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Brain Rattled, Heart Shackled: Ictal Asystole in a Patient without Prior History of Epilepsy or Arrhythmia

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Abstract

We present a case of ictal asystole in an 81-year-old female, with no prior history of epileptic activity, or cardiac history suggestive of arrhythmia, who suffered several seemingly unrelated epileptic and asystolic episodes prior to finally having a witnessed seizure followed by an asystolic event. Following this event, all atrioventricular (AV) nodal blockers, and medications with potential seizure threshold lowering activity were stopped, and anti-epileptic medication was optimized. Due to the wishes of the patient's family, no invasive interventions were pursued. However, the patient continued to be medically treated with anti-epileptic therapy and had no further asystolic events. Unfortunately, the patient's overall clinical status deteriorated, and she subsequently passed during her hospital stay after being made do not resuscitate and do not intubate (DNR/DNI) by the family and then subsequently comfort care. Prior to her passing, however, she had remained free of epileptic events for 10 days and free of asystolic events for 21 days.

Keywords

Seizure, Epilepsy, Asystole, Cardiac Arrest, Ictal Asystole, Arrhythmia, Cardiac Pacing, Electroencephalogram, Ertapenem

1. Introduction

Ictal asystole (IA) is a phenomenon well-known by Neurologists, however, less often discussed in the Cardiology community [1]. It is defined as EKG evidence of prolongation of the R-R interval longer than 3 seconds, accompanied by sei-

zure activity [2]. The rate of ictal asystole in individuals with a history of epilepsy who underwent surveillance with video EEG monitoring ranged from 0.25% to 0.40% [3]. The condition is considered rare, both due to its pathophysiology and difficulty in detection secondary to the need for dual monitoring with electrocardiogram (EKG) and electroencephalogram (EEG). However, it must be noted that the rarity may be overstated due to the limits of the population being tested [1].

The physiology behind IA is uncertain but is thought to be due to the central nervous system's effect on the heart and the possibility of epileptic activity synchronizing with cardiac activity [1]. An estimated 80% of these cases are associated with temporal lobe epilepsy, while the remainders occur with extratemporal lobe seizures. The most common type of arrhythmia noted during epileptic events is ictal tachycardia making up 80% - 100%, with ictal bradycardia making up less than 6% of the seizure cases [4]. The bradycardia can be severe enough to cause asystole. Paradoxically, the loss of cerebral perfusion and cortical functioning from a lack of blood flow to the brain during asystole is believed to facilitate the termination of the epileptic event [1]. Our patient had an episode of ictal asystole, which highlights the importance of timely diagnosis and recognition of IA with solely clinical evidence, and EKG monitoring.

2. Case Presentation

Written informed consent was obtained from the patient's immediate family authorizing this report.

Our patient is an 81-year-old female with a past medical history of Alzheimer's disease (on olanzapine), Parkinson's disease (on carbidopa/levodopa), non-insulin-dependent diabetes mellitus, hypertension, chronic anemia, urinary retention with chronic indwelling catheter and glaucoma, who presented to the emergency department, altered, with initial labs showing leukocytosis, bacteriuria, and elevated creatinine. A presumptive diagnosis of urinary tract infection (UTI) was made, and due to her prior history of *Proteus mirabilis* extended-spectrum beta-lactamase (ESBL) UTI, she was started on meropenem then switched to ertapenem.

Three days following admission, a rapid response was called due to the patient being non-responsive, however, the patient slowly regained consciousness, computed tomography (CT) head scan was negative for acute pathology, however, it did show a moderate degree of diffuse cerebral atrophy with sulcal widening and ventricular dilation as well as chronic hypodense changes throughout the periventricular white matter indicative of small vessel ischemia. No anti-epileptic medication was started at this time as the seizure was not believed to be the cause. The following day, the patient suffered a grand-mal seizure, and neurology ordered an electroencephalogram (EEG) and started levetiracetam 750 mg twice a day and subsequently increased to 1000 mg twice a day, with lorazepam as needed for breakthrough activity. Olanzapine was held due to its ef-

fect on lowering the seizure threshold [5].

Continuous video EEG was unfortunately not available, however a single EEG was performed using an 18-channel digital EEG machine with standard 10/20 electrode placement [6]. The recorded time was 22.3 minutes, and it was interpreted by the same neurologist attending to the patient. The EEG showed no spikes, and no response to photic stimulation, however, did show evidence of potential underlying diffuse encephalopathy. There was no reported seizure activity noted during the test.

The patient continued antibiotic and anti-epileptic therapy for 6 more days at which point another rapid response was called due to the patient being unresponsive. The patient was bradycardic down to 45 beats per minute (bpm), with a regular rhythm, and was somnolent but arousable. Immediately following this, her telemetry showed a pause of 15.38 seconds (Figure 1). Heart rate returned to normal rhythm without intervention, and atropine was ordered for bedside. Cardiology was consulted and a Zoll automated external defibrillator with pacing pads was attached to the patient with a demand rate set at 30 beats per minute. Electrophysiology was also consulted at this time.

