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Comparison of Clinical, EEG, and Neuroimaging Findings in Autoimmune and Viral Encephalitis: A Single-center Experience

Merve Melodi Çakar, Şule Şenveli, Özden Kamışlı

University of Health Sciences Türkiye, Bursa City Hospital, Department of Neurology, Bursa, Türkiye

Merve Melodi Çakar MD,

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Corresponding Author: Merve Melodi Çakar, MD, University of Health Sciences Türkiye, Bursa City Hospital, Department of Neurology, Bursa, Türkiye **E-mail:** mervemelodicakar@gmail.com

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Abstract

Objective: Autoimmune encephalitis (AE) and viral encephalitis (VE) may present with overlapping clinical manifestations, whereas confirmatory laboratory testing is often delayed. We aimed to compare the clinical characteristics, cerebrospinal fluid (CSF) findings, electroencephalographic (EEG) features, and neuroimaging patterns of patients with AE and VE who were followed at a tertiary neurology center.

Methods: Medical records of patients diagnosed with encephalitis between January 2022 and January 2026 were retrospectively reviewed. Patients with positive neuronal autoantibodies in serum or CSF were classified as AE, whereas patients with positive neuropathogen polymerase chain reaction results in CSF were classified as VE. Clinical findings, CSF parameters, EEG findings, neuroimaging features, intensive care requirements, and discharge modified Rankin scale (mRS) scores were evaluated.

Results: A total of 24 patients were included, comprising 13 AE and 11 VE cases. Mean age was 50.7±17.0 years in the AE group and 55.0±15.4 years in the VE group. In the AE group, the most frequent antibodies were contactin-associated protein-like 2, anti-N-methyl-D-aspartate receptor, and anti-leucine-rich glioma-inactivated protein 1 (n=3 each). Herpes simplex virus (HSV) was the most common pathogen in the VE group (n=8). CSF pleocytosis and protein elevation were more frequent in VE patients (90.9% each) than in AE patients (54.5% and 45.5%, respectively). Limbic involvement on magnetic resonance imaging (MRI) scans was observed more frequently in AE (58.3% vs. 20.0%). Temporal epileptiform EEG abnormalities were also more frequent in AE (54.5% vs. 40.0%). Requirements for intensive care and mechanical ventilation were higher in the VE group, and discharge mRS scores were worse in these patients.

Conclusion: HSV-predominant VE was associated with more prominent CSF inflammatory findings and greater disease severity, whereas limbic MRI abnormalities and temporal epileptiform EEG discharges were more characteristic of AE. Early integration of clinical, EEG, and neuroimaging findings may facilitate the differential diagnosis before laboratory confirmation becomes available.

Keywords: Autoimmune encephalitis, viral encephalitis, herpes simplex encephalitis, EEG, limbic encephalitis, cerebrospinal fluid

INTRODUCTION

Encephalitis—inflammation of the brain parenchyma—is a neurological emergency that continues to carry substantial morbidity and mortality.[1] Patients may present with altered consciousness, seizures, focal deficits, or neuropsychiatric features, and this clinical heterogeneity makes early aetiological characterization both essential and difficult.[2]

For many decades, viral pathogens, herpes simplex virus (HSV) in particular, were regarded as the dominant cause of encephalitis. The picture has shifted considerably over the past twenty years, with the identification of a growing list of neuronal surface and synaptic antibodies; autoimmune aetiologies now occupy a central place in the differential.[3] Anti-N-methyl-D-aspartate receptor (NMDA-R) encephalitis is now among the most frequently recognized forms in younger patients, and antibodies directed against leucine-rich glioma-inactivated protein 1 (LGI1), contactin-associated protein-like 2 (CASPR2), gamma-aminobutyric acid B (GABA-B) receptor, and glutamic acid decarboxylase (GAD) are increasingly encountered in routine practice.[4]

Even with this expanded awareness, separating autoimmune from viral encephalitis (VE) at the bedside remains far from straightforward. Seizures and encephalopathy are common to both, while serological or virological confirmation typically takes time.[5] The therapeutic stakes of getting this right are high: HSV encephalitis demands rapid antiviral therapy, whereas autoimmune cases require immunotherapy.[6] Late initiation of the appropriate treatment—in either direction—is linked to worse neurological outcomes.

