); ♀≈♂ (adults);	Acute or subacute onset	Hallucinations, delusions, agitation	Cognitive dysfunction (memory deficits)	Generalized tonic-clonic seizures, focal seizures with impaired awareness
Anti-LGI1	Middle-aged/older adults (>50 yrs); ♂>♀	Acute or subacute onset	Depression, anxiety	Short-term memory impairment	Temporal lobe seizures
Anti-CASPR2	Older adults (~60 yrs); Relatively rare	Acute or subacute onset	Mood swings, personality changes	Short-term memory impairment	Multiple seizure types
Anti-GABA _B R	Older adults (~60 yrs); ♂>♀;	Acute onset (symptoms peak within days to weeks)	Irritability, delirium	Short-term memory impairment	Generalized tonic-clonic seizures; highly refractory to AEDs; frequent progression to status epilepticus
Pediatric AE (predominantly anti-NMDAR)	children (4-18 yrs)	Acute or subacute onset (similar to adults)	Similar to adults, but psychiatric symptoms may be initial presentation	Similar to adults but may be subtle/atypical;	Similar to adults, but may present with seizure as first manifestation

3. Diagnostic advances and challenges

3.1. Current diagnostic criteria

3.1.1. Three-tier framework of Graus criteria (2016)

In 2016, Graus et al. proposed a systematic three-tier diagnostic framework for AE, including "possible AE", "probable AE" and "definite AE". This framework emphasizes the importance of clinical evaluation, cerebrospinal fluid (CSF) analysis, neuroimaging (e.g., MRI) and antibody testing. Specifically, definite AE requires meeting specific clinical manifestations (such as subacute onset of memory impairment, psychiatric symptoms or seizures) and at least one abnormal ancillary test (e.g., CSF pleocytosis, specific antibody positivity or MRI showing limbic system involvement). This framework has significantly improved the early recognition rate and treatment response rate of AE [1].

3.1.2. Adjustments in Chinese consensus

The Chinese expert consensus (2022 edition) made adjustments based on the Graus criteria to better adapt to domestic clinical practice. The consensus emphasizes the importance of early diagnosis and comprehensive treatment, and proposes an integrated diagnostic workflow based on clinical manifestations, antibody testing and ancillary examinations. The consensus establishes diagnostic criteria for various autoimmune encephalitis subtypes, encompassing both NMDAR encephalitis and LGI1 antibody-associated cases, offering clinicians enhanced diagnostic specificity [4].

3.2. Novel biomarkers

3.2.1. Sensitivity of CSF sCD27/sBCMA

Recent studies have shown that levels of soluble CD27 (sCD27) and soluble B-cell maturation antigen (sBCMA) in CSF are significantly elevated in AE patients and demonstrate high diagnostic sensitivity. In untreated NMDA AE and LGI1 AE patients, CSF sCD27 levels were significantly higher than in symptomatic controls, with ROC curve analysis showing its diagnostic performance was superior to sBCMA (AUC values of 0.97 and 0.69, respectively). This finding provides new biomarkers for early diagnosis of AE [3].

3.2.2. Oxidative stress proteins

Oxidative stress plays an important role in the pathogenesis of AE. Studies have shown that serum levels of antioxidant proteins such as albumin (ALB), glutathione peroxidase 3 (GPX3) and superoxide dismutase 3 (SOD3) are significantly decreased in AE patients, while their expression in the central nervous system is correspondingly reduced. Through proteomic analysis, researchers found these oxidative stress-related proteins may serve as potential diagnostic biomarkers for AE and could become novel therapeutic targets in the future (Table 2) [8].

