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Fifty-second flat-line: A dramatic case of ictal asystole

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Introduction

Ictal asystole is a rare complication of refractory epilepsy. It is clinically significant given its potential connection to sudden unexpected death in epilepsy (SUDEP). We report here an observed 50-second episode of ictal asystole, and the subsequent clinical management of this patient.

Case report

A 31-year-old woman with a history of medically intractable epilepsy was admitted to the Epilepsy Monitoring Unit for evaluation ahead of potential resective epilepsy surgery. She had an extensive oncologic history most notable for a left chest Askin tumor at age 13 for which she underwent en bloc resection and 5400 cGy radiation to the chest wall. She was also treated with a regimen of ifosfamide, etoposide, vincristine, actinomycin-D, and cyclophosphamide. This course of chemotherapy was complicated by a left superior temporoparietal stroke from which she initially recovered with no residual deficits. The patient experienced her first seizure at age 26 and subsequently developed medically refractory epilepsy. Her seizures emanated from the left superior temporoparietal cortex, the region of her prior stroke.

On admission to the Epilepsy Monitoring Unit, the patient's antiseizure medications were tapered to facilitate capture of her stereotypic seizures. A complete blood count and comprehensive metabolic panel were normal. Review of baseline electrocardiogram (ECG) demonstrated sinus rhythm with a first degree atrioventricular block and a QTc interval of 485 milliseconds (Figure 1). Shortly after admission, the patient experienced 3 focal unaware seizures, which subsequently evolved into bilateral convulsive seizures, all recorded on continuous video, electroencephalogram (EEG), and ECG monitoring. During the second seizure in this cluster, she became cyanotic and lost consciousness. The semiology of this seizure as captured on video monitoring demonstrated right-sided head deviation and facial clonic movements, which evolved into a bilateral convulsive seizure lasting 60 seconds. The EEG correlate revealed evolving, slow ictal rhythmic activity over the left temporoparietal region that subsequently spread bilaterally. At 15 seconds following the resolution of the convulsive phase, telemetry monitoring demonstrated a short period of progressive sinus bradycardia, which gave way to 50 seconds of asystole. There was corresponding diffuse global attenuation of EEG activity during the postictal period. The patient then experienced spontaneous return of sinus bradycardia (Figure 2, Supplemental Video). Shortly following resolution of this episode, she again experienced 1 minute of seizure activity, during which she became bradycardic. Although the patient experienced additional seizures during this hospitalization, she had no further episodes of ictal bradycardia or asystole.

KEY TEACHING POINTS

- Ictal asystole is a rare cause of syncope in patients with medically refractory, temporal lobe epilepsy.
- Permanent pacemaker implantation should be pursued in all patients who have experienced an episode of ictal asystole lasting >6 seconds.
- Medically refractory epilepsy is a risk factor for both ictal asystole and sudden unexpected death in epilepsy (SUDEP), but there is no evidence to support ictal asystole as a direct cause of SUDEP.

KEYWORDS Bradyarrhythmia; Bradycardia; Cardiac arrest; Epilepsy; Seizure
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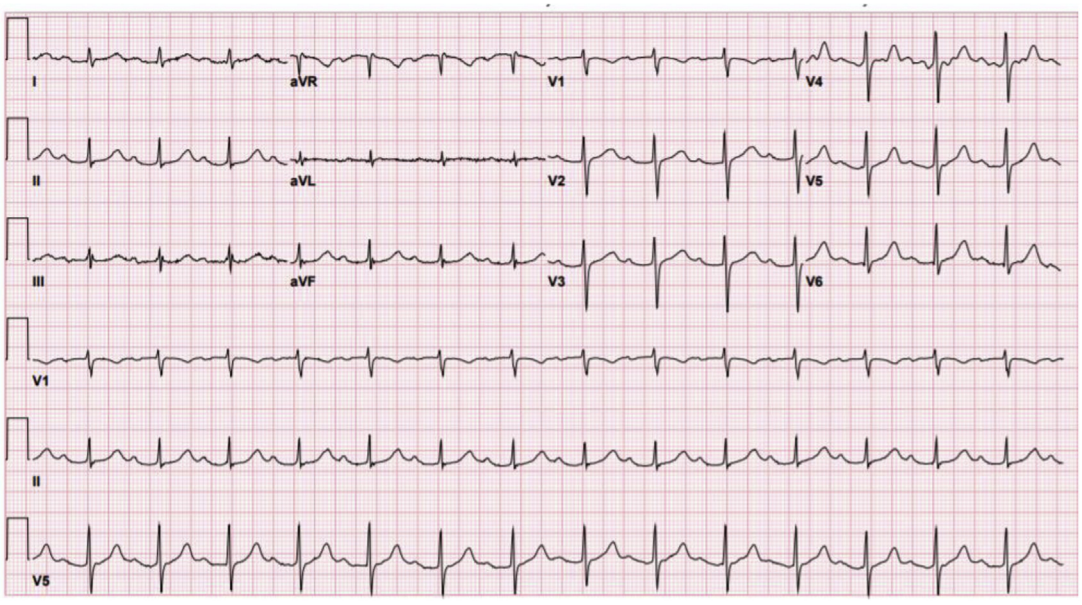