Two readily available bedside tools—electroencephalography (EEG) and magnetic resonance imaging (MRI)—can offer early clues. On imaging, limbic autoimmune encephalitis (AE) tends to involve the mesiotemporal structures; HSV encephalitis preferentially produces

frontotemporal signal changes; and varicella-zoster virus (VZV) may extend into the thalami.[7] EEG can be similarly informative: temporal epileptiform discharges and the extreme delta brush pattern in anti-NMDA-R encephalitis are particularly worth recognising.[8]

Against this background, this study aimed to describe and compare the clinical features, cerebrospinal fluid (CSF) profiles, MRI findings, EEG patterns, intensive care unit (ICU) requirements, and short-term functional outcomes of patients with autoimmune and VE managed at a single tertiary neurology center.

METHODS

Study Design and Patient Selection

This was a retrospective, single-center study carried out in a tertiary neurology department. We reviewed the medical records of patients who were admitted with a clinical diagnosis of encephalitis between January 2022 and January 2026. Ethical approval was granted by University of Health Sciences Türkiye, Bursa City Hospital Scientific Research Ethics Committee (approval no: 2026-07/3, date: 01.04.2026). Patient confidentiality was safeguarded throughout, in line with the Declaration of Helsinki. Given the retrospective design, not all variables were available for every patient, and the analyses below reflect this limitation.

Patients were grouped into AE and VE. For inclusion in the AE group, a recognised neuronal autoantibody had to be detected in serum or CSF in line with established criteria.[7] A diagnosis of VE required a positive viral polymerase chain reaction (PCR) in CSF obtained using a comprehensive neuropathogen panel. Cases in which the two diagnoses overlapped, or in which a definite aetiology could not be reached, were not included.

Data Collection

The following information was extracted from the records: age, sex, presenting symptoms (psychiatric features, focal neurological deficits, seizures), CSF white cell count and protein concentration, autoantibody type, viral PCR results, cranial MRI findings (categorised as normal, limbic involvement, or other patterns including thalamic or frontotemporal lesions), EEG results, ICU admission, and length of stay, mechanical ventilation requirement, and modified Rankin scale (mRS) score at discharge.

EEG and Neuroimaging Analysis

Video-EEG was carried out during hospitalisation, and the timing of recording relative to symptom onset was noted. All studies were recorded using 20-channel digital video-EEG systems, with T1, T2, and ECG electrodes added to the scalp electrodes, which were placed according to the international 10-20 system. Depending on each patient's clinical condition, recordings were acquired in one of three settings: at the bedside in the ICU, using a portable device; in the EEG laboratory, as standard 20-minute recordings; or in the video-EEG monitoring unit, as prolonged recordings lasting 4-24 hours. Only EEGs recorded within 60 days of symptom onset were included. Tracings were classified as diffuse slowing, focal slowing, temporal epileptiform activity, multifocal epileptiform activity, or normal. Cranial MRI was performed at 1.5 Tesla and routinely included T2-weighted, FLAIR, diffusion-weighted imaging, and post-gadolinium T1-weighted sequences.

MAIN POINTS

- Cerebrospinal fluid (CSF) pleocytosis, elevated CSF protein, and intensive care requirement were more common in viral encephalitis.
- Limbic magnetic resonance imaging involvement and temporal epileptiform electroencephalography (EEG) abnormalities were more prominent in autoimmune encephalitis.
- Early integration of clinical, EEG, and neuroimaging findings may support differential diagnosis before laboratory confirmation.

Statistical Analysis

Given the modest sample size and the retrospective design, the data are reported descriptively. Continuous variables are presented as mean ± standard deviation, and categorical variables as frequency and percentage based on the number of cases with available data. Exploratory statistical comparisons were performed where appropriate, and findings were interpreted cautiously because of the limited sample size.

