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Severe cardioinhibitory vasovagal syncope in sleep and supine posture

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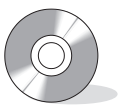
ABSTRACT – Severe cardioinhibitory vasovagal syndrome is characterised by syncope accompanied by cardiac asystole which may lead clinically to seizure-like motor activity. Vasovagal syncope usually occurs in erect posture and is often provoked by emotional or physical triggers. We report two patients who presented with severe cardioinhibitory vasovagal syncope accompanied by cardiac asystole resulting in seizure-like motor manifestations in sleep and supine posture. Both cases were initially diagnosed as epilepsy and treated with antiepileptic drugs. We discuss the putative mechanisms of this rare condition and its potential for misdiagnosis as epilepsy. [*Published with video sequences*]

Key words: convulsive syncope, epilepsy, cardiac, nocturnal seizure, diagnosis, EEG

Vasovagal syncope is a common cause of transient loss of consciousness, haemodynamically characterised by decreases in blood pressure with or without bradycardia (Alboni *et al.*, 2002). During syncope, some patients develop clinical features such as myoclonic jerks, gaze deviation, nystagmus, automatisms, and extensor posturing, which could be mistaken for epileptic seizures (Lempert *et al.*, 1994; Wieling *et al.*, 2009). A subgroup of patients with vasovagal syncope has been found to present with cardiac asystole (Milstein *et al.*, 1989). Malignant vasovagal syndrome is the term often used to identify those patients (Maloney *et al.*, 1988). "Severe cardioinhibitory vasovagal syncope" is perhaps a better term for this group, in contrast to "vasodepressive vasovagal syncope" characterised by blood pressure decrease with little or no drop in heart rate (van Dijk *et al.*, 2009). Vasovagal syncope is usually situation related and rare in sleep and supine posture (Iskos *et al.*, 1998; Krediet *et al.*, 2004). We report two patients who presented with severe cardioinhibitory vasovagal syncope and motor activity, mimicking seizures in sleep and supine posture.

Case 1

A 26-year-old female presented with a history of convulsions over a period of seven years. The events



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had been stereotypic, occurring mostly nocturnally in supine posture (while drifting into sleep) and in sleep. The patient could not recall a specific trigger. She was aware of a preceding "aura" which she described as a butterfly sensation in the chest, associated with her heart "missing a beat" and diaphoresis, before progressing within seconds to loss of consciousness and jerking of the limbs, occasionally accompanied by biting the edge of the tongue and urinary incontinence. She had occasionally experienced "auras" on prolonged standing without loss of consciousness. There was no family history of epilepsy, cardiac arrhythmias or sudden death.

The cardiovascular and neurological examinations were normal. The ECG, 24-hour ECG monitoring, and transthoracic echocardiogram were normal. Tilt-table testing was not performed. The routine EEG and MRI of the brain were normal.

At that stage, these events were diagnosed as seizures and she was commenced on lamotrigine. However, she had a few more events and was admitted for inpatient video-EEG monitoring (VEM). A typical event was captured during light sleep. While lying in bed, she experienced a typical aura followed by loss of consciousness associated with convulsive-type movements (*video sequence 1*). This was characterised by cardiac asystole lasting for 47 seconds. The EEG did not show any epileptic ictal rhythm (*figure 1*). The evolution of semiology along with corresponding ECG and EEG changes is detailed in *table 1*. The VEM for the entire duration did not reveal any interictal or ictal epileptiform EEG abnormalities. She underwent emergency dual-chamber pacemaker implantation and lamotrigine was ceased. She has so far remained event-free for over 12 months.

Case 2

A 75-year-old male presented with a history of recurrent convulsions occurring mostly in sleep and rarely when awake, over five years. The events were characterised by an "aura" which he described as a peculiar feeling in his head and nausea, followed by loss of consciousness and jerking of limbs. The occasional daytime events had occurred in the supine and sitting position. His neurological and cardiovascular examinations were normal. Investigations including 12-lead ECG, 24-hour ECG monitoring, transthoracic echocardiogram, tilt-table testing, and routine EEG and brain MRI were unremarkable.