That evening, while being seen by the cardiac electrophysiologist in attendance, the patient developed recurrent asystolic pauses that were reported to be correlated with seizures. The locations of the pacer pads were physically adjusted as they were not capturing correctly. Immediately following this, the patient had a witnessed seizure, involving involuntary ocular movements as well as involuntary movements of the upper and lower extremities. Telemetry during seizure activity demonstrated 1:1 AV node conduction at 70 bpm. A loading dose of levetiracetam 1000 mg was given. Following abatement of her seizure, the patient became bradycardic and then demonstrated three distinct asystolic events (Figure 2). She subsequently regained AV conduction without intervention showing a normal sinus rhythm of 64 beats per minute. The Zoll automatic external defibrillator settings were re-evaluated and adjusted so that there was demonstrated capture at 15 milliamps with a demand rate set of 30 beats per minute.

A clinical diagnosis of ictal asystole was made with treatment goals of anti-epileptic therapy, electrolyte repletion and medication optimization. All AV-nodal blockers were held. Ertapenem was held due to its potential effect on seizure threshold [7]. Discussions for potential permanent pacemakers were made in the event of treatment failure but were declined by the patient and family. Electrolytes were maintained at potassium 4.0 - 4.5 millimoles per liter and magnesium 2.0 - 2.5 milligrams per deciliter.

The following day, a rapid response was called due to reported seizure activity, however, there were no pauses or asystolic events, and the patient continued to be managed medically. Again, ten days later, the patient had a similar episode of reported seizure activity, with no cardiac changes. Phenobarbital 20 milligrams, three times a day, was started at this time for improved medical control of her epileptic activity. Subsequently, there were no further episodes of seizure activity.
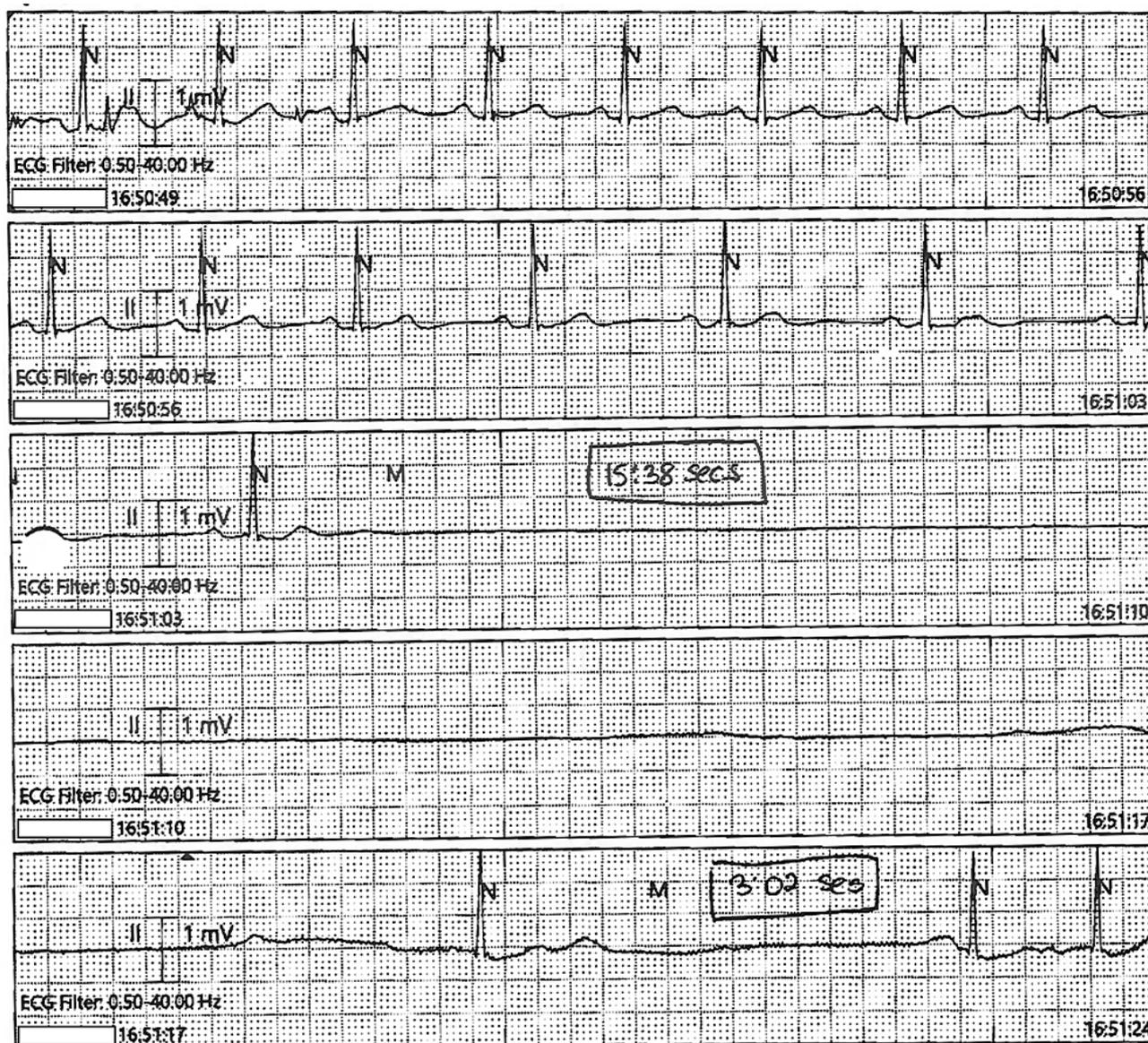
Figure 1. Initial episode of asystole with two distinct events lasting 15.38 seconds and 3.02 seconds.

