

Research Article

Link Between Autoimmunity and Epilepsy: Neuronal Autoantibodies

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Abstract

Introduction: Autoimmune epilepsy remains under-recognized, and its true incidence remains uncertain. **Objective:** This study aimed to determine the prevalence of neuronal autoantibodies in patients with epilepsy of unknown etiology. **Materials and Methods:** An observational, longitudinal, prospective, and analytical study was conducted to assess the presence of autoantibodies associated with autoimmune encephalitis, glutamic acid decarboxylase-65 (GAD65), and onconeural antibodies in the serum and cerebrospinal fluid of consecutive patients with epilepsy of unknown etiology. **Results:** Sixty patients and 80 controls (30 healthy individuals, 30 with multiple sclerosis, 10 with systemic lupus erythematosus, and 10 with Sjögren's syndrome) were included to detect neuronal antibodies. Among epilepsy patients, 28 out of 60 (47%) tested positive for antibodies against N-methyl-D-aspartate receptor (NMDAR), contactin-associated protein 2 (CASPR2), leucine-rich glioma-inactivated 1 (LGI1), and glutamic acid decarboxylase (GAD), which was significantly higher ($p < 0.001$) than in the combined control cohort. No onconeural antibodies were detected in epilepsy patients except for 6 cases of epilepsy, 1 case of multiple sclerosis, and 3 cases of lupus with positive GAD by immunofluorescence assay and immunoblotting. There was no significant difference in antibody incidence between male and female epilepsy patients. The incidence of positive autoantibodies was significantly higher in patients with focal epilepsy compared to those with generalized epilepsy ($p < 0.01$). **Conclusions:** The findings indicate the presence of antibodies against NMDAR, VGKC-associated proteins (LGI1, CASPR2), and intracellular antigens (GAD65) in the serum and cerebrospinal fluid of patients with epilepsy, suggesting an autoimmune etiology. These results underscore the need for further research to elucidate the role of autoantibodies in epilepsy pathogenesis and to explore immunotherapeutic interventions.

Keywords

Established Epilepsy, New-Onset Epilepsy, Neuronal Autoantibodies, Voltage-Gated Potassium Channel Complex, Glutamic Acid Decarboxylase, NMDA Receptor

1. Introduction

Epileptic seizures are frequently encountered in autoimmune encephalitis, sometimes presenting as the sole symptom. The prevalence of neuronal autoantibodies in epilepsy of

unknown origin varies among studies. These antibodies have been identified in conditions such as limbic encephalitis (LE) [1] and, more recently, in faciobrachial dystonic seizures

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(FBDS) [2]. These encephalopathies often exhibit a monophasic course with antibody titers that typically decrease significantly within 1 to 2 years [3]. Autoantibodies against neuronal antigens play a crucial role in synaptic signal transduction, contributing to seizures and neuropsychiatric manifestations. Associated autoimmune conditions include specific forms of limbic encephalitis, neuromyotonia, and Morvan's syndrome, which can be severe and potentially life-threatening, with both non-paraneoplastic and paraneoplastic etiologies.

Paraneoplastic neurological syndromes (PNS) encompass a spectrum of nervous system disorders associated with malignancies, not attributable to direct tumor effects. Instead, they are mediated by immunological mechanisms and are diagnosed based on specific antibodies known as onconeural antibodies (ONA). Graus et al. categorize ONAs against intracellular antigens as well-characterized (e.g., anti-Hu or ANNA-1, anti-Ri or ANNA-2, anti-Yo, anti-CV2/CRMP5, anti-Ma2, anti-amphiphysin, and anti-Tr or PCA-Tr) and partially characterized (e.g., anti-Zic4, anti-SOX, anti-ANNA-3, and PCA-2) antibodies. The prevalence of underlying tumors associated with these antibodies ranges from 10% to 70%, depending on the antibody type, suggesting a causal role in pathogenesis.