Table 2. Current major diagnostic approaches

Comparison Dimension	Conventional CSF Tests	Novel CSF Biomarkers	Conventional Serum Tests	Novel Serum Biomarkers
Targets	Routine CSF analysis (cell count, protein levels) + Known antibody testing (e.g., anti-NMDAR, anti-LGI1)	CSF sCD27/sBCMA levels	Serum antibody testing + routine biochemical tests	GPX3 SOD3
Specificity	High specificity for antibody detection (but potential false positives from contamination/technical factors)	Relatively good specificity (particularly when combining multiple biomarkers)	High specificity but limited to known antigen types	Potential high specificity as molecular markers
Applicability	Essential for antibody-confirmed AE cases; required when clinical presentation suggests AE	Atypical early-stage presentations; Antibody-negative suspected AE cases	Typical antibody-confirmed cases; Selected abnormal biochemical findings	Early-stage or antibody-negative suspected cases; Slowly progressive AE variants
Limitations	Limited diagnostic value in seronegative cases; Invasive sampling procedure (lumbar puncture)	High sample processing requirements; Currently only available in specialized centers	Limited diagnostic value in antibody-negative cases; Most biochemical changes are non-specific	Requires specialized assay platforms; Currently limited to research centers
Clinical Value	Remains diagnostic cornerstone, but requires integration with other biomarkers and clinical evaluation	Supplemental early diagnostic tool	Remains an essential component but requires comprehensive evaluation with other indicators	Early detection in prodromal phases; Precision medicine approaches

3.3. Causes of misdiagnosis

3.3.1. Serum false positives

False-positive results in serum antibody testing are one of the common causes of AE misdiagnosis. Since the presence of antibodies in serum can be influenced by various factors (such as infections or other autoimmune diseases), a single serum antibody test result cannot serve as definitive evidence for AE diagnosis. It must be combined with clinical manifestations, CSF analysis, and neuroimaging for comprehensive evaluation [2].

3.3.2. Antibody-negative cases

Some AE patients may test negative for antibodies, which poses diagnostic challenges [2]. Antibody-negative AE may involve unknown antigens or antibody titers below the detection threshold. For such patients, diagnosis relies on detailed clinical assessment, exclusion of other etiologies, and possibly repeated antibody testing. Additionally, the discovery and application of novel biomarkers (such as CSF sCD27) may help improve diagnostic accuracy in antibody-negative AE [9].

3.3.3. Diverse clinical manifestations

AE exhibits highly variable clinical presentations, with significant symptom differences among patients, further increasing diagnostic difficulty [2]. For example, anti-NMDAR encephalitis patients may primarily present with psychiatric symptoms, seizures, or consciousness impairment, while anti-LGI1 antibody-associated encephalitis patients may predominantly exhibit faciobrachial dystonic seizures (FBDS) and memory deficits [1]. Therefore, clinicians require extensive expertise and keen clinical acumen to accurately identify AE amid such complex and diverse manifestations. [2]

In summary, AE diagnosis faces challenges including limited application of novel biomarkers and relatively high misdiagnosis rates. Future efforts should focus on optimizing diagnostic criteria, exploring novel biomarkers, and strengthening multidisciplinary collaboration to improve diagnostic accuracy and treatment outcomes.

4. Immunotherapy strategies

The immunotherapy strategies for AE are key to improving patient prognosis and reducing relapse rates. With the deepening understanding of AE pathogenesis, immunotherapy approaches have become increasingly diverse and precise.

4.1. First-line immunotherapy

First-line immunotherapy for AE mainly includes glucocorticoids, intravenous immunoglobulin (IVIG), and plasma exchange, which modulate the immune system and alleviate inflammatory responses through different mechanisms.

Glucocorticoids, as the preferred treatment option, primarily mitigate immune responses through nonspecific cytokine suppression. Clinically, intravenous methylprednisolone is commonly used, with dosage adjusted according to disease severity, and the standard treatment course is 6 months [4].

IVIG exerts immunomodulatory and anti-inflammatory effects by providing polyclonal IgG, and is often combined with glucocorticoids in severe cases to form a synergistic treatment regimen of glucocorticoid pulse therapy and IVIG [4].