Seven days later, a rapid response was called for hypoxia to 80% and increased work of breathing. Imaging was done, and antibiotics and steroids were administered for presumed aspiration pneumonia. There were no signs of epileptic or ictal activity. Following extensive family discussions, the patient was made DNR/DNI and eventually comfort care as her clinical status deteriorated despite appropriate medical management. At this time, non-necessary medical interventions were ceased per their wishes. The patient continued to decline and subsequently passed, twenty-one days after her recorded episode of ictal asystole, and ten days after her last reported epileptic event.

3. Discussion

We present a case of ictal asystole in an 81-year-old female, with no prior history
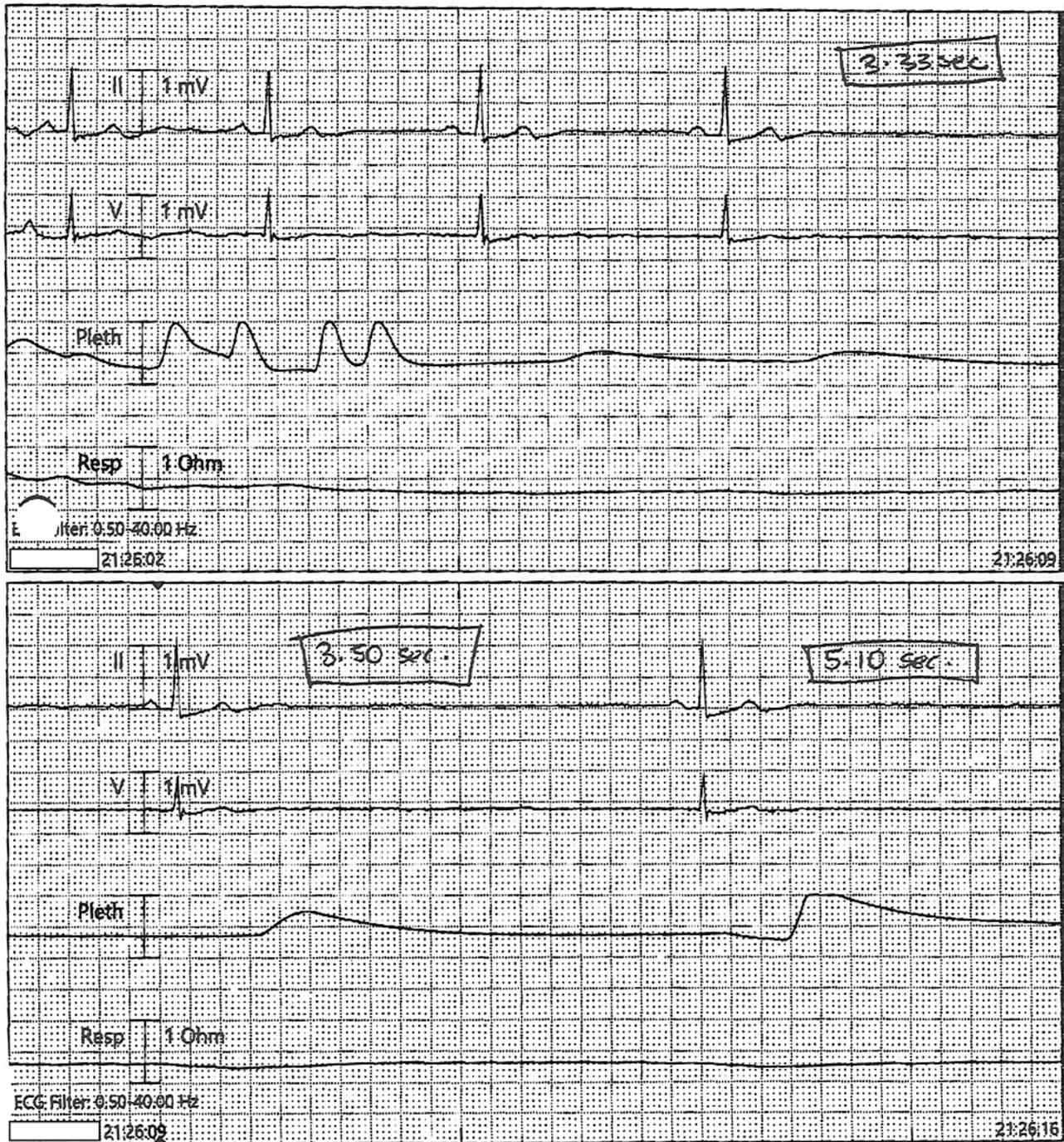
Figure 2. Ictal asystole captured on telemetry following a witnessed seizure with 3 distinct episodes lasting 3.33 seconds, 3.50 seconds and 5.10 seconds.