These events were initially diagnosed as epileptic seizures and treated with several antiepileptic drugs,

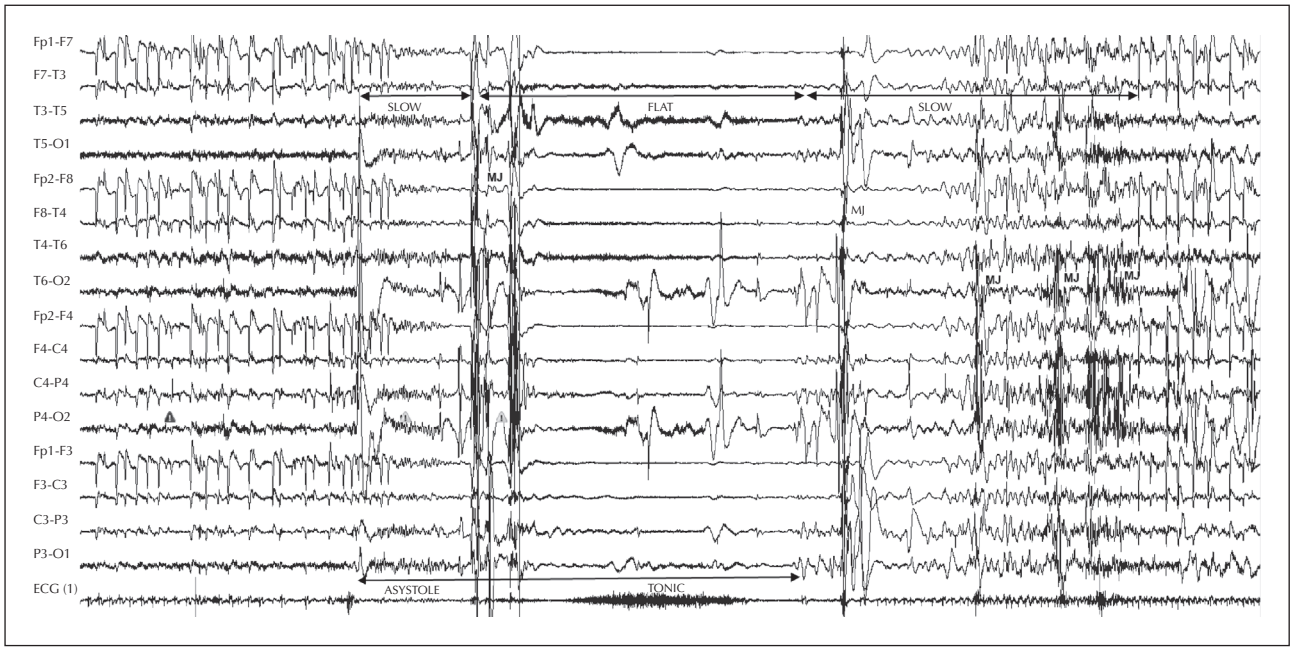

Figure 1. Representation of a single page of the video-EEG recording of Case 1, incorporating a single-channel ECG corresponding to 120 seconds (time-base compressed to 120 seconds/page).
The EEG demonstrates "slow" and "flat" phases during cardiac asystole, followed by the second "slow" phase after resumption of cardiac sinus rhythm. Myoclonic jerks (MJ) occur during asystole and after resumption of sinus rhythm. Tonic posturing (TONIC) occurs during asystole. Note the tonic muscle artefact captured on the ECG channel.

Table 1. Evolution of ECG, EEG, and clinical observations with time.

Time	ECG	EEG	Clinical Observations
00:25:22	Sinus rhythm	Normal	Feeling of typical aura while lying in bed Patient presses the alarm button and sits up
00:25:40	Sinus bradycardia (24 bpm)	Normal	Sitting up in bed
00:25:48	Asystole	Normal	Patient lies down
00:25:51	Asystole	Generalised 5-Hz theta slowing	Tachypnoea
00.25.57	Asystole	Generalised 3-Hz delta slowing	Tachypnoea
00:25:59	Asystole	Generalised suppression	Eyes roll back. Myoclonic jerking of the torso in the anterior-posterior direction
00:26:07	Asystole	Muscle artefact	Stiffening of the body, legs stretched, arms bent at elbows
00.26.32	Asystole	Generalised suppression	Relaxation of muscles
12.26.35	Resumption of cardiac rhythm	Generalised suppression	No movements
00:26:45	Sinus bradycardia	Generalised delta slowing	No movements
00:26:52	Sinus rhythm	Generalised delta slowing	Myoclonic jerks
00:27:08	Sinus rhythm	Generalised theta slowing	Sitting up
00:27:11	Sinus rhythm	Normal EEG with return of alpha rhythm	Able to communicate

