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Autoimmune Encephalitis and Musicogenic Epilepsy: A Case of GAD65 Antibody-Associated Seizure

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ABSTRACT

Musicogenic epilepsy (ME) is a rare form of reflex epilepsy with a prevalence of 1 in 10,000,000. Recent research suggests a potential link between ME and autoimmune encephalitis, particularly involving glutamic acid decarboxylase 65-isoform (GAD65) antibodies. A 48-year-old female presented with a one-year history of music-triggered seizures. Her episodes were characterized by an initial aura followed by unresponsiveness and oral automatisms. Electroencephalography revealed abnormalities in the left anterior temporal lobe and temporal leads. Laboratory studies showed positive anti-GAD65 antibodies. The patient was treated with a combination of antiepileptic medication (Lamotrigine) and corticosteroids and intravenous immunoglobulin. This case contributes to the growing evidence supporting an association between ME and autoimmune mechanisms, particularly GAD65 antibody-mediated autoimmunity. It highlights the importance of screening autoimmune factors in ME patients and highlights the need for further research into targeted treatment strategies.

1 | Background

Epilepsy is a neurological condition characterized by recurrent, unprovoked seizures. While many epileptic seizures arise spontaneously, some are triggered by certain stimuli like stress, light, or music [1]. Musicogenic epilepsy (ME), an uncommon type of epilepsy with a prevalence rate of 1 in 10,000,000 people, is specifically induced by musical stimuli, highlighting the intricate interaction between auditory processing and neural excitability. The pervasive nature of music in everyday life renders ME particularly challenging for individuals affected [2].

The temporal lobes, located just above the ears, play a pivotal role in auditory perception and music comprehension. In ME, it is believed that exposure to specific musical stimuli leads to abnormal electrical activity within the auditory pathways of the temporal lobe, leading to a seizure [3].

The precise etiology of ME remains controversial. However, recent research has suggested a potential link between ME and autoimmune encephalitis (AE). AE is an autoimmune disorder characterized by the aberrant targeting of healthy brain cells by the immune system. Glutamic acid decarboxylase 65-isoform (GAD65) is a crucial enzyme for brain function, and the presence of GAD65 antibodies in the blood or cerebrospinal fluid can serve as a biomarker for AE. Studies have shown that a significant proportion of patients with ME tested positive for GAD65 antibodies, suggesting a potential autoimmune mechanism underlying some cases of ME [4].

Summary

- This case highlights musicogenic epilepsy as a rare presenting manifestation of autoimmune encephalitis associated with anti-GAD65 antibodies.
- Recognition of this association is essential as early identification and immunotherapy can improve outcomes.
- This report emphasizes the importance of autoimmune screening in unusual seizure presentations.

This case report presents a unique instance of a patient with ME who tested positive for GAD65 antibodies. This article aims to shed light on the underlying mechanisms linking musicogenic seizures and GAD65 antibody positivity, contributing to the deeper understanding of this uncommon epilepsy type.

2 | Case History

A 48-year-old woman is presented to a neurological clinic with a one-year history of abnormal movement episodes after playing music. The most recent episode occurred while listening to romantic music, during which she initially experienced crying followed by a specific aura of right upper extremity heat sensation. Subsequently, she developed forward staring, unresponsiveness, and motionlessness. Previous episodes were notable for oral automatisms. The seizures typically lasted 45 s and were accompanied by post-ictal amnesia. She is under maintenance treatment of Lamotrigine 100 mg twice a day for the past 1 year. Her family history was positive for seizure disorder in one of her eight siblings. She was married and employed and fully independent for routine daily activities. She had no history of any type of medical disorders and central nervous system disease like meningitis, febrile seizure, or head trauma. She had no history of smoking or drug abuse. In the physical examination, she had a pulse rate of 84 beats per min, a respiratory rate of 12 breaths per min, blood pressure of 113/64 mmHg, and body temperature of 36.4°C. Neurological examination showed normal muscle tone. The muscle force is 5/5 in all muscle groups, and deep tendon reflexes were normal. Gait and psychiatric examinations were unremarkable.

