Ictal syncope or isolated syncope? A case report highlighting the overlap

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Background
Ictal bradyarrhythmia is a rare condition defined by temporal lobe epilepsy resulting in bradycardia or asystole and can result in syncope. This needs to be differentiated from isolated syncope in patients with seizure disorder, as treatment strategies differ.

Case summary
A 50-year-old female with well-controlled temporal epilepsy and a 20-year seizure-free period presented to her neurologist with abrupt onset of sudden drop attacks thought to be ictal events with potential underlying ictal bradyarrhythmia and was initially treated with escalation of anticonvulsant therapy. However, her workup was consistent with a diagnosis of cardiac syncope. She subsequently underwent successful insertion of a pacemaker, with no recurrence of her presenting episodes at a 13-month follow-up.

Discussion
Ictal syncope and isolated syncope may share a common terminal pathway and may have similar presenting symptoms. In patients with known seizure disorder, loss of consciousness may be attributable to epileptic events, ictal syncope, or isolated syncope—which can be difficult to differentiate. This case highlights the ambiguous nature of such episodes and the importance of simultaneous electroencephalogram/electrocardiogram monitoring, as this can have implications on treatment.

Keywords
Ictal bradyarrhythmia • Cardiac pacing • Neurology • Electrophysiology • Case report

Learning points
- Ictal bradyarrhythmia is a rare condition characterized by a causal relationship between an ictal event and a bradyarrhythmia episode, resulting in sudden drop attacks.
- This syndrome may be difficult to distinguish from isolated syncope. The absence of typical semiological features of epilepsy may be deceiving.
- Continuous electroencephalogram/electrocardiogram monitoring is required to adequately evaluate ‘sudden drop attacks’ in patients with known seizures, to avoid undertreating implicated arrhythmias.
**Introduction**

Ictal bradyarrhythmia, including asystole or bradycardia, is a rare condition with arrhythmic manifestations induced by epileptic episodes. Such events are most often associated with temporal lobe epilepsy and can result in syncope with associated injury or death. Episodes of sudden loss of consciousness in patients with known seizure disorder can present ambiguously and may be secondary to an epileptic event, ictal bradyarrhythmia, or isolated syncope. While anticonvulsant therapy is the first-line therapy for seizures and ictal bradyarrhythmia, it does not address independent underlying arrhythmias or isolated syncope.

**Timeline**

| Time                  | Event                                                                 |
|-----------------------|-----------------------------------------------------------------------|
| Five months before the presentation | Abrupt onset of ‘unusual’ sudden drop attacks                          |
| Initial presentation  | Recurrence of seizure activity was presumed, with up-titration of antiepileptic medication but no improvement |
| Within 1 month of presentation | Change of antiepileptic drugs from carbamazepine to brivaracetam     |
| Within 1 month of presentation | Electroencephalographic study shows sinus arrest and asystole before onset of seizures |
| One month after presentation | Insertion of a dual-chamber pacemaker                                |
| 13 months after presentation | No recurrences of the presenting events                             |

**Case presentation**

A 50-year-old female with a history of well-controlled focal epilepsy presented to her neurologist with new symptoms of recurrent ‘sudden collapse’. At the age of 30, the patient had been diagnosed with non-lesional temporal lobe epilepsy characterized primarily by episodes of tonic–clonic seizures preceded by a sensation of déjà vu. She had been started on carbamazepine at that time with excellent seizure control. Her medical history was positive for hypertension and dyslipidaemia. She also maintained a family history of cardiac disease, unspecified. The patient had not suffered from any seizures or syncopal events until 5 months before her presentation. She complained of ‘unusual’ episodes, witnessed by her husband, of sudden drop attacks with brief loss of consciousness and postural tone associated with urinary incontinence. The syncopal episodes occurred without warning and without an associated trigger. She sustained no significant injuries from her syncopal events. Her clinical examination and biochemical profile on blood work were unremarkable. Magnetic resonance imaging of the head did not reveal evidence of acute changes to explain her presentation. Her carbamazepine dose was escalated in an attempt to control these episodes but failed to result in any improvement. Her antiepileptic medication was then changed from carbamazepine 200 mg p.o. t.i.d. to brivaracetam 75 mg p.o. b.i.d., again with no improvement. The patient underwent a continuous video-electroencephalographic study to characterize these events further.

During observation in the epilepsy unit, the patient was observed to have an episode of sudden loss of consciousness and urinary incontinence without any tonic–clonic activity or a prominent postictal state. Continuous electrocardiogram (ECG) monitoring revealed a concurrent episode of asystole lasting ~20 s, followed by sinus bradycardia at a rate of 20–30 beats/min (Figure 1). There was no evidence of seizure activity on the electroencephalogram (EEG) preceding, during or following this event. The patient recovered and was subsequently admitted to the coronary care unit. On examination, her heart rate was 82 per minute, blood pressure was 128/74 mmHg, 86 kg, body mass index 32.1, and the systems examination was normal. She was recorded to have two episodes of symptomatic Mobitz type I atrioventricular (AV) block. Overall, her findings were consistent with isolated symptomatic bradyarrhythmia rather than ictal bradyarrhythmia or seizures. An echocardiogram was completed, which did not reveal any abnormalities. She underwent the successful implantation of a dual-chamber pacemaker. Her device was programmed to AAi-DDD with lower and upper rates of 50–130. Paced AV delay was set to 220 ms, and sensed AV delay 200 ms. Rate drop response was programmed ‘on’ to both low rate and rate drop. At 13-month follow-up, the patient was symptom free with no recurrence of her presenting events. Interrogation of her pacemaker revealed atrial pacing at 15.2% and ventricular pacing at 11%, suggesting a bradyarrhythmia of atrial aetiology.