Early diagnosis is critical for favorable outcomes, as timely intervention with immunomodulatory therapies or tumor resection can lead to substantial symptom improvement in most patients. Neuronal protein antibodies are frequently detected in patients presenting with acute seizures suspected to have an autoimmune basis, identified by cerebrospinal fluid inflammation or abnormal neuroimaging findings [4]. Antibodies against proteins of the voltage-gated potassium channel complex (VGKC) and glutamic acid decarboxylase (GAD) have also been reported in a subset of patients where seizures are the primary or sole manifestation, often in the absence of overt autoimmune disease [5]. However, these studies typically recruit patients from tertiary centers, potentially biasing towards those with refractory and long-standing epilepsy. Consequently, it remains uncertain whether the elevated prevalence of neuronal autoantibodies in these contexts reflects a causal link to epilepsy or merely arises secondary to uncontrolled seizures and associated neurologic damage.

Recent reports have identified antibodies against other brain-expressed proteins, including N-methyl-D-aspartate receptor (NMDAR), α -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPA), γ -aminobutyric acid B receptor (GABA-B), and glycine receptors (GLY-Rs) in patients with encephalopathies [6]. However, the incidence of these newer antibodies in larger cohorts of sporadic epilepsy remains poorly understood. Moreover, it is unclear whether these antibodies coexist with more established antibodies like VGKC and GAD in broader autoimmune profiles associated with seizure disorders.

This study aimed to assess the prevalence of both estab-

lished and newly recognized neuronal autoantibodies in a cohort of epilepsy patients.

2. Materials and Methods

An observational, longitudinal, prospective, and analytical study was conducted to assess the presence of autoantibodies associated with autoimmune encephalitis, glutamic acid decarboxylase-65 (GAD), and onconeural antibodies in both serum and cerebrospinal fluid (CSF) of consecutive patients diagnosed with established epilepsy or recent-onset epilepsy of unknown etiology. Exclusion criteria included individuals with a history of alcohol abuse, recreational drug use, suspected non-epileptic seizures, or progressive neurological disorders. Laboratory analyses were performed based on clinical indications by the patients' neurologists as part of the differential diagnostic workup for suspected autoimmune neuroinflammatory diseases.

Serum and CSF samples underwent analysis using the following methods:

1. Tissue-based assay (IIF-TBA): Serum samples were diluted at 1:10 and 1:100, and CSF at 1:1 and 1:5, and applied onto primate cerebellum substrate. Following a 30-minute incubation and phosphate-buffered saline (PBS) wash, the substrate was further incubated with anti-IgG-fluorescein for another 30 minutes. Slides were visualized using fluorescence microscopy at 400x magnification by two independent operators.
2. Immunoblotting: A commercial immunoblotting kit (EUROLINE Paraneoplastic Neurological Syndromes 12 Ag; Euroimmun, Lübeck, Germany) was utilized according to manufacturer instructions. Reactive strips were scanned, and band intensities of Hu (ANNA1), Yo (PCA1), CV2 (CRMP5), Ri (ANNA2), Ma2, Tr (DNER), Zic-4, SOX1, recoverin, GAD, titin, and amphiphysin were evaluated using EUROLineScan software (Euroimmun, Lübeck, Germany). Band intensities ≤ 10 were considered negative for onconeural antibodies.
3. Cell-based assay (CBA): Serum was diluted 1:10 and CSF 1:1 and screened for antibodies against N-methyl-D-aspartate receptor (NMDAR), α -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor type B (AMPA), dipeptidyl aminopeptidase-like protein 6 (DPPX), voltage-gated potassium channels (VGKC), or VGKC-associated proteins (leucine-rich glioma-inactivated protein 1 LGI1, contactin-associated protein 2 CASPR2) using Autoimmune Encephalitis Mosaic 1 Biochip 6 (Euroimmun, Lübeck, Germany).

3. Statistical Analysis

Antibody results were expressed as relative incidence

throughout the study period and analyzed using appropriate statistical tests. Categorical variables were compared using the chi-square test or Fisher's exact test, while continuous variables were assessed using the Mann-Whitney test. Demographic data and clinical characteristics were statistically compared to evaluate potential associations.

4. Results

Between January 2017 and March 2023, sixty patients with established or recent-onset epilepsy were analyzed, including serum ($n = 60$) and cerebrospinal fluid (CSF) samples ($n = 60$). The median age of the cohort was 48 years (range 15–65), with 27 patients (45%) being female.