Plasma exchange serves as a supplementary treatment that produces therapeutic effects in specific AE patients by removing pathogenic antibodies from the blood [4]. These three fundamental therapies constitute a complete system for AE immunotherapy, and personalized treatment plans should be developed based on individual patient conditions in clinical practice.

4.2. Second-line immunotherapy

For severe AE patients with poor response to first-line immunotherapy, timely escalation to second-line immunotherapy is necessary, which mainly includes two biological agents: rituximab and tocilizumab.

Rituximab, as an anti-CD20 monoclonal antibody, significantly reduces pathogenic antibody production by targeting B cell depletion, and has demonstrated marked efficacy in refractory AE, especially in anti-NMDAR encephalitis patients [4,10].

Tocilizumab, as an anti-IL-6 receptor monoclonal antibody, exerts therapeutic effects by blocking the IL-6-mediated inflammatory signaling pathway. Clinically, it is recommended to consider switching to this treatment regimen for severe patients who show no significant improvement after 1-2 months of second-line immunotherapy [4,10].

These two targeted biological agents provide important treatment options for AE patients unresponsive to first-line therapy, and their application requires strict evaluation of individual patient conditions and monitoring of treatment responses.

4.3. Immunotherapy for refractory cases

The treatment of refractory AE requires a stepwise intensification strategy, and third-line treatment should be initiated for patients unresponsive to first- and second-line immunotherapy.

Currently, the main clinical third-line drugs are bortezomib and daratumumab: bortezomib targets plasma cell clearance through proteasome inhibition, while daratumumab specifically eliminates plasma cells as an anti-CD38 monoclonal antibody, both of which can significantly reduce pathogenic antibody production [11].

In terms of treatment strategy, a multi-target combination approach is recommended, such as the synergistic use of tocilizumab and rituximab, or long-term maintenance therapy with additional immunosuppressants like mycophenolate mofetil or azathioprine [4].

Notably, timely resection of associated tumors is a key measure to improve prognosis for AE patients with concurrent tumors. Additionally, comprehensive management should include targeted rehabilitation therapy and psychological intervention to promote neurological recovery and social reintegration [4,5]. This multidimensional, personalized comprehensive treatment model provides an important clinical pathway for improving prognosis in refractory AE patients.

5. Breakthroughs in mechanism research

The pathogenesis of AE is complex, involving multiple aspects such as antibody-mediated neuronal damage, immune cell infiltration, and neuroinflammation. In recent years, with the deepening of AE research, several breakthrough advances have been made in mechanistic studies.

5.1. Antibody pathogenic mechanisms

GluN1-NTD is the primary binding site for anti-NMDAR antibodies. Further experiments have demonstrated that the binding of anti-NMDAR antibodies to NMDARs not only blocks the receptor's normal function but, more importantly, induces receptor internalization. Studies using immunostaining and electrophysiological recordings have found that prolonged incubation with anti-NMDAR antibodies (such as mAbsF6 and mAb2G7) significantly reduces the density of NMDARs on the neuronal surface without affecting the levels of postsynaptic density protein 95 (PSD95). Additionally, whole-cell patch-clamp recordings revealed that neurons incubated with anti-NMDAR antibodies exhibit markedly reduced NMDAR-mediated currents, indicating that antibody binding not only causes NMDAR internalization but also further impairs receptor function [12].

Anti-NMDAR antibody-induced NMDAR internalization represents a key pathogenic mechanism underlying AE development. NMDARs are important excitatory glutamate receptors in the central nervous system, involved in various physiological processes such as learning, memory, and synaptic plasticity. By inducing NMDAR internalization, anti-NMDAR antibodies reduce the number of NMDARs on the postsynaptic membrane, thereby disrupting normal neurotransmission and synaptic function, leading to a range of neuropsychiatric symptoms in AE patients [12].

5.2. Role of PV neurons

PV neurons are a crucial class of interneurons in the medial prefrontal cortex (mPFC) that regulate gamma oscillations and play key roles in cognitive functions such as working memory, attention, and decision-making. In neuropsychiatric disorders like schizophrenia and autism, PV neuron dysfunction is often closely associated with cognitive impairments [13].