RESULTS

Patient Characteristics

Twenty-four patients met the inclusion criteria: 13 with AE and 11 with VE. Their demographic and clinical features are shown in Table 1. Mean age was broadly similar in the two groups (AE: 50.7±17.0 years; VE: 55.0±15.4 years), as was sex distribution (AE: 6F/7M; VE: 5F/6M). Psychiatric symptoms at onset were more common in AE (8/13, 61.5%) than in VE (3/11, 27.3%). Seizures at presentation were seen in 6 AE patients (46.2%) and in 4 VE patients (36.4%); focal neurological deficits were documented in 2 AE patients (15.4%) and 4 VE patients (36.4%), respectively.

Autoantibody and Virological Findings

In the AE group, the antibodies identified were CASPR2 (n=3), anti-NMDA receptor (n=3), and anti-LGI1 (n=3), anti-GAD (n=2), GABA-B (n=1). One additional patient' had co-occurring CASPR2 and LGI1 antibodies. Among viral agents, HSV was clearly dominant (n=8, 72.7%), while VZV accounted for the remaining three cases (27.3%).

CSF and Neuroimaging Findings

CSF data were available for 11 of the 13 AE patients; in the remaining two, lumbar puncture had been performed at outside institutions and the records could not be retrieved. Of those with available data, pleocytosis was present in 6/11 AE patients (54.5%) and 10/11 VE patients (90.9%). Elevated CSF protein followed a similar pattern, occurring in 10/11 VE patients (90.9%) versus 5/11 AE patients (45.5%). Although statistical significance was not reached, CSF protein elevation and limbic MRI involvement showed trends toward differences between groups. The detailed CSF and MRI findings are shown in Table 2.

MRI was available for review in 12 AE patients and 10 VE patients. Limbic involvement was seen in 7/12 AE patients (58.3%) and in 2/10 VE patients (20.0%). Other lesion patterns were noted

Table 1. Demographic and clinical features

Variable	Autoimmune encephalitis (n=13)	Viral encephalitis (n=11)
Age, mean ± SD (years)	50.7±17.0	55.0±15.4
Sex (female/male)	6F/7M	5F/6M
Psychiatric symptoms at onset, n (%)	8 (61.5%)	3 (27.3%)
Seizures at onset, n (%)	6 (46.2%)	4 (36.4%)
Focal neurological deficit, n (%)	2 (15.4%)	4 (36.4%)
ICU admission, n (%)	4 (30.8%)	6 (54.5%)
Mechanical ventilation, n (%)	3 (23.1%)	4 (36.4%)
Discharge mRS, median	1	2

ICU: Intensive care unit, mRS: Modified Rankin scale, SD: Standard deviation

Table 2. CSF and neuroimaging findings

Variable	Autoimmune encephalitis (n=13)	Viral encephalitis (n=11)
CSF pleocytosis, n (%)*	6/11 (54.5%)	10/11 (90.9%)
CSF protein elevated, n (%)*	5/11 (45.5%)	10/11 (90.9%)
MRI limbic involvement, n (%)**	7/12 (58.3%)	2/10 (20.0%)
MRI other lesion pattern, n (%)**	3/12 (25.0%)	6/10 (60.0%)
MRI normal, n (%)**	2/12 (16.7%)	2/10 (20.0%)

*: Percentages are calculated based on cases with available data for each variable, **: Denominator reflects patients who underwent cranial MRI at our center. CSF: Cerebrospinal fluid, MRI: Magnetic resonance imaging

in 3/12 AE patients (25.0%) and 6/10 VE patients (60.0%); in the VE group, these lesions were typically frontotemporal signal abnormalities with restricted diffusion, in keeping with HSV encephalitis, along with thalamic involvement in the VZV cases. Representative imaging is provided in Figure 1.

