CASO CLÍNICO/CASE REPORT

# When Seizures Signal the Heart: Diagnosing Brugada Syndrome in a Neurological Presentation

## Quando as Crises Epiléticas Sinalizam o Coração: Diagnóstico da Síndrome de Brugada numa Apresentação Neurológica

Bárbara Lage Garcia [1,*]; Emídio Mata [1]; Lucy Calvo [1]; António Lourenço [1]

1-Serviço de Cardiologia, Unidade Local de Saúde do Alto Ave, Guimarães, Portugal

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**Abstract**

Brugada syndrome is an inherited cardiac channelopathy associated with sudden cardiac death, particularly during sleep, and characterized by a distinctive electrocardiographic pattern. Emerging evidence suggests overlap with epilepsy due to shared ion channel dysfunction. Differentiating seizures from arrhythmic syncope remains clinically challenging.

A 30-year-old woman presented with a sleep-related motor paroxysmal event. She had a family history of sudden cardiac death and a prior similar event. ECG prompted an ajmaline challenge revealing a type 1 Brugada pattern. A subcutaneous implantable cardioverter-defibrillator was implanted. During follow-up, the patient experienced a recurrent episode of loss of consciousness, without documented arrhythmia. A spontaneous type 1 Brugada pattern was subsequently observed during treadmill cardiac stress testing, though no additional events occurred thereafter.

This case highlights the overlap between Brugada syndrome and epilepsy and its diagnostic complexity, underscoring the need for ECG screening in seizure-like presentations and the importance of multidisciplinary evaluation.

**Resumo**

A síndrome de Brugada é uma canalopatia cardíaca hereditária associada à morte súbita cardíaca, sobretudo durante o sono, com padrão eletrocardiográfico distinto. Evidência crescente sugere uma sobreposição com epilepsia, por disfunção partilhada dos canais iónicos. A distinção clínica entre crises epiléticas e síncopes disrítmicas continua um desafio.

Uma mulher de 30 anos apresentou-se com episódio motor paroxístico relacionado com o sono. Apresentava antecedentes familiares de morte súbita e episódio semelhante prévio. O ECG motivou um teste de provocação com ajmalina, revelando padrão Brugada tipo 1. Foi implantado um cardio-desfibrilhador subcutâneo. Durante o seguimento, apresentou nova perda de consciência, sem documentação de arritmias. Posteriormente, foi identificado um padrão espontâneo de Brugada tipo 1 durante a prova de esforço, sem ocorrência de novos eventos.

Este caso realça a sobreposição entre síndrome de Brugada e epilepsia e a complexidade diagnóstica, reforçando a importância do rastreio com ECG em crises epiléticas e avaliação multidisciplinar.

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***Autor Correspondente / Corresponding Author:**
Bárbara Lage Garcia
Serviço de Cardiologia,
Unidade Local de Saúde do Alto Ave,
Rua dos Cutileiros, Creixomil
4835-044 Guimarães, Portugal
barbara1234@live.com.pt

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## Introduction

Brugada syndrome (BrS) is an inherited cardiac channelopathy characterized by a distinct electrocardiographic (ECG) pattern and an increased risk of sudden cardiac death (SCD) due to ventricular arrhythmias, particularly in structurally normal hearts and while sleeping.[1,2]

It was first described in 1992, with an estimated prevalence of ~1:2000.[2] It is estimated that BrS is responsible for up to 12% of all SCD and up to 50% of SCD in patients without structural heart disease.[2]

Emerging evidence suggests an association between BrS and epilepsy, as both involve dysfunctional ion channels, raising the possibility of a shared systemic channelopathy rather than distinct entities.

Notably, epilepsy carries a significantly increased risk of sudden unexplained death in epilepsy (SUDEP), with up to a 24-fold risk, compared with the general population.[3]

Clinically, differentiating seizures from syncope remains challenging due to overlapping features like transient loss of consciousness (TLOC), convulsive movements, or postictal confusion. As such, enhanced awareness of BrS is essential to ensure accurate diagnosis, appropriate risk stratification, and timely intervention, potentially preventing fatal outcomes.

We describe a 30-year-old woman who presented with a seizure-like episode and was concurrently diagnosed with both BrS and epilepsy.

## Case Report

A 30-year-old female patient experienced a nocturnal episode during the first third of the night, without preceding aura or prodromal symptoms and characterized by sudden arousal from sleep, head turning, ocular retroversion and shallow breathing, followed by repetitive jerky movements. No lateralizing signs or asymmetries of motor activity were documented.