In addition to the epilepsy cohort, were included 80 controls: 30 healthy volunteers, 30 patients with multiple sclerosis (MS), and 20 individuals with other autoimmune conditions (10 systemic lupus erythematosus, 10 Sjögren's syndrome). Serum and CSF samples were evaluated for antibodies against NMDAR, AMPAR, CASPR2, LGI1, DPPX, GABAB, and GAD in patients with epilepsy, whereas only serum samples were analyzed in healthy controls. Detailed results are summarized in Table 1.

Among the epilepsy patients, 28 out of 60 (47%) tested positive for serum and CSF antibodies against NMDAR, CASPR2, LGI1, and GAD, representing a significantly higher incidence compared to the combined control cohort ($p < 0.001$) (Table 1, Figure 2). The most prevalent antibody was anti-NMDAR, detected in 15 epilepsy patients (25% of total), compared to 4 controls (5% of total). Antibodies against CASPR2, LGI1, and GAD were also identified in 3.3%, 8.3%, and 10% of epilepsy patients, respectively (Figure 1).

None of the epilepsy patients or controls tested positive for onconeural antibodies, except for 6 epilepsy cases, 1 MS case, and 3 SLE cases showing anti-GAD positivity detected by IIF-TBA and immunoblotting (Figure 3).

There was no significant difference in the incidence of studied autoantibodies between male and female epilepsy patients (Table 2). However, a notably higher incidence of positive autoantibodies was observed in patients with focal epilepsy compared to those with generalized epilepsy ($p < 0.01$; Table 2).

5. Discussion

Previous studies have highlighted the presence of autoantibodies against NMDAR [7] and GAD [8] in cross-sectional cohorts of patients with epilepsy, particularly in well-defined epileptic syndromes and those with suspected pre-existing neurological autoimmunity [4]. More recently, investigations into CASPR2 [9] and LGI1 [10] antibodies have expanded our understanding within the autoimmune epilepsy population, with limited studies focusing on pediatric cases of limbic encephalitis and status epilepticus [11].

In the study, antibodies in a consecutive, unselected cohort of epilepsy patients were systematically examined. A significantly higher incidence of NMDAR, CASPR2, LGI1, and GAD antibodies was observed compared to healthy and diseased controls. Specifically, 28 out of 60 epilepsy patients (47%) tested positive for antibodies against these neuronal antigens.

Notably, none of the patients in ~~our~~ this study exhibited clinical evidence of limbic encephalitis (LE) or anti-NMDAR encephalitis, emphasizing that several neurologic autoantibodies associated with subacute onset encephalopathies may also precipitate sporadic epilepsy, corroborating previous reports in young patients with unexplained-onset epilepsy [12]. Among the six patients positive for anti-GAD antibodies, all had focal epilepsy, evenly split between men and women, consistent with existing literature [13] and recent findings linking anti-GAD antibodies to temporal lobe epilepsy and mild cognitive impairments [14–16].

After anti-NMDAR antibodies, anti-GAD emerged as the second most prevalent autoantibody in our analysis. This aligns with historical data linking anti-GAD antibodies to drug-resistant epilepsies that do not meet criteria for limbic encephalitis [17], a criterion consistent with our study's selection criteria.

Our findings also revealed that 7 out of 60 patients diagnosed with epilepsy—both focal and generalized—tested positive for anti-CASPR2 (3.3%) and anti-LGI1 (8.3%) antibodies, consistent with the relative prevalence observed in other studies. While generalized epilepsies are often genetically rooted, the potential overlap between genetic epilepsy and autoimmune mechanisms warrants further investigation. The International League Against Epilepsy (ILAE) has acknowledged this evolving understanding in its recent classification updates, recognizing "Immune" as an etiological factor in epilepsy for the first time [18].

Anti-NMDAR encephalitis, the most common autoimmune encephalitis associated with anti-neuronal surface antibodies (ANSA) [19], underscores the autoimmune etiology within the broader spectrum of neurological disorders. A prospective, multicenter study supports autoimmune disorders as the third most prevalent cause of encephalitis after viral infections and acute disseminated encephalomyelitis [20]. Diagnostic confirmation of anti-NMDAR encephalitis hinges on cerebrospinal fluid antibody detection against the GluN1 subunit of NMDAR, given the less reliable serum tests that yield false negatives in up to 14% of cases [21]. Conversely, cases presenting with positive serum and negative cerebrospinal fluid antibodies should be carefully re-evaluated for accuracy [22, 23].