Figure 1 Baseline electrocardiogram demonstrating normal sinus rhythm, first-degree atrioventricular block with a PR interval of 256 ms, and a QTc interval of 485 ms.

The patient's seizures were initially treated with intravenous boluses of diazepam and levetiracetam. She was subsequently initiated on clobazam and restarted on her home levetiracetam and lacosamide. She experienced no further seizures on this medication regimen. The electrophysiology service was consulted. Transthoracic echocardiogram demonstrated a left ventricle ejection fraction of 60% and no valvular pathology. Given the patient's history of medically refractory epilepsy, prolonged period of ictal asystole, and high risk of SUDEP, she underwent implantation of a Medtronic (Minneapolis, MN) single-chamber pacemaker without complication. A single-chamber device was selected as the patient had minimal anticipated pacing needs. A leadless pacemaker is an appropriate consideration in this case, but at the time these devices were not yet approved for standard care.

A pacemaker device interrogation completed 3 months following implantation demonstrated that the patient's underlying rhythm was sinus with normal atrioventricular conduction and a ventricular pacing burden of $<0.1\%$ (VVI with the device's lower rate limit programmed at 50 beats per minute). In the months following this hospitalization, the patient underwent placement of a vagal nerve stimulator. Although she continued to experience seizures, she endorsed a reduction in the frequency and duration of these episodes following this procedure.

Discussion

Cardiac arrhythmias are often provoked by seizures. While sinus tachycardia is the most common seizure-associated arrhythmia, tachyarrhythmias and bradyarrhythmias as well as atrial and ventricular fibrillation can be associated with seizure activity.[1] Seizure-associated arrhythmias are of particular clinical importance given their potential contribution to SUDEP.[1]

Ictal asystole has an estimated prevalence of 0.2%–0.4% among seizure patients and occurs predominantly in young patients with a longstanding history of temporal lobe epilepsy refractory to ≥ 2 antiepileptic medications.[1,2] Episodes typically occur during the course of focal dyscognitive seizures, on average starting 30 seconds following onset of epileptic activity.[1] Ictal asystole is defined by an R-R interval >3 seconds, and previous case series have described a mean duration of 20 seconds, although there have been witnessed episodes lasting up to 96 seconds.[1] Ictal asystole lasting >6 seconds is strongly associated with syncope.[2] Identifying a syncopal episode during a seizure is challenging. While myoclonic jerks can be observed in both states, loss of tone favors syncope and can aid in identification of episodes of ictal asystole.[3] Continuous ECG is needed to definitely detect ictal asystole. ECG recordings preceding ictal asystole typically reveal a progressive bradycardia representing a possible neurocardiogenic mechanism characterized by vagal activation.[4] The exact pathophysiology of ictal asystole is debated, with some evidence suggesting that left temporal seizure activity may trigger asymmetrically distributed parasympathetic neuronal networks located in the adjacent insula and other hypotheses invoking overactivation of reflex pathways intended to counteract seizure-induced tachycardia.[5,6] The consequent loss of cerebral blood flow is thought to facilitate termination of epileptic activity.[7]

SUDEP is defined as a sudden, unexpected, nontraumatic, and nondrowning death in an epilepsy patient with or without evidence of seizure but excluding status epilepticus, in which autopsy does not identify a cause of death. It typically occurs in the postictal phase of a generalized tonic-clonic seizure and is characterized by respiratory dysfunction, arousal failure, and bradyarrhythmias.[8] SUDEP accounts for 8%–17% of deaths in epilepsy patients.[9] While many SUDEP risk factors have been identified, the most important of these is