The witnessed episode lasted approximately one minute, during which she remained unresponsive. A postictal state with confusion and prostration lasted for about 2 minutes before she returned to baseline. There was no evidence of sphincter incontinence, and the patient denied fever or any other associated symptoms.

She reported poor sleep quality and reduced sleep duration over the past week, with no history of alcohol or substance use.

A similar episode had occurred in the month prior, with a witnessed sudden episode of TLOC and suspected generalized tonic-clonic seizure, but with a longer postictal phase, for which she had been started on levetiracetam, with outpatient follow-up with Neurology.

The patient had a family history of SCD in a second-degree maternal cousin at the age of 40. Her usual medication included levetiracetam 500 mg twice daily and an oral contraceptive.

On admission to the emergency department, the patient was alert and responsive, with stable vital signs and no fever. There were no focal neurological deficits or signs of meningism. Oral examination revealed evidence of tongue biting. Initial laboratory tests were unremarkable except for elevated myoglobin, and cranial computed tomography (CT) was normal.

ECG changes suggestive of Brugada pattern prompted cardiology consultation. While the baseline ECG was non-diagnostic (**Fig. 1**), ajmaline challenge unmasked a classic type 1 Brugada pattern with coved ST elevation ≥2 mm. No prior ECG was available for comparison. Transthoracic echocardiography revealed no abnormalities.

The patient was then transferred to the Cardiology department for further monitoring. Continuous telemetry monitoring during the hospital stay showed no arrhythmic events or seizure recurrence. An electroencephalogram was performed under levetiracetam therapy and showed no epileptiform abnormalities. Cranial magnetic resonance imaging (MRI) was also unremarkable.

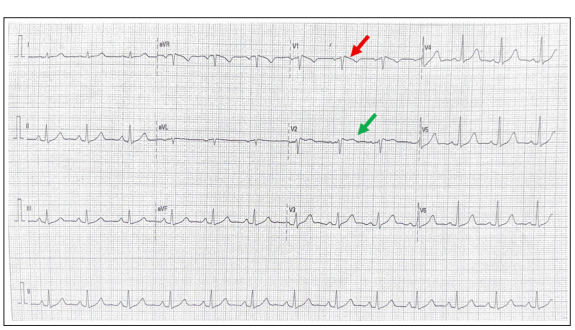

**Figure 1.** Twelve lead electrocardiogram using standard leads, upon admission to the emergency.

Given the drug-induced Brugada pattern, possible cardiogenic syncope mimicking seizure activity, and a Shanghai score[4] of 4.5 indicating probable diagnosis of BrS, a multidisciplinary team recommended subcutaneous implantable cardioverter-defibrillator (ICD) implantation, which occurred without complications. The

discharge regimen consisted of levetiracetam 1000 mg twice daily, with scheduled neurology follow-up.

One month post-discharge, the patient returned to the emergency department following a new episode of TLOC occurring during sleep, in the first third of the night, lasting approximately 2 minutes and resolving spontaneously. Notably, there was no postictal phase, tongue biting, or sphincter incontinence, and no associated palpitations, chest pain, dyspnea, headache, nausea or vomiting. ICD interrogation revealed no dysrhythmic events, supporting a probable diagnosis of a seizure episode and prompting optimization of antiepileptic therapy.

During subsequent follow-up, the patient developed a spontaneous type 1 Brugada pattern during treadmill stress testing (**Fig. 2**), providing further evidence and reinforcing the BrS diagnosis. No exertional arrhythmias were recorded. Genetic testing yielded inconclusive results, identifying no clearly pathogenic variants but detecting a heterozygous variant of uncertain significance in the *SCN5A* gene (*c.4498C>G, p.Leu1500Val*).

This case exemplifies a complex diagnostic challenge between neurological and cardiac disorders, where TLOC may reflect either epileptic or arrhythmic events. It underscores the importance of ECG evaluation in seizure presentations, particularly to screen for BrS given its potential overlap with epilepsy.

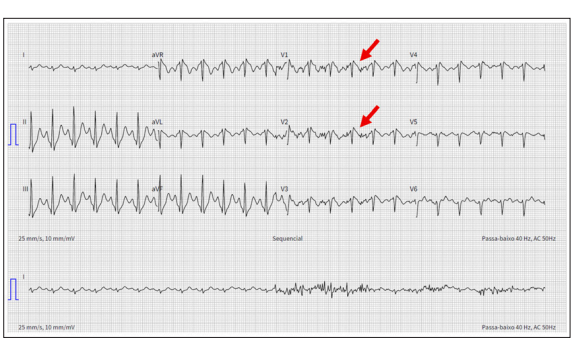

**Figure 2.** Twelve lead electrocardiogram at treadmill cardiac stress testing, showing a spontaneous type 1 Brugada pattern in modified intercostal positions.