with no improvement. He was subsequently admitted for inpatient video-EEG monitoring which captured several typical events in light sleep. He woke up with an aura followed by loss of consciousness associated with generalised hyperkinetic and clonic movements of the arms and legs (*video sequence 2*). All the events were associated with cardiac asystole, but no ictal rhythm on EEG (*figure 2*). The VEM for the entire duration did not reveal any interictal or ictal epileptiform abnormalities. He underwent emergency dual-chamber pacemaker implantation and antiepileptics were ceased. He has so far remained event-free for five years.

Discussion

We present two unusual cases of recurrent, severe, cardioinhibitory vasovagal syncope accompanied by cardiac asystole occurring in sleep and supine posture with preceding aura-like sensation and motor manifestations mimicking seizure activity, captured on VEM. Seizure-like movements occurred in two phases: during asystole (cerebral hypoperfusion) and after resumption of sinus rhythm (cerebral reperfusion). Both patients had no evidence of epilepsy and the events completely resolved after dual-chamber pacemaker implantation. Supine and sleep syncope is rarely described in the literature. To our knowledge, vasovagal syncope with cardiac asystole and convulsive movements occurring in light sleep has not been reported previously.

Nocturnal episodes of unconsciousness could be due to seizures, sleep disorders, cardiac arrhythmias, or hypoglycaemia. Vasovagal syncope usually occurs in upright posture due to orthostatic stress or provoked by emotional and physical triggers such as pain, fear, and instrumentation. Transient loss of consciousness in the supine posture argues against vasovagal syncope and may favour other conditions, such as generalised seizures and cardiac arrhythmias (Moya *et al.*, 2009; Thijs *et al.*, 2009). However, vasovagal