3 | Investigations

Patient was admitted to the neurology ward and underwent some lab tests and magnetic resonance imaging (MRI) and ictal brain perfusion single photon emission computed tomography scan with a computed tomography scan (SPECT–CT) and electroencephalography (EEG) with provocation procedures. All lab results were in the normal range. Interictal SPECT–CT showed local hyperperfusion in the left anterior temporal lobe. Moreover, in EEG with provocation, in the interictal phase there is a Frequent left temporal 3–4 Hz sharp/sharp and slow max T1T3 repeating every 10–20 min. Furthermore, Occasional right temporal 4 Hz sharp/sharp and slow max T2 repeating every 1–2 h. Also, Intermittent left temporal irregular/rhythmic delta slowing max T1T3 60% is seen. An intermittent right temporal irregular rhythmic delta slowing Max F8T2 30% is reported. In addition, 4 s after the aura onset of ictal EEG started as left temporal LPDs max T1, T3 consisted of 5 Hz sharp waves with an inter-discharge

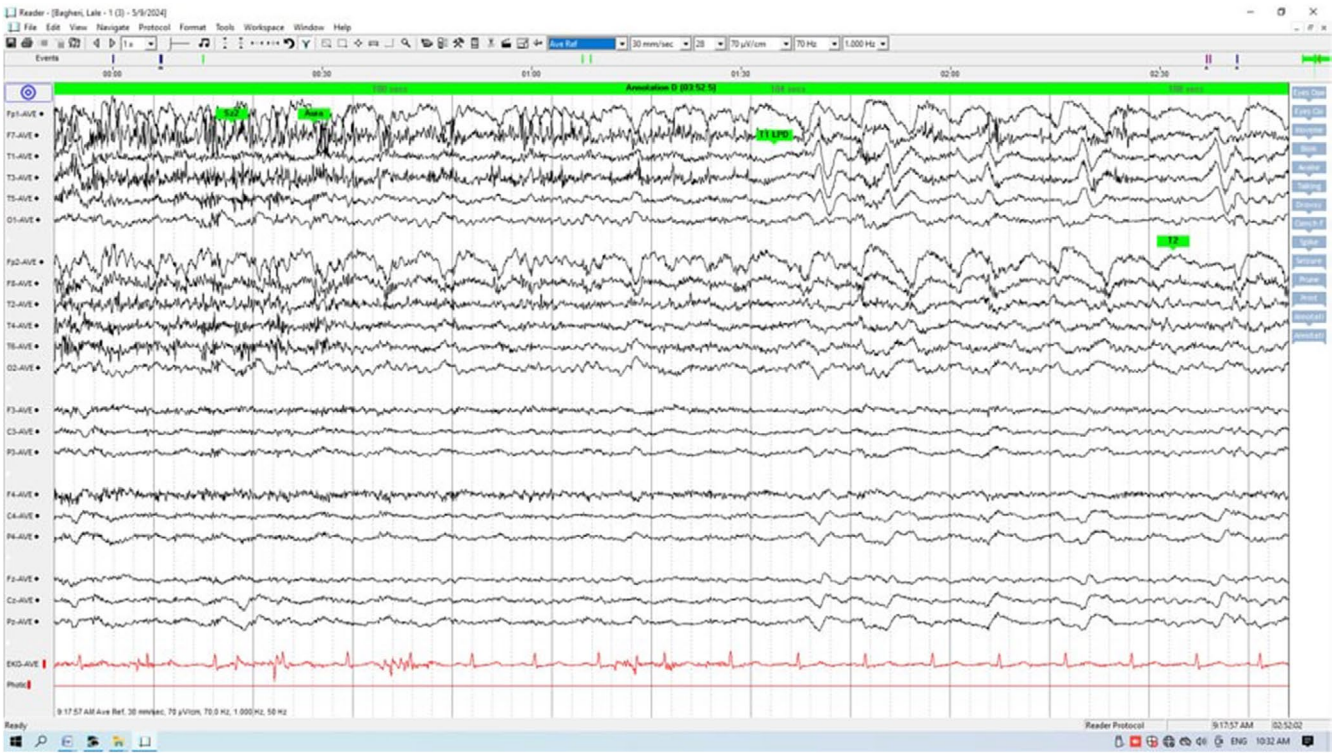

FIGURE 1 | Bipolar montage. seizure began 5 s after the patient's habitual aura, with periodic left temporal discharges starting at the eighth second. By the twelfth second, it had evolved to the right temporal region.