The anti-LGI1 antibody, previously identified as anti-VGKC, underscores the complexity of antibody characterization. While initially detected via radioimmunoassay targeting VGKC, subsequent studies revealed LGI1 and CASPR2 as true antigenic epitopes. This realization prompted the reclassification to anti-VGKC complex antibodies, urging

a shift towards direct antigen naming rather than the VGKC complex. Such nuances highlight the importance of updated methodologies, such as cell-based assays (CBA), in accurately diagnosing autoimmune epilepsies [24, 25].

This study's antibody incidence data offer insights for future research directions and clinical considerations. Given the variability in antibody types and detection methodologies across studies, standardized protocols for neuronal autoantibody testing are crucial to obtain accurate prevalence estimates and improve clinical management strategies for patients with epilepsy of unknown origin.

In summary, our consecutive prospective study of epilepsy patients revealed a notable proportion with detectable neuronal antibodies in serum and cerebrospinal fluid, indicating a potential autoimmune basis. This study underscores the under-recognition and prevalence of autoimmune epilepsy. However, limitations, such as the unavailability of glycine receptor antibody testing and potential under-recognition of certain neurological autoantibodies, warrant further investigation to refine our understanding and clinical management of autoimmune epilepsy.

6. Conclusion

In conclusion, our study identifies antibodies against neuronal receptors (NMDAR), VGKC-associated proteins (LGI1, CASPR2), and intracellular antigens (GAD65) in the serum and cerebrospinal fluid of epilepsy patients, indicating potential responsiveness to immune-modulatory treatments. Future research should focus on prospective cohorts of newly diagnosed epilepsy patients to further elucidate the role of autoantibodies in epilepsy pathophysiology, aiming to enhance diagnostic accuracy and explore alternative treatment

options, such as immunotherapies.

7. Recommendations

Based on this study, several recommendations can be made:

1. **Enhanced Screening Protocols:** Implement enhanced screening protocols to routinely test for neuronal antibodies (NMDAR, LGI1, CASPR2, GAD65) in both serum and cerebrospinal fluid of epilepsy patients, especially those with refractory epilepsy or atypical presentations.
2. **Early Diagnosis and Intervention:** Encourage early diagnosis by incorporating autoantibody testing into the diagnostic workup of epilepsy patients, potentially leading to earlier intervention with immunomodulatory therapies.
3. **Educational Initiatives:** Conduct educational initiatives for healthcare providers to increase awareness of autoimmune etiologies in epilepsy and the clinical significance of neuronal antibodies.
4. **Collaborative Research Efforts:** Foster collaborative efforts between neurologists, immunologists, and researchers to further investigate the pathophysiological roles of neuronal antibodies in epilepsy and develop targeted treatment strategies.
5. **Longitudinal Studies:** Support longitudinal studies to monitor the efficacy and long-term outcomes of immunomodulatory therapies in epilepsy patients positive for neuronal antibodies.

Implementing these recommendations can potentially improve diagnostic accuracy, optimize treatment outcomes, and advance our understanding of autoimmune contributions to epilepsy.

Table 1. Presence of neuronal autoantibodies in cases and controls.

	n	a-NMDAR (CBA)	a-AMPA (CBA)	a-CASPR2 (CBA)	a-LGI1 (CBA)	a-DPPX (CBA)	a-GABA _B (CBA)	a-GAD (IIF-TBA-IT)	Total, Ac +	p
Cases										
Epilepsy	60	15	0	2	5	0	0	6	28	
Controls										
Healthy	30	0	0	0	0	0	0	0	0	<0,001*
MS	30	1	0	0	0	0	0	1	2	<0,001*
Autoimmune	20	3	0	0	0	0	0	3	6	<0,01*

Results are expressed as the number of samples showing a positive titer. Statistical comparisons (*total positive antibodies in cases vs controls) were conducted using the chi-square test or Fisher's exact test as appropriate.