The patient was maintained on brivaracetam as her antiepileptic and was well tolerated. A decision was made not to switch back to her original anticonvulsant, carbamazepine, despite the non-ictal aetiology of her event. Carbamazepine exerts its therapeutic function through sodium channel blockade and can therefore theoretically affect depolarization currents within cardiomyocytes. Its use has been reported by the Food and Drug Administration (FDA) to be associated with AV block. As such, given the patients bradyarrhythmia, she was maintained on the alternative agent.

**Discussion**

Epileptic-seizure-induced cardiac arrhythmias are not uncommon but usually manifest as tachyarrhythmias. Ictal asystole is a rare phenomenon reported to occur in 0.002–0.4% of patients with epilepsy undergoing monitoring. These ictal bradyarrhythmias may be challenging to appreciate given that the clinical manifestations may be mistakenly attributed to the seizure. Moreover, distinguishing ictal syncope from neurally mediated reflex syncope may pose a challenge, particularly in patients with no known history of seizures, well-controlled seizures with no apparent triggers, or in unwitnessed events. Likewise, in patients with a known history of seizure activity, such episodes may be mistakenly attributed to underlying epilepsy or ictal arrhythmia and incorrectly treated by escalation of anticonvulsant therapy.

Risk factors for the occurrence of ictal bradyarrhythmia are largely unknown, although it appears that a female preponderance exists in patients with new-onset ictal bradyarrhythmia. The presence of
underlying cardiac disease does not appear to increase the risk of occurrence. \(^6\) The exact mechanisms driving the pathogenesis of this phenomenon are yet to be elucidated. However, the involvement of excessive vagal stimulation has been proposed. It is postulated that propagation of ictal activity from the temporal lobes to the adjacent insular cortex, or to brainstem autonomic reflex centres results in an ensuing ‘vagal storm’ that precipitates cardiac syncope. This event, under the proposed mechanism, operates as a self-terminating loop. Ictal activity precipitates bradyarrhythmia and vasodepression, which subsequently results in cerebral hypoperfusion and hypoxia. The hypoxia results in decreased cerebral activity, which in turn may terminate the seizure and release the inappropriate activation of the autonomic reflex centres. \(^6\) Ictal asystole does not always lead to ictal syncope. However, a strong association was found when the ictal-induced asystole lasted longer than 6 s. \(^7\)

In our case, the patient’s presentation was mistakenly classified as an ictal episode and possible ictal bradyarrhythmia and treated initially with escalation of antiepileptic therapy. This case highlights the ambiguous nature of syncope in patients with known seizure disorders and the overlap of ictal syncope with isolated syncope, given the shared terminal mechanism. Of note, the anoxic seizure activity noted was not associated with an epileptiform discharge. To the best of the authors’ knowledge, no association between epilepsy and a propensity for anoxic seizure activity has been described in the literature.

While antiepileptic therapy is the cornerstone of treating ictal syncope, it plays no role in the treatment of coincidental isolated syncope of cardiac aetiology. Thorough evaluation of epileptic patients with syncope is required to differentiate ictal syncope from isolated syncope. The role of pacemaker’s is yet to be strongly established in ictal syncope. In the absence of official guidelines on the prevention and management of ictal bradyarrhythmias, a general consensus exists amongst experts that prolonged pauses implicated in the loss of consciousness during these events may be a reasonable indication for implantation of a pacemaker device.\(^6,7\) A contention exists in that if the proposed mechanism of a vagal storm is in fact the primary driving mechanism of ictal bradyarrhythmia, a vasodepressor component to the loss of consciousness is unlikely to be responsive to cardiac pacing. A paucity of robust evidence exists for the use of cardiac pacing in the treatment of ictal asystole. However, in uncontrolled case reports, the seizure-related injury was noted to decrease substantially after the insertion of a pacemaker in patients with ictal asystole.\(^3,8\) Conversely, the role of permanent pacemakers in the treatment of cardiac syncope is well established.
**Conclusion**

Ictal syncope is a rare, underrecognized phenomenon that can be associated with significant morbidity in epilepsy. Epileptic events, ictal syncope, and isolated cardiac syncope may be difficult to differentiate and will require different targeted therapy. This case highlights the ambiguous nature of such episodes and the importance of simultaneous EEG/ECG monitoring.

**Lead author biography**

Dr. Yehia Fanous received his medical degree from the University of Toronto and is currently a senior internal medicine resident at the University of Western Ontario, Canada. He has interests in the fields of cardiac arrhythmia and device therapy.

**Supplementary material**

Supplementary material is available at European Heart Journal - Case Reports online.

**Slide sets**: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

**Consent**: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

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