interval of 2 s evolved to high-voltage sharply contoured 5 Hz theta waves. Spreading to the right temporal was revealed after 3 s and F3 was involved after 10 s as rhythmic 6 Hz theta activity (Figures 1–3). As well, her heart rate did not change.

The highly probable diagnosis for the patient based on clinical workup is ME in the left anterior temporal lobe. Because of the high correlation of ME and GAD65 activity, GAD65 antibody tests were done, and the result showed a quantity of 57.

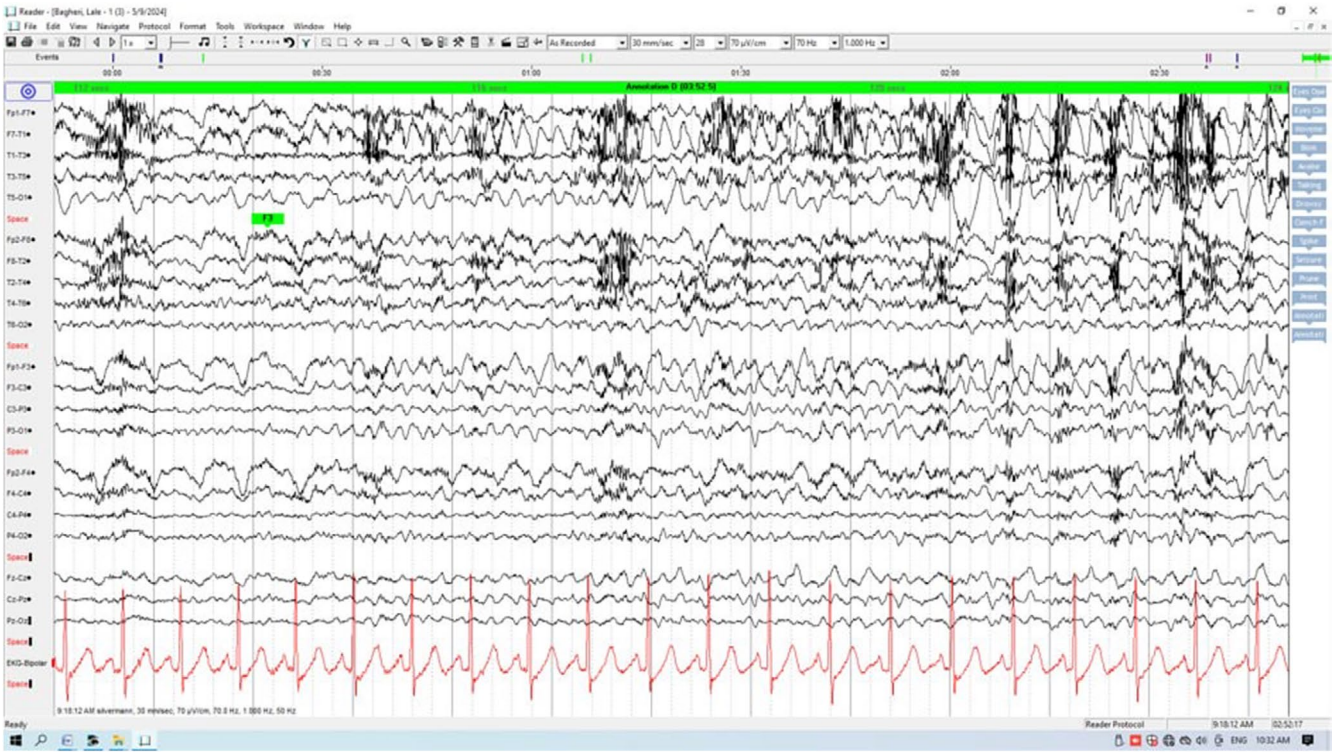

FIGURE 2 | Bipolar montage. Evolution in frequency and morphology is evident in the left temporal region. At the third second, a location evolution occurs with involvement of the right frontal region. Subsequently, generalized sharply contoured rhythmic theta waves with a frequency of 5–6 Hz persist.