EEG Findings

EEG was available for 11 of the 13 AE patients and 10 of the 11 VE patients. The findings are summarised in Table 3. Diffuse background slowing was the most frequent abnormality in both groups. Temporal epileptiform activity was identified in 6/11 AE patients (54.5%) and 4/10 VE patients (40.0%), most often arising from the left, right, or bilateral temporal regions. One AE patient with anti-LGI1 antibodies had electrographically confirmed faciobrachial dystonic seizures, with ictal onset in the left temporal area on video-EEG. Periodic lateralized epileptiform discharges (PLEDs) were recorded in one further AE patient and are illustrated in Figure 2.

ICU Admission, Ventilatory Support, and Functional Outcomes

Admission to the ICU was required in 4/13 AE patients (30.8%) and 6/11 VE patients (54.5%). Mechanical ventilation was required in 3 AE patients (23.1%) and in 4 VE patients (36.4%); ICU stays ranged from 4 to 84 days in the AE group and from 4 to 26 days in the VE group. At hospital discharge, the median mRS was 1 in the AE group and 2 in the VE group; several VE patients left the hospital with residual cognitive or motor deficits.

DISCUSSION

This single-center retrospective study describes the clinical, CSF, neuroimaging, and EEG profiles of 24 patients diagnosed with either autoimmune or VE. Three observations stand out. First, VE—overwhelmingly driven by HSV in our cohort—was associated with more pronounced CSF inflammatory changes and a higher rate of ICU admission and mechanical ventilation. Second, the autoimmune group more frequently presented with psychiatric features at onset and showed limbic involvement on MRI. Third, temporal epileptiform abnormalities on EEG were observed in both groups, but were numerically more frequent in AE group.

That HSV was the most common viral pathogen in our cohort aligns well with population-based and registry data, in which HSV-1 is consistently identified as the leading viral cause of sporadic encephalitis.[9] The disease characteristically produces hemorrhagic necrosis of the medial temporal lobes and insular cortex, and this is reflected in the frontotemporal signal change and restricted diffusion that we observed.[10] VZV, identified in three patients, is the second most frequent herpesvirus to cause encephalitis in immunocompetent adults and may extend into the thalami, a pattern seen in one of our cases.[11]

The autoantibody profile in the AE group mirrors the heterogeneity reported in larger published series. CASPR2, anti-NMDA-R, and anti-LGI1 antibodies were each found in three patients. Anti-LGI1 encephalitis warrants particular emphasis given its association with faciobrachial dystonic seizures, which we confirmed electrographically in one case a useful reminder of the value of video-EEG monitoring when AE is suspected.[12] One patient was diagnosed with GABA-B encephalitis and subsequently found to have prostate adenocarcinoma. Although GABA-B receptor encephalitis is most commonly associated with small-cell lung carcinoma, rare associations with prostate adenocarcinoma have also been reported in the literature.[13]

The contrast in CSF findings was striking: pleocytosis and protein elevation were each observed in approximately 90% of VE