Detected autoantibodies include: NMDAR, N-methyl-D-aspartate receptor; AMPAR, alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid

receptor; CASPR2, contactin-associated protein-like 2; LGI1, leucine-rich glioma inactivated 1 protein; DPPX, dipeptidyl-peptidase-like protein 6; GABA_B, gamma-aminobutyric

acid type B receptor; GAD, glutamic acid decarboxylase.

Methods for antibody determination were CBA: cell-based assay, IIF-TBA: immunofluorescence tissue-based assay, IT: immunotransfer; MS, multiple sclerosis; p, p-value. -n Number of cases and controls. -Total: Number of positive autoantibodies. -Autoimmune: Controls from other autoim-

mune diseases (systemic lupus erythematosus and Sjögren's syndrome).

This table provides a structured overview of the presence of specific neuronal autoantibodies in different groups of patients and controls, highlighting significant findings through statistical comparisons.

Table 2. Incidence of neuronal autoantibodies by demographic and clinical characteristics.

	n	a-NMDAR (CBA)	a-AMPA R (CBA)	a-CASPR2 (CBA)	a- LGI1 (CBA)	a-DPPX (CBA)	a-GABAb (CBA)	a-GAD (IIF-TBA-IT)	Total Ac +	p
Sex										
Male	33	8 (24%)	0 (0%)	1 (3%)	3 (9%)	0 (0%)	0 (0%)	3 (9%)	15 (45%)	ns
Female	27	7 (26%)	0 (0%)	1 (4%)	2 (7%)	0 (0%)	0 (0%)	3 (11%)	13 (48%)	
Epilepsy Type										
Generalized	20	5 (25%)	0 (0%)	0 (0%)	1 (5%)	0 (0%)	0 (0%)	1 (5%)	7 (35%)	<0,01*
Focal	40	10 (25%)	0 (0%)	2 (5%)	4 (10%)	0 (0%)	0 (0%)	5 (12%)	21 (52%)	

Results are expressed as the number of samples showing a positive titer in clinical cohorts. Statistical comparisons were performed using the chi-square test or Fisher's exact test as appropriate. -ns: not significant, *: statistically significant.

Detected autoantibodies include: NMDAR, N-methyl-D-aspartate receptor; AMPAR, alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor; CASPR2, contactin-associated protein-like 2; LGI1, leucine-rich glioma inactivated 1 protein; DPPX, dipeptidyl-peptidase-like protein 6; GABAb, gamma-aminobutyric acid type B receptor; GAD, glutamic acid decarboxylase.

Methods for antibody determination were CBA: cell-based assay, IIF-TBA: immunofluorescence tissue-based assay, IT: immunotransfer; p, p-value. -n Number of cases. -Total: Number of positive autoantibodies.

This table summarizes the incidence of specific neuronal autoantibodies categorized by sex and epilepsy type, demonstrating significant associations through statistical analysis.

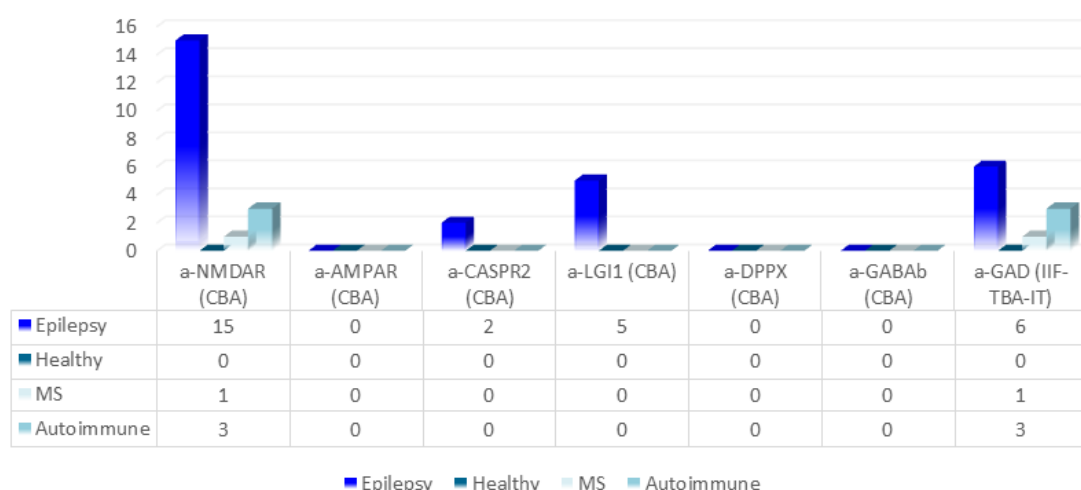


Figure 1. Neuronal autoantibodies in cases and controls.