Using anti-NMDAR IgG purified from the serum of AE patients, the research team delivered it precisely to the mPFC of mice via stereotaxic injection. After seven consecutive days of injection, significant morphological damage to PV neurons was observed, characterized by reduced dendritic complexity, decreased synaptic density, and impaired NMDAR-mediated gamma oscillations [13].

Behavioral tests showed that mice injected with anti-NMDAR IgG exhibited significant working memory and recognition memory deficits in the Y-maze and novel object recognition tests. These cognitive impairments coincided with the timeline of PV neuron damage, suggesting that PV neuron injury may be a major contributor to cognitive deficits in anti-NMDAR encephalitis patients [13].

The study also found that optogenetic and chemogenetic activation of PV neurons in the mPFC significantly improved cognitive deficits in mice injected with anti-NMDAR IgG. This discovery provides important clues for developing novel therapeutic strategies targeting cognitive impairments in anti-NMDAR encephalitis, such as restoring cognitive function by modulating PV neuron activity [13].

5.3. Research on immune pathways

Beyond antibody-mediated mechanisms, the role of immune pathways in AE pathogenesis has garnered significant attention. Cytokines such as IL-6 play important roles in AE development. Studies have found that tocilizumab (an anti-IL-6 receptor antibody) demonstrates good efficacy in treating refractory AE, further confirming the importance of the IL-6 signaling pathway in AE pathogenesis [10].

5.4. Oxidative stress and neuroinflammation

The roles of oxidative stress and neuroinflammation in AE pathogenesis have also gained increasing recognition. Proteomic analyses have revealed abnormal expression of oxidative stress-related proteins in the serum of AE patients, which may serve as biomarkers for AE. Additionally, studies have shown that the antioxidant N-acetylcysteine (NAC) can improve clinical symptoms and neuronal damage in experimental autoimmune encephalitis (EAE) mice, suggesting a potential role of oxidative stress in AE pathogenesis [8].

6. Future directions

AE, as a complex and variable neurological disorder, still faces numerous challenges in diagnosis and treatment. With the deepening understanding of AE pathogenesis and the application of new technologies, future research will focus on precision diagnosis, targeted therapy, long-term management, and multidisciplinary collaboration.

6.1. Precision diagnosis

Current AE diagnosis primarily relies on antibody detection in CSF, but single antibody testing has limitations in sensitivity and specificity. Future research should aim to integrate multiple biomarkers, including but not limited to antibody titers, inflammatory markers in CSF (such as sCD27 and sBCMA) [3], oxidative stress-related proteins (such as ALB and GPX3) [8], and neuroimaging features, to improve diagnostic accuracy and timeliness. By combining multimodal biomarker analysis, a more comprehensive understanding of AE pathophysiology can be achieved, providing robust support for clinical decision-making [8,12].

6.2. Targeted therapy

For AE immunotherapy, current first-line treatments include steroids, IVIG, and plasma exchange, but some patients show poor response or experience relapse. Future research should explore more precise targeted therapeutic strategies, such as developing neutralizing antibodies that specifically counteract pathogenic antibodies to block their binding to neuronal receptors and reduce neuronal damage [12]. Additionally, for refractory AE patients, early introduction of third-line immunotherapies, such as tocilizumab, should be considered to improve outcomes [10].

6.3. Long-term management

Even after effective treatment, AE patients may still face long-term cognitive dysfunction and relapse risks. Therefore, establishing long-term cognitive rehabilitation programs and relapse monitoring systems is crucial. Future research should focus on personalized cognitive training, pharmacological interventions, and psychological support to promote cognitive recovery and reduce relapse rates. Concurrently, antibody titer monitoring and neuroimaging follow-ups can help detect early signs of relapse and adjust treatment plans accordingly [4,6].