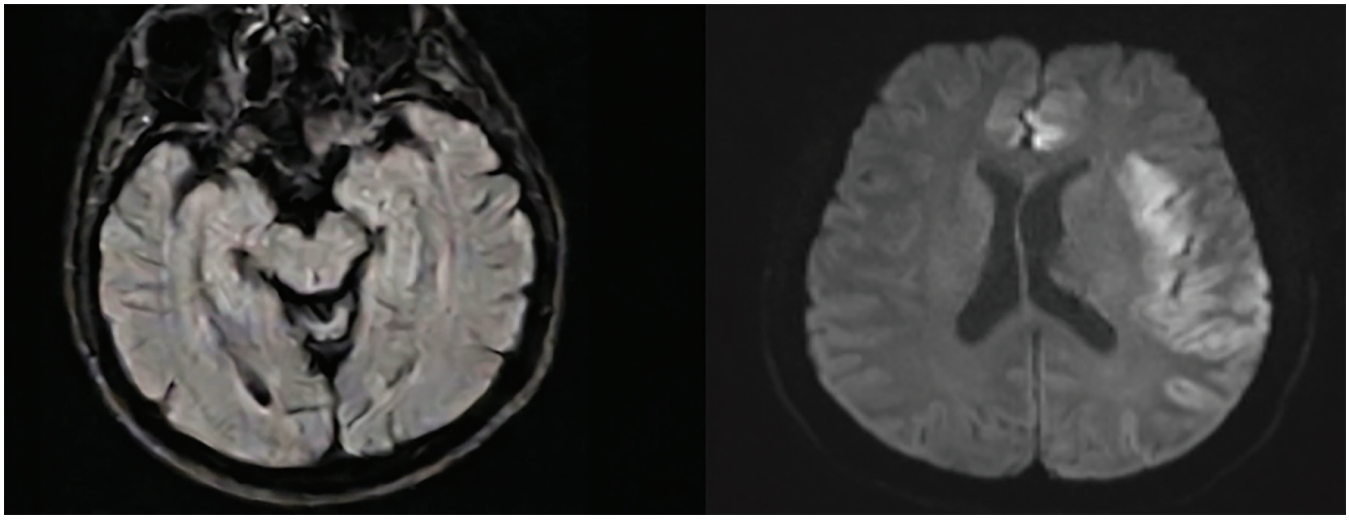

Figure 1. Representative cranial magnetic resonance imaging findings. Autoimmune encephalitis: FLAIR hyperintensity in the mesiotemporal region consistent with limbic encephalitis. Viral encephalitis (HSV): frontotemporal signal abnormality with restricted diffusion on DWI
FLAIR: Fluid-attenuated inversion recovery, DWI: Diffusion-weighted imaging, HSV: Herpes simplex virus

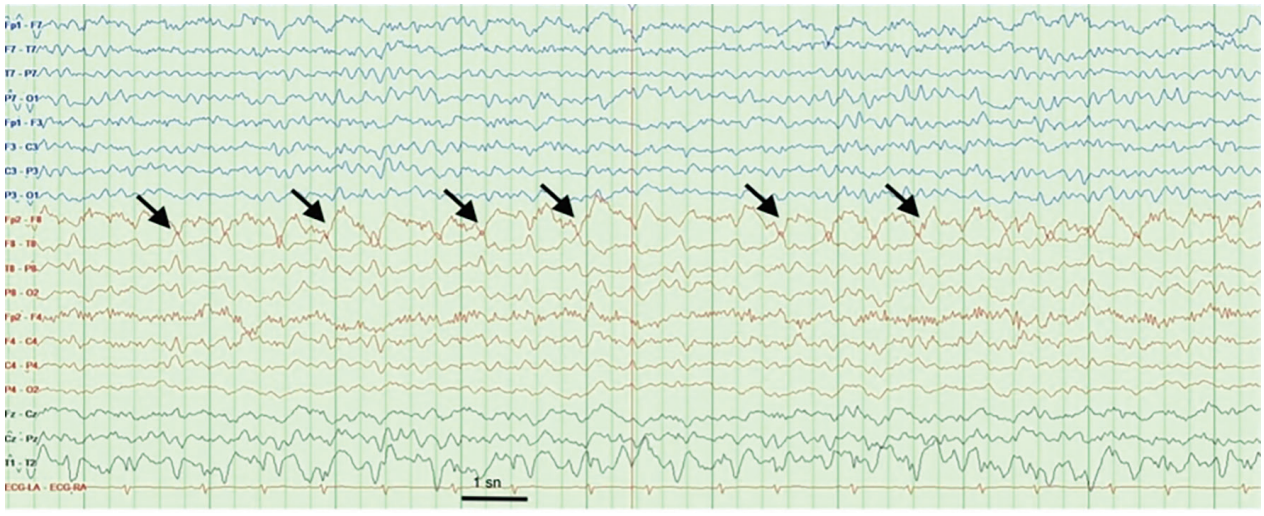

Figure 2. Periodic lateralized epileptiform discharges over the right hemisphere, maximal in the right frontotemporal derivations (F8-T8), in a patient with autoimmune encephalitis. Arrows indicate the periodic discharges. Longitudinal bipolar montage; sensitivity 10 µV/mm, low-frequency filter 0.5 Hz, high-frequency filter 60 Hz, 50-Hz notch filter; sweep speed 15 mm/s