Patients with epilepsy (n = 60), disease controls [multiple sclerosis (MS) n = 30, autoimmune diseases, systemic lupus erythematosus (SLE) + Sjögren's syndrome (SS) n = 20], and

healthy controls (n = 30) were analyzed for autoantibodies against various neuronal proteins. The figure depicts the results of autoantibody detection against NMDAR,

N-methyl-D-aspartate receptor; AMPAR, alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor; CASPR2, contactin-associated protein-like 2; LGI1, leucine-rich glioma inactivated 1 protein; DPPX, dipeptidyl-peptidase-like protein 6; GABAb, gamma-aminobutyric acid type B receptor, by cell-based assay (CBA), and GAD,

glutamic acid decarboxylase by immunoblot and immunofluorescence tissue-based assay (IIF-TBA). This description summarizes the autoantibody detection against various neuronal proteins in patients with epilepsy and control groups, indicating the methodology used for each antibody type.

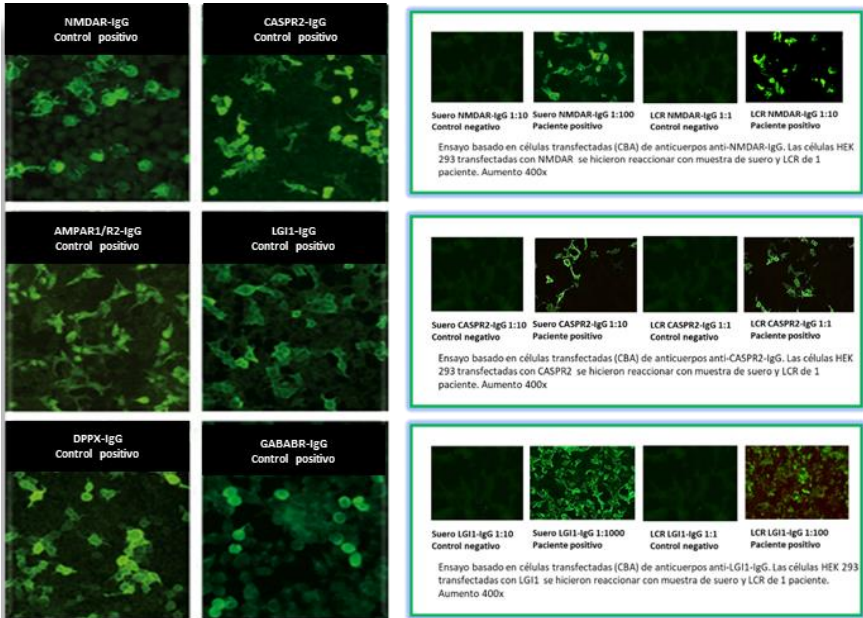


Figure 2. Autoimmune encephalitis mosaic. Cell-based assay.

Mono-specific determination of autoantibodies targeting neuronal surface antigens using indirect immunofluorescence assay based on transfected cells presenting the relevant antigens in their authentic or conformational form. Different transfected cellular substrates can be combined in multiplex. The left panel displays positive controls for detecting antibodies against NMDAR, N-methyl-D-aspartate receptor; AM-

PAR, alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor; CASPR2, contactin-associated protein-like 2; LGI1, leucine-rich glioma inactivated 1 protein; DPPX, dipeptidyl-peptidase-like protein 6; GABAb, gamma-aminobutyric acid type B receptors. On the right, images of positive immunofluorescence from three patients are shown.



Figure 3. Anti-glutamic acid decarboxylase (GAD) autoantibodies.

(a) Immunofluorescence findings in a case of epilepsy associated with anti-GAD antibodies. Micrograph showing immunofluorescence using patient serum diluted 1:100 on cerebellum (400x magnification). The typical fluorescence pattern of anti-GAD antibodies shows prominent staining in the granular cell layer, unlike anti-amphiphysin antibodies, which do not stain the molecular layer.