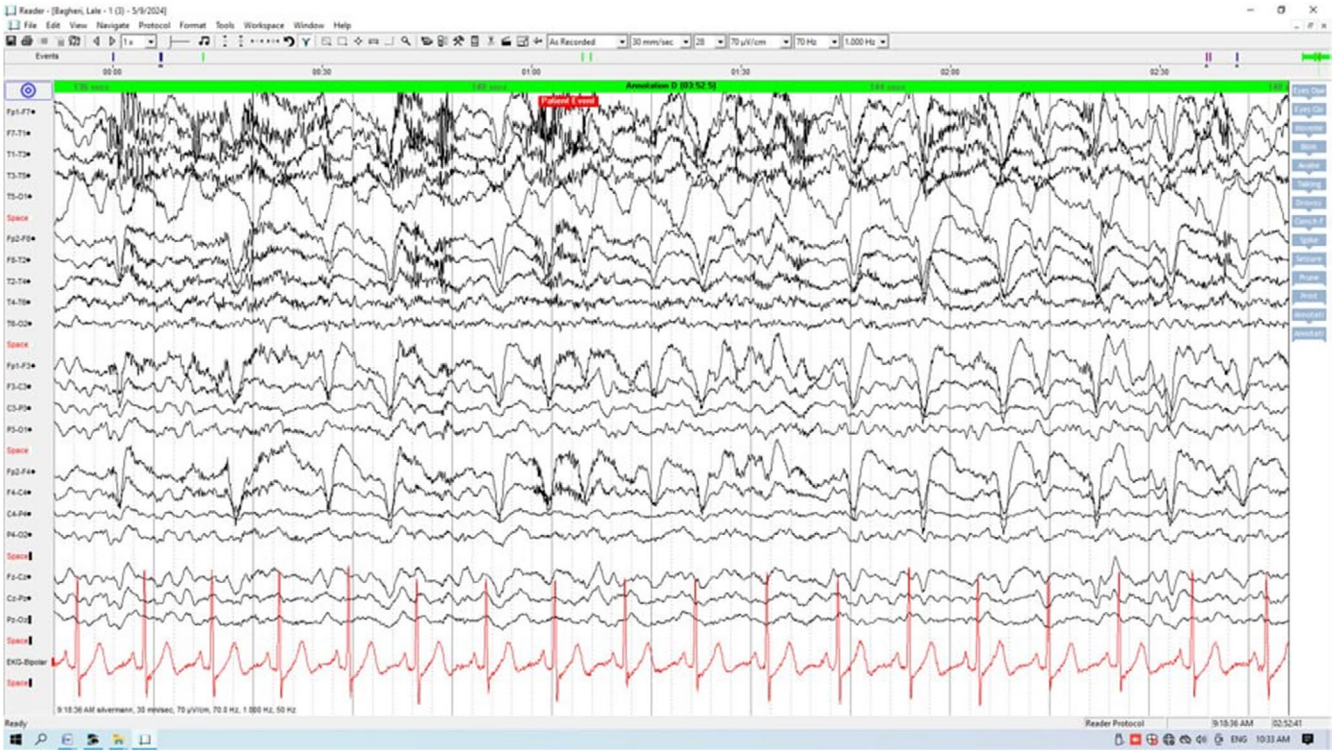

FIGURE 3 | Bipolar montage. The seizure terminates at 2 s. Slow waves persist in the left temporal region in the postictal period.