Table 3. EEG findings

EEG finding	Autoimmune encephalitis (n=13)	Viral encephalitis (n=11)
Diffuse slowing, n (%)*	7/11 (63.6%)	7/10 (70.0%)
Focal slowing, n (%)*	3/11 (27.3%)	2/10 (20.0%)
Temporal epileptiform activity, n (%)*	6/11 (54.5%)	4/10 (40.0%)
Multifocal epileptiform activity, n (%)*	2/11 (18.2%)	1/10 (10.0%)
Normal EEG, n (%)*	2/11 (18.2%)	2/10 (20.0%)
EEG not performed, n	2	1

*: Percentages are calculated based on cases with available data for each variable. EEG: Electroencephalography

patients, but in only about half of AE cases. This is consistent with the more vigorous intrathecal inflammatory response expected with viral pathogens. A relatively bland CSF in a patient who is encephalopathic and has psychiatric symptoms should, by the same token, raise suspicion for an autoimmune process.[14]

On MRI, limbic involvement was identified in 58.3% of AE patients with available imaging, compared with only 20.0% in the VE group. While mesiotemporal signal change is the classical hallmark of autoimmune limbic encephalitis, anti-NMDA-R encephalitis often presents with normal or extra-limbic imaging findings.[7] The frontotemporal and thalamic patterns seen in the VE group are in line with the known neurotropism of herpesviruses.[10,11]

EEG provided diagnostic information in most patients in both groups. Temporal epileptiform discharges were somewhat more common in AE (54.5%) than in VE (40.0%). When such discharges—particularly unilateral periodic or ictal rhythmic patterns—are seen in a patient with possible VE, empirical aciclovir should be started without waiting for CSF PCR.[15] In AE, by contrast, temporal epileptiform activity reflects the predilection of antibodies such as LGI1 and CASPR2 for mesiotemporal circuits.[16] The PLEDs we recorded in one AE patient (Figure 2) are also a reminder that prolonged EEG monitoring is worthwhile in the ICU setting.[15]

Functional outcomes at discharge favored the AE group (median mRS score of 1 vs. 2). Two factors plausibly contributed to this: the generally favorable response of AE to early immunotherapy and the fulminant course of HSV encephalitis, which in some patients required prolonged ventilatory support.[17]

Study Limitations

The study has several limitations. Its retrospective design and a relatively small sample size limit the statistical power and generalizability of the findings. In addition, some CSF, MRI, and EEG data were incomplete or were obtained at outside institutions prior to transfer. Accordingly, the observed differences between AE and VE should be interpreted cautiously. Larger prospective multicenter studies with standardized diagnostic and EEG protocols will be necessary to validate these observations.

CONCLUSION

HSV-predominant VE in our cohort was characterized by more pronounced CSF inflammation and a greater need for intensive care, while AE more often presented with psychiatric symptoms at onset, limbic involvement on MRI, and temporal epileptiform discharges on EEG. Bringing clinical, CSF, imaging, and EEG findings together early — rather than waiting for definitive laboratory results — can help guide the differential diagnosis and inform empirical management decisions.

Ethics

Ethics Committee Approval: Ethical approval was granted by University of Health Sciences Türkiye, Bursa City Hospital Scientific Research Ethics Committee (approval no: 2026-07/3, date: 01.04.2026).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Ö.K., Ş.Ş., Concept: M.M.Ç., Ö.K., Design: M.M.Ç., Ö.K., Ş.Ş., Data Collection or Processing: M.M.Ç., Ş.Ş., Analysis or Interpretation: M.M.Ç., Ö.K., Ş.Ş., Literature Search: M.M.Ç., Ş.Ş., Writing: M.M.Ç., Ö.K., Ş.Ş.

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