of epileptic activity. *Ictal asystole* is defined as EKG evidence of prolongation of the R-R interval longer than 3 seconds, accompanied by seizure activity [2]. It is a rare condition, difficult to quantify due to the temporal nature of the events and thought to affect an estimated 0.3% of individuals with refractory epilepsy [8]. Further complicating the diagnosis is the potential for asymptomatic asystole, that is, ictal asystole, without a syncopal episode. A systematic review of

published ictal asystole cases done in 2018 by Hampel revealed that the short-term recurrence rate of IA is 40.4%. Furthermore, the same review noted that in patients with recurrent IA, only 63.8% of episodes were symptomatic. Notably however, the rate of future ictal episodes decreased with the total number of recorded seizures. Age, sex, type, and duration of the seizure, as well as lateralization, and duration of the ictal event were not found to be a significant determinant in predicting future ictal events. Both clinical and empirical evidence including EKG and video EEG are important in the diagnosis [9].

Most cardiac arrhythmias occur in the setting of temporal lobe epilepsy, which suggests that this area may play a role in regulating the cardiac rate and rhythm [10]. The most common arrhythmia associated with epilepsy is ictal tachycardia (80% - 100% of all seizures) with ictal bradycardia occurring in fewer than 6% of cases and ictal asystole in only 0.25% - 0.4% of patients undergoing video-EEG [3] [4]. The pathophysiology of ictal-induced bradyarrhythmia and asystole is uncertain currently, however, studies do not link it to a definite prior cardiac conduction defect but associate it more with activation of certain areas of the brain with subsequent effect on the heart via efferent neural pathways, possibly synchronizing cardiac autonomic input with seizure activity. Of particular importance are the insular cortex and the amygdalae. It was previously thought that the left brain was more prominent in this condition; however, research now supports that both sides are equally as important. The pathophysiology is likely that of a "vagal storm" which induces bradycardia and anoxia which may be ironically beneficial as it may result in the termination of the seizure. It should be noted that the increased brain activity that leads to a bradyarrhythmia may also have the potential to cause a tachyarrhythmia. However, this was not noted in our patient [1].

Our case is notable in that prior to this incident, the patient had no prior episodes of seizure or syncope and no cardiac history suggestive of arrhythmia. Seizure-related syncope is uncommon, and constant telemetry monitoring was critical to the diagnosis. Cardiac arrest, bradycardia and syncope do not always manifest with every seizure complicating the diagnosis further [11]. Additionally, isolating and removing potential offending agents including ertapenem and olanzapine were paramount [5] [7]. Due to the unavailability of continuous EEG monitoring at the time of the event and no evidence of seizures on subsequent EEG, we were unable to quantify the location of the seizure.

Treatment for IA is two-fold, directed at epilepsy prevention as well as cardiac stabilization. The three mainstays of treatment are anti-epileptic medication, epilepsy surgery, and pacemaker placement. Research shows that pacemaker placement can be considered in patients who have longer periods of asystole [3].

Following extensive discussion with our patient's family, her wishes were changed to DNR/DNI and the patient continued to be managed medically. Subsequently, the patient's family chose to pursue comfort care measures and forewent any invasive intervention, after which she passed.

4. Conclusion

The incidence of ictal asystole is rare both in part due to its pathophysiology as well as the need for concomitant EKG and EEG monitoring. Our patient, with no history of epileptic or cardiac arrhythmia, suffered a witnessed ictal episode followed by transient asystole documented on continuous telemetry monitoring. It was believed that the seizure threshold was reduced by her antibiotic therapy with improvement when the medications were adjusted. It is of paramount importance with ictal asystole that the clinician recognizes the temporal nature of the events so that proper diagnostic tests and treatment may be administered in an expedient manner.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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