4 | Conclusion and Treatment

Based on AE diagnosis, she underwent a 5-day period of 1 mg methylprednisolone once daily. Because there has not been any improvement, intravenous immunoglobulin (IVIG) started for the patient by a dose of 0.4 mg/kg for 5 days. By improvement of lab tests and patient clinical evaluation, the patient was discharged by administration of Lamotrigine 100 twice a day, Clobazam 10 twice a day, and Azathioprine 50 twice a day. Also, bridging therapy continued until the Azathioprine reached proper plasma concentration.

5 | Discussion

This case report provides a unique instance of musicogenic epilepsy (ME) in a 48-year-old woman with positive GAD65 antibodies, suggesting a potential autoimmune component to her condition. The patient's characteristics of seizures triggered by music, coupled with characteristic EEG and ictal SPECT–CT findings, align with the typical features of ME, while the GAD65 antibody positivity adds an intriguing aspect to the case.

ME is an uncommon form of reflex epilepsy, characterized by seizures induced by musical stimuli with an estimated prevalence of 1 in 10,000,000 [2]. The patient's description of experiencing an aura, followed by impaired awareness and oral automatisms, is consistent with focal motor seizure originating from the temporal lobe. This aligns with the current understanding of ME, which often involves the temporal lobe auditory pathways [4]. Also, triggering of patient seizures by romantic music, highlight the role of the limbic system and some areas of the temporal lobe. The ictal SPECT–CT results showing local hyper perfusion in the left anterior temporal lobe, coupled with the ictal EEG which showed seizure onset zone in left mid-temporal region. This is consistent with previous studies that have implicated the temporal lobe in ME cases [2]. Of particular interest in this case is the positive GAD65 antibody test. Glutamic acid decarboxylase 65-isoform (GAD65) is an enzyme crucial for the synthesis of γ-aminobutyric acid (GABA), the primary inhibitory neurotransmitter in the central nervous system. The presence of GAD65 antibodies suggests a potential autoimmune mechanism underlying this patient's ME that was ignored in previous case reports of ME [3]. In Recent years, research has proposed a link between ME and autoimmune encephalitis, with several case reports and small studies demonstrating GAD65 antibody positivity in ME patients [5]. The presence of these antibodies may lead to decreased GABA synthesis, resulting in neuronal hyperexcitability and lowered seizure threshold [6]. This could explain the patient's susceptibility to seizures triggered by musical stimuli.

The patient's positive family history of seizures in one sibling raises the question of a potential genetic predisposition to epilepsy. However, the late onset of seizures at 47 years of age and the specific triggering by music suggest that the autoimmune component may have played a crucial role in the development of ME in this case.

Therapeutic approaches in this case should take into account both the epileptogenic and potential autoimmune mechanisms. Although the patient's focal seizures showed a partial response to Lamotrigine, the addition of immunotherapy would be beneficial due to the GAD65 antibody positivity [5]. Options such as intravenous immunoglobulins, corticosteroids, or other immunosuppressive agents could be considered, although their efficacy in GAD65 antibody-associated epilepsy remains a subject of ongoing research [7].

In conclusion, this case contributes to the expanding evidence-based linking of musicogenic epilepsy with autoimmune mechanisms, particularly GAD65 antibody-mediated autoimmunity. It emphasizes the importance of autoimmune screening in adult-onset reflex epilepsies and suggests potential therapeutic implications. Further research is warranted to elucidate the precise pathophysiological mechanisms and develop targeted treatment protocols for this distinct subset of ME patients.

Author Contributions

Ali Mohammadi-Asl: writing – original draft. **Amir Reza Bahadori:** methodology, writing – original draft, writing – review and editing. **Iman Sabzgolin:** conceptualization, methodology. **Afshan Davari:** methodology. **Mohammad Razmafrooz:** methodology. **Abbas Tafakhori:** conceptualization. **Mehrdad Sheikhvatan:** writing – review and editing. **Sara Ranji:** conceptualization, writing – review and editing.

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The authors have nothing to report.

Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

If supporting data is needed, contact the corresponding author.

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