7. Conclusion

This study systematically reviews recent advances in the diagnosis and immunotherapy of AE. In terms of diagnosis, with the deepening understanding of AE pathogenesis, diagnostic criteria have

been continuously refined. The discovery of novel biomarkers, such as sCD27, sBCMA in CSF, and oxidative stress-related proteins, has provided new tools for early AE diagnosis. In terms of treatment, immunotherapy strategies have become increasingly diverse and precise. First-line immunotherapies, including glucocorticoids, intravenous immunoglobulin (IVIG), and plasma exchange, have become the foundation of AE treatment. For severe AE patients with poor response to first-line therapy, second-line immunotherapies such as rituximab and tocilizumab have significantly improved outcomes. Furthermore, for refractory cases, exploration of third-line immunotherapies and combination therapies continues to deepen, providing more options to improve patient prognosis.

Despite significant progress in AE diagnosis and treatment, each patient's condition is unique, highlighting the importance of personalized medicine. Future research should focus on understanding individual differences through genetic testing and proteomic analysis to develop more precise treatment plans. Additionally, AE diagnosis and treatment involve multiple disciplines, including neurology, immunology, psychiatry, and rehabilitation medicine. Multidisciplinary collaboration not only facilitates comprehensive patient assessment but also improves diagnostic accuracy and treatment efficacy. By establishing integrated care teams, specialists from various fields can collaboratively discuss cases, develop personalized treatment plans, and monitor therapeutic outcomes.

References

- [1] B, F. G. A., et al. (2016). A clinical approach to diagnosis of autoimmune encephalitis. *The Lancet Neurology*, 15(4), 391–404.
- [2] Dalmau, J., & Graus, F. (2023). Autoimmune encephalitis—Misdiagnosis, misconceptions, and how to avoid them. *JAMA Neurology*, 80(1), 12–14.
- [3] Cobanovic, S., et al. (n.d.). Cerebrospinal fluid soluble CD27 is a sensitive biomarker of inflammation in autoimmune encephalitis. *Journal of the Neurological Sciences*, 466.
- [4] Guan, H. Z., Wang, J. W., & Zhao, G. (2022). Chinese expert consensus on diagnosis and treatment of autoimmune encephalitis. *Chinese Journal of Neurology*.
- [5] Dalmau, J., et al. (2011). Clinical experience and laboratory investigations in patients with anti-NMDAR encephalitis. *The Lancet Neurology*, 10(1), 63–74.
- [6] Varley, J. A., et al. (2023). Autoimmune encephalitis: Recent clinical and biological advances. *Journal of Neurology*.
- [7] De Bruijn, M. A. A. M., et al. (2020). Pediatric autoimmune encephalitis: Recognition and diagnosis. *Neurology Neuroimmunology & Neuroinflammation*, 7(3), e682.
- [8] Zhang, F., et al. (2025). Proteomic profiling and therapeutic targeting of oxidative stress in autoimmune encephalitis. *Journal of Molecular Neuroscience*, 75(2), 1–16.
- [9] Dalmau, J., & Graus, F. (2023). Diagnostic criteria for autoimmune encephalitis: Utility and pitfalls for antibody-negative disease. *The Lancet Neurology*, 22(6), 12.
- [10] Lee, W. J., et al. (2016). Tocilizumab in autoimmune encephalitis refractory to rituximab: An institutional cohort study. *Neurotherapeutics*, 13(4), 824–832.
- [11] Kelly, M. J., & Irani, S. R. (2023). Autoimmune encephalitis: Should we consider third-line immunotherapies earlier? *European Journal of Neurology*.
- [12] Wang, H., et al. (2024). Structural basis for antibody-mediated NMDA receptor clustering and endocytosis in autoimmune encephalitis. *Nature Structural & Molecular Biology*, 11(2024), 31.
- [13] Feng, Y. F., et al. (2025). Parvalbumin neurons mediate neurological phenotypes of anti-NMDAR encephalitis. *Brain*, 5(2025), 5.