## Discussion

BrS is an autosomal dominant arrhythmogenic disorder characterized by a distinctive electrocardiographic pattern: coved-type ST segment elevation ≥2mm with a negative T-wave, in the right pre-cordial leads.[1]

Epilepsy, in contrast, is a neurological disorder characterized by abnormal neuronal excitability leading to unprovoked seizures.[5]

Though traditionally considered distinct entities, there is increasing evidence of pathophysiological overlap between BrS and epilepsy, particularly in cases where both disorders may be linked to mutations in ion channel genes.

Although other genetic variants have also been implicated in BrS, the most reported until date, remains mutations on the *SCN5A* gene, which encodes voltage-gated sodium channels, implicated in ~20% of cases.[1] It involves primarily loss-of-function, which results in an imbalance in inward sodium currents and calcium currents and/or outward potassium currents during the early phase of the action potential, creating an arrhythmogenic substrate located in the anterior aspect of the right ventricular outflow, exacerbated by fever and an increase in vagal tone.[6]

The *SCN5A* gene, while primarily expressed in cardiomyocytes, is also present in the limbic regions of the brain, including the piriform cortex, an area with a low threshold for epileptogenesis.[7] Supporting this, a rat model of temporal lobe epilepsy demonstrated increased *SCN5A*/*Nav1.5* expression in the brain, including the hippocampus.[8] Additionally, a reported family carrying the *SCN5A-p.W1095X* mutation exhibited both BrS and epilepsy, reinforcing the concept of a shared cardiocerebral channelopathy.[9] This molecular overlap raises the possibility that certain mutations could produce phenotypic features of both BrS and epilepsy, especially in cases where a variant of uncertain significance is identified, as occurred here with the *SCN5A c.4498C>G (p.Leu1500Val)* variant.

Although direct causal evidence linking SCN5A mutations to epilepsy remains lacking, this overlap has been increasingly implicated in the context of SUDEP, defined as a sudden, non-traumatic, and unexplained death in individuals with epilepsy. Recognized risk factors include frequent and recent seizures, particularly nocturnal generalized tonic–clonic seizures. The underlying pathophysiology is likely multifactorial, involving respiratory dysfunction, autonomic instability, and cardiac mechanisms. Notably, variants in cardiac arrhythmia-related genes, including SCN5A, have been identified in SUDEP cases, supporting the hypothesis that underlying channelopathies may predispose to malignant arrhythmias during or following seizures, thereby contributing to seizure-related mortality.[7]

A key challenge of this overlap is differentiating syncope from epileptic seizures, as both share overlapping clinical features.

Both can present with TLOC, abnormal movements, incontinence, and postictal confusion, which can complicate early clinical distinction, particularly when the event is unwitnessed or occurs during sleep. Nevertheless, careful semiological assessment may provide important diagnostic clues. Epileptic seizures are more frequently associated with a preceding aura (including sensory, psychic, or autonomic symptoms), lateral tongue biting, sustained and rhythmic tonic-clonic movements, and a prolonged postictal phase with confusion, fatigue, and amnesia. Conversely, syncope is often preceded by prodromal symptoms of global cerebral hypoperfusion such as lightheadedness, nausea, diaphoresis, visual blurring, or auditory changes. During syncope, transient motor phenomena may occur, including brief myoclonic or tonic jerks, which reflect acute cerebral hypoperfusion. The duration of TLOC is generally short, with rapid, complete and spontaneous recovery and minimal or absent post-event confusion. In contrast, epileptic seizures are more often abrupt in onset, may occur without identifiable triggers and are followed by a clearly defined postictal phase.[10]

Eyewitness reports and video monitoring can be critical, as can the presence or absence of postictal features. Rarely, seizures may induce ictal asystole, further blurring the distinction. Conversely, cerebral hypoperfusion during syncope may provoke convulsive activity, resulting in a convulsive syncope, which can mimic epilepsy. This phenomenon is not epileptic in origin and reflects brainstem disinhibition due to acute global hypoxia rather than cortical epileptogenic activity.[10]

This case illustrates a syncopal episode with features initially suggestive of a neurological origin, but with atypical elements that raised suspicion of an underlying arrhythmic cause.

The 12-lead ECG played a pivotal role by revealing abnormalities that prompted a pharmacological challenge with ajmaline, which unmasked a type 1 Brugada pattern. This diagnosis was later reconfirmed by the spontaneous appearance of a type 1 pattern during exercise testing.