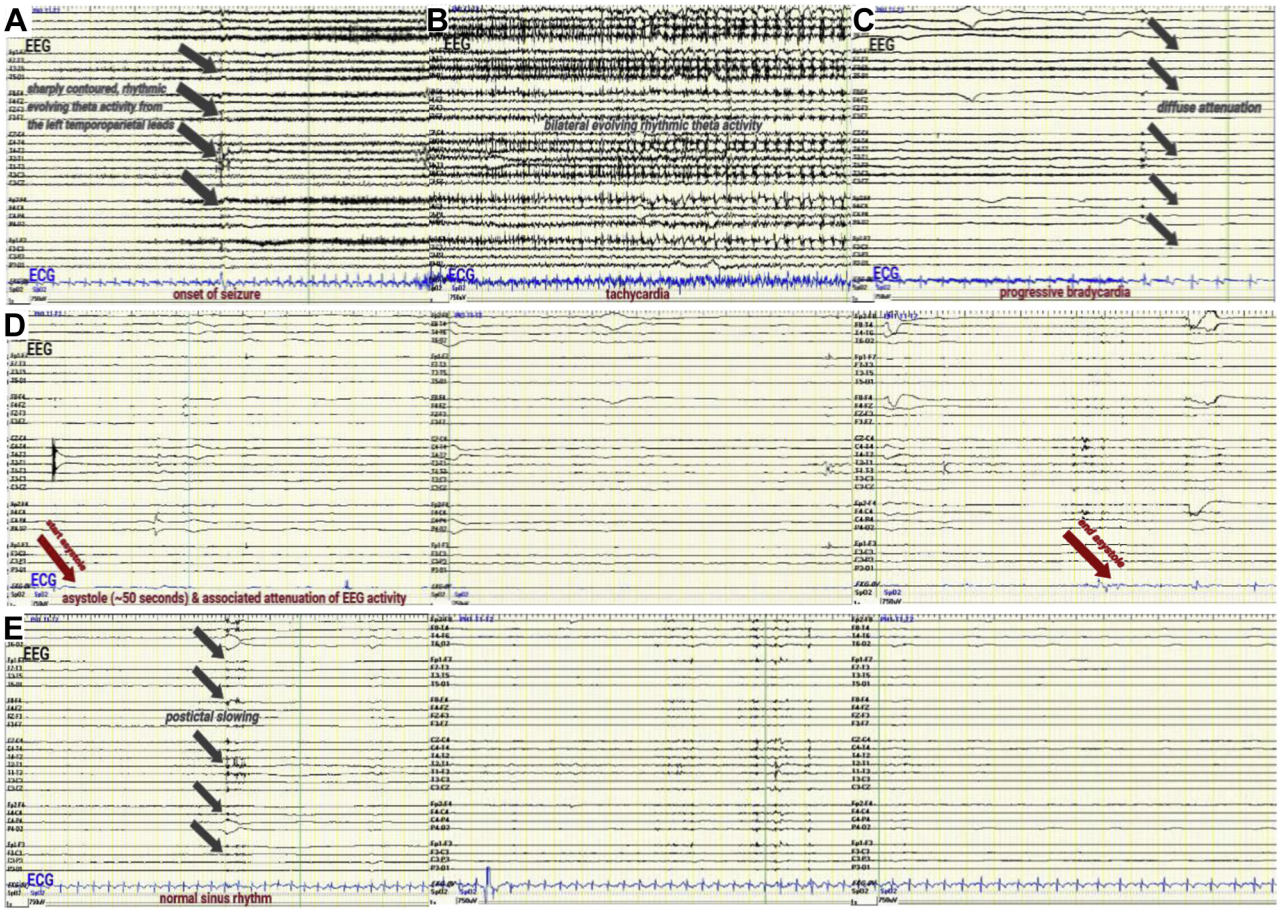

Figure 2 Seizure complicated by ictal asystole captured on video, electroencephalogram (EEG), and electrocardiogram (ECG) monitoring (see supplementary materials for full video). Unless otherwise specified, the above tracings are not continuous in time but rather represent snapshots at various stages of seizure progression. EEG/ECG tracings represent 25mm/s paper speed. **A:** Onset of seizure. EEG demonstrates sharply contoured, rhythmic evolving theta activity arising out of the left temporoparietal leads (*gray arrows*). **B:** EEG demonstrates bilateral evolving theta activity, which becomes obscured by muscle artifact. ECG demonstrates tachycardia. **C:** EEG demonstrates global slowing followed by diffuse attenuation (*gray arrows*) of activity after termination of the convulsive phase. ECG demonstrates progressive bradycardia. **D:** EEG/ECG tracings are continuous in time and demonstrate 50 seconds of asystole with onset and resolution marked by red arrows. A short period of bradycardia follows. There is ongoing attenuation of EEG activity during this time. **E:** Observed return of spontaneous breathing. EEG demonstrates sustained postictal slowing (*gray arrows*). ECG demonstrates normal sinus rhythm.