(b) Anti-GAD detected by immunoblot in serum and cerebrospinal fluid (CSF) of the same patient. Serum dilution 1:100, CSF dilution 1:2. CV2: CV2/collapsin response mediator protein (CRMP) 5; PNMA2/Ma2: paraneoplastic Ma antigen family (PNMA) represented by at least fifteen family members, with PNMA1-3 associated with paraneoplastic disorder; Ri: 55 and 80 kDa proteins named Nova-1 and Nova-2, involved in pre-mRNA regulation; Yo: cytoplasmic proteins in Purkinje cells of cerebellum, 34 and 62 kDa; Hu: RNA-binding protein family (Hu-D, Hu-C, and Hel N1), 35-40 kDa, located in nuclei and cytoplasm of all neurons and also in tumor cells; SOX1: antigen localized in Bergmann glial cell nuclei of adult cerebellum; Zic4: proteins in granular layer nuclei, part of a zinc-finger protein family crucial in nervous system (NS) development; GAD65: glutamic acid decarboxylase, Tr (DNER): antigen expressed in Purkinje cell cytoplasm, axons, and dendrites.

Abbreviations

GlyR	Anti-glycine Receptor Antibodies
AMPA	α -amino-3-Hydroxy-5-Methyl-4-Isoxazolepropionic Acid Receptor
anti-Amphiphysin	Antibodies Against a 128 kDa Protein Called Amphiphysin
Anti-ANNA-3	Anti-Neuronal Nuclear Type 3 (ANNA-3) Antibodies
anti-CV2/CRMP5	Antibodies Against CV2/Collapsin Response Mediator Protein 5
anti-Hu or ANNA-1	Antibodies Against RNA-binding Protein Family (Hu-D, Hu-C, and Hel N1)
anti-Ma2/PNMA2	Antibodies Against Brain and Testis Proteins Including Ma1, Ma2, and Others
anti-NSA	Anti-Neuronal Surface Antigen Antibodies
Anti-PCA-2	Antibodies Identified in a Small Group of Patients with Paraneoplastic Cerebellar Degeneration (PCD) Associated with Small-Cell Lung Cancer
anti-Ri or ANNA-2	Antibodies Against Nova-1 and Nova-2 Proteins (55 and 80 kDa)
Anti-SOX1	Anti-Glial Nuclear (AGNA) Antibodies
anti-Tr (PCA-Tr)	Antibodies Associated with Paraneoplastic Cerebellar Degeneration (PCD) and Hodgkin's Disease
anti-Yo	Antibodies Against Cytoplasmic Proteins of Purkinje Cells (34 and 62 kDa)
Anti-Zic4	Antibodies Against Zic4 Proteins

AON	Onconeural Antibodies
CASPR2	Contactin-Associated Protein 2
CBA	Cell-Based Assay
CDFB	Faciobrachial Dystonic Seizures
AE	Autoimmune Encephalitis
LE	Limbic Encephalitis
MS	Multiple Sclerosis
GABABR	γ -aminobutyric Acid B Receptor
GAD	Glutamic Acid Decarboxylase
GLY-Rs	Glycine Receptors
IIF-TBA	Indirect Immunofluorescence Assay Using Primate Cerebellar Tissue
ILAE	International League Against Epilepsy
Kv1	Potassium Voltage-Gated Channel Subfamily A member 1
CSF	Cerebrospinal Fluid
SLE	Systemic Lupus Erythematosus
LGI1	Leucine-rich Glioma-Inactivated Protein 1
NMDAR	N-methyl-D-Aspartate receptor
PBS	Phosphate-Buffered saline
NS	Nervous System
PNS	Paraneoplastic Neurological Syndromes
VGKC	Voltage-Gated Potassium Channel Complex

Author Contributions

Silvia Graciela Ramos: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Supervision, Validation, Writing – original draft Writing – review & editing

Viviana Novoa: Conceptualization, Investigation, Supervision, Writing – review & editing

Claudio Aranda: Conceptualization, Supervision, Visualization

Conflicts of Interest

The authors declare no conflicts of interest.

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