It is important to note that although a 12-lead ECG is essential for identifying Brugada patterns, particularly the type 1 pattern in right precordial leads, as these changes can be transient and concealed, as seen in this case. Provocative testing with sodium channel blockers such as ajmaline may be required to unmask the phenotype. However, unlike pharmacologically induced patterns, spontaneous type 1 Brugada are more strongly associated with arrhythmic risk.[1]

Similarly, interictal electroencephalogram, though helpful in diagnosing epilepsy, is often normal, especially under antiepileptic treatment, which can suppress epileptiform discharges.[11]

About one-third of BrS patients present with syncope, which is associated with a fourfold increased risk of arrhythmic events. Despite thorough history-taking, the cause remains unclear in up to 30% of cases.[12]

Notably, some antiarrhythmics, anesthetic agents, excessive alcohol content or fever are potential triggers to exacerbate the type 1 pattern and trigger ventricular arrhythmias, such as ventricular fibrillation.[12] In fact, certain antiepileptics, particularly those that block sodium or calcium channels (like carbamazepine, lamotrigine, phenytoin) may also trigger cardiac arrhythmias.[13] This makes drug selection critical in patients with dual concerns of seizure and arrhythmic risk.

ICD is the only proven therapy to prevent SCD but is not indicated in all patients with BrS.[12] If the patient has purely isolated epilepsy, inappropriate shocks due to misclassification of seizures as ventricular arrhythmias must be avoided. Hence, in cases of diagnostic uncertainty, careful multidisciplinary evaluation is crucial.

Since the patient had induced type 1 Brugada pattern, with suspected arrhythmic syncope, nocturnal agonal respiration and a family history of SCD at a young age, the diagnosis of BrS should be considered.[12] A family history of early sudden death, as in our patient, raises concern for inherited arrhythmia syndromes and should weigh into risk stratification and consideration of ICD therapy, even in the absence of clear arrhythmic events. As per European Society of Cardiology guidelines, ICD implantation should be considered in this case, since there was suspicion of cardiac syncope/nocturnal agonical respirations, with a positive ajmaline test.[12]

As for genetic testing, even when the identified variant is of uncertain significance, the absence of functional studies or strong segregation data leaves its pathogenicity unclear, thereby warranting cascade screening of relatives. This highlights the limitations of current genetic panels and reinforces the need for comprehensive

genetic counselling to appropriately guide patients and families, particularly in the context of these findings.

Several published case reports have described BrS presenting as refractory epilepsy or misdiagnosed seizures,[14-17] highlighting the importance of considering cardiac causes in atypical or treatment-resistant epilepsy or even as a coexisting condition. This case contributes to this growing body of literature.

Even in patients presenting with classic seizure presentations, clinicians should routinely perform an ECG in the initial work-up. Epileptic seizures may represent the initial manifestation of BrS, particularly in cases where no clear neurological etiology is identified or when there is a family history of SCD. As BrS can mimic or coexist with epilepsy, early detection through ECG screening is critical to avoid misdiagnosis, ensure appropriate risk stratification, and prevent potentially fatal arrhythmic events.

## Conclusion

This case highlights the diagnostic complexity in distinguishing between epileptic and arrhythmic causes of transient loss of consciousness, particularly in the context of overlapping clinical features between BrS and epilepsy.

Given the shared pathophysiological pathways, especially involving ion channel dysfunction, clinicians should maintain a high index of suspicion for BrS in patients with atypical seizures or a family history of sudden cardiac death. Early identification and appropriate risk stratification are essential to prevent potentially fatal outcomes. Routine ECG screening in patients with new-onset seizures may be a crucial step in avoiding misdiagnosis and guiding effective, life-saving interventions. ■

**Contributorship Statement / Declaração de Contribuição**

BLG and EM: Contribution: Participation in the drafting and preparation of the article, as well as in the final and critical review of the manuscript.

LC: Participation in the drafting of the manuscript, review of drafts, and critical review of the content.

AL: Responsible for the critical review of the content and approval of the final version.

All authors approved the final version of the manuscript for publication and assume responsibility for all aspects of the work, ensuring the accuracy and integrity of the data presented.

BLG e EM: Contribuição: Participação na redação e elaboração do artigo, bem como na revisão final e crítica do manuscrito.

LC: Participação na redação do manuscrito, revisão de versões e revisão crítica do conteúdo.

AL: Responsável pela revisão crítica do conteúdo e aprovação da versão final.

Todos os autores aprovaram a versão final do manuscrito para publicação e assumem responsabilidade por todos os aspetos do trabalho, garantindo a exatidão e a integridade dos dados apresentados.

**Responsabilidades Éticas**

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