poor control of primary or secondary generalized tonic-clonic seizures. The exact mechanism of SUDEP is debated, and it remains unclear why some postictal states progress to SUDEP while most recover to baseline.[8] Postictal generalized EEG suppression has been observed in conjunction with terminal respiratory dysfunction but has not been definitively shown to initiate events leading to SUDEP.[10] Additionally, there is no clear evidence linking ictal bradycardia or asystole to SUDEP, although these complications of epilepsy all share similar risk factors.[4] The 2013 Incidence and Mechanisms of Cardiorespiratory Arrests in Epilepsy Monitoring Units (MORTEMUS) study reviewed 11 monitored SUDEP events and found that many of these patients experienced initial postictal tachypnea and tachycardia that subsequently devolved into apnea, bradycardia, and finally asystole. In some patients this sequence of events led to immediate death while, for others, terminal cardiorespiratory arrest was delayed several minutes.[11] This observed variable time to terminal arrest distinguishes SUDEP from seizure-induced sudden cardiac death and suggests that although postictal cardiorespiratory instability is an important contributor, other pathophysiological mechanisms are also at play.[8]

There are no standardized guidelines regarding the long-term management of patients with epilepsy complicated by ictal asystole. Given the known association between ictal asystole and refractory epilepsy as well as the established link between SUDEP and generalized tonic-clonic seizures with associated prolonged postictal attenuation, adequate seizure control is paramount. Some patients achieve this with medical management alone, while others may also require epilepsy surgery. Cardioneuroablation is an additional possible treatment modality. This novel technique, first described for the management of ictal asystole in 2018, involves radiofrequency ablation of epicardial parasympathetic ganglia to achieve partial denervation of the sinus or atrioventricular node to mitigate the cardiac consequences of increased ictal parasympathetic tone.[12] Implantation of a

permanent pacemaker (PPM) should also be pursued, given demonstrated morbidity benefit. Case reports and small observational studies have found that PPM implantation in patients who have experienced ictal asystole lasting >6 seconds decreases the risk of future syncopal episodes and consequent falls.[7]

Conclusion

In conclusion, we report a striking case of ictal asystole lasting 50 seconds in a patient with classic risk factors for this complication, most notably medically refractory epilepsy characterized by recurrent temporal lobe seizures. The mainstay of management in cases such as these is improved seizure control, which this patient achieved with titration of her antiseizure medication regimen. PPM implantation was pursued given her extended episode of ictal asystole and high risk for future SUEDP.

Appendix

Supplementary data

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.hrcr.2020.08.002.

References

1. van der Lende M, Surges R, Sander JW, Thijs RD. Cardiac arrhythmias during or after epileptic seizures. J Neurol Neurosurg Psychiatry 2016;87:69–74.
2. Bestawros M, Darbar D, Arain A, et al. Ictal asystole and ictal syncope. Circ Arrhythm Electrophysiol 2015;8:159–164.
3. Shmuely S, Bauer PR, van Zwet EW, van Dijk JG, Thijs RD. Differentiating motor phenomena in tilt-induced syncope and convulsive seizures. Neurology 2018;90:e1339–e1346.
4. Marynissen T, Govers N, Vydt T. Ictal asystole: case report with review of literature. Acta Cardiol 2012;67:461–464.
5. Duplyakov D, Golovina G, Lyukshina N, Surkova E, Elger CE, Surges R. Syncope, seizure-induced bradycardia and asystole: two cases and review of clinical and pathophysiological features. Seizure 2014;23:506–511.
6. Li W, Jayagopal LA, Taraschenko O. Ictal asystole with isolated syncope: A case report and literature review. Epilepsy Behav Case Rep 2019;11:47–51.
7. Wittekind SG, Lie O, Hubbard S, Viswanathan MN. Ictal asystole: an indication for pacemaker implantation and emerging cause of sudden death. Pacing Clin Electrophysiol 2012;35:e193–e196.
8. Devinsky O, Hesdorffer DC, Thurman DJ, Lhatoo S, Richerson G. Sudden unexpected death in epilepsy: epidemiology, mechanisms, and prevention. Lancet Neurol 2016;15:1075–1088.
9. Velagapudi P, Turagam M, Laurence T, Kocheril A. Cardiac arrhythmias and sudden unexpected death in epilepsy (SUDEP). Pacing Clin Electrophysiol 2012;35:363–370.
10. Rajakulendran S, Nashef L. Postictal generalized EEG suppression and SUDEP: a review. J Clin Neurophysiol 2015;32:14–20.
11. Ryvlin P, Nashef L, Lhatoo SD, et al. Incidence and mechanisms of cardiorespiratory arrests in epilepsy monitoring units (MORTEMUS): a retrospective study. Lancet Neurol 2013;12:966–977.
12. Antolic B, Gorisek V, Granda G, Lorber B, Sinkovec M, Zizek D. Cardioneuroablation in ictal asystole—new treatment method. HeartRhythm Case Rep 2018;4:523–526.