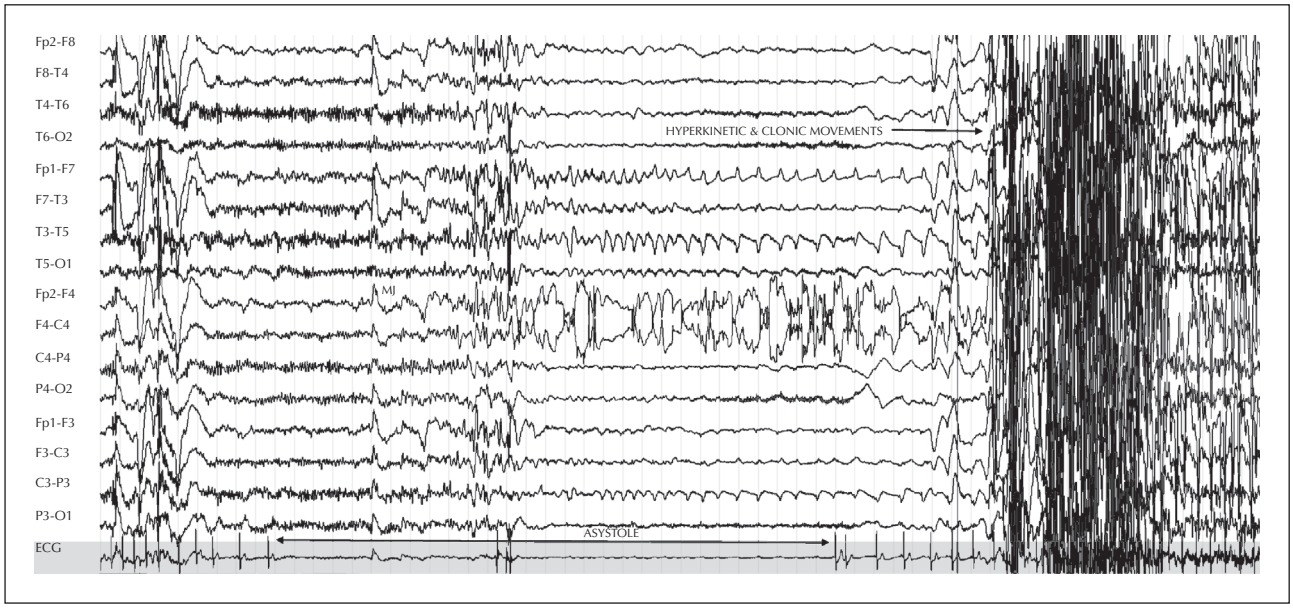

Figure 2. Representation of a single page of the video-EEG recording of Case 2, incorporating a single-channel ECG corresponding to 60 seconds (time-base compressed to 60 seconds/page).
Myoclonic jerks (MJ) occur during cardiac asystole whilst hyperkinetic and clonic movements appear after resumption of sinus rhythm.

syncope may occur while lying down in people undergoing instrumentation or shortly after awakening from sleep ("sleep syncope") (Iskos *et al.*, 1998; Krediet *et al.*, 2004; Marrison and Parry, 2007). Our two cases share some similarities with the recently described case series of 13 patients described with "vasovagal syncope interrupting sleep", although important differences exist (Krediet *et al.*, 2004). None of those 13 patients had sinus arrest. Our two patients had markedly prolonged cardiac asystole accompanied by convulsive movements. In the series of 13 patients with vasovagal syncope interrupting sleep, all cases awoke with a prodrome of nausea and the urge to defecate, with a short duration syncope occurring in the supine position or immediately after leaving the bed. Importantly, the period of loss of consciousness reported in that series was brief with only one case of isolated myoclonic jerks, whereas our two cases experienced recurrent events lasting greater than 30 seconds associated with prominent convulsive and hypermotor movements mimicking seizure activity.

Convulsive movements accompanying syncope are not uncommon, making the differentiation between epilepsy and vasovagal syncope particularly challenging (Wieling *et al.*, 2009). Motor phenomena such as flaccidity, tonic spasms, automatisms, and myoclonic jerking can occur at different phases of reflex syncope (Lempert *et al.*, 1994; Wieling *et al.*, 2009). In our patients, seizure-like movements were seen in two stages; cerebral hypoperfusion and reperfusion. The movements may have been misinterpreted as psychogenic non-epileptic seizures. However, tongue biting (Case 1) and occurrence during sleep are useful clues indicating that the events are more likely to be organic than psychogenic. These two cases provide useful insight into the correlation between cerebral haemodynamics, EEG changes, and clinical manifestations during vasovagal syncope.

There are two EEG patterns described in reflex syncope; "slow-flat-slow" and "slow" patterns (Gastaut, 1974). The "slow-flat-slow" pattern is most commonly described in reflex syncope associated with asystole. It is recognised to occur as a consequence of cerebral hypoperfusion and reperfusion (Gastaut, 1974; Breningstall, 1996; Brenner, 1997). The first "slow" phase is characterised by slow wave activity of increased amplitude, replacing the alpha rhythm during cerebral hypoperfusion, before disappearing abruptly to produce a "flat" EEG. The restoration of cerebral blood flow results in the reappearance of slow wave activity before the alpha rhythm returns (Gastaut, 1974; Breningstall, 1996; Brenner, 1997). In Case 1, no motor manifestations were seen during the first "slow" phase on EEG. Tonic activity and myoclonic jerking were seen in the "flat" phase, followed by marked myoclonic jerks during the second "slow" phase (*video sequence 1*, *figure 1*). The second patient had a single burst of myoclonic jerking during the first "slow" phase, but none in the "flat" phase. He

developed prominent hyperkinetic and clonic movements during the second "slow" phase of the EEG (*video sequence 2 and figure 2*). These two cases demonstrate that seizure-like motor manifestations occur during both cerebral hypoperfusion and reperfusion.

Cardiac arrhythmias, both physiological and pathological, can occur in sleep. In our patients, cardiac asystole occurred in non-rapid eye movement (NREM) sleep, and no other cardiac arrhythmias were seen during other stages of sleep, during wakefulness on VEM, or 24-hour-ECG monitoring.

Various cardiac arrhythmias are known to occur during seizures (Moseley *et al*., 2011), but our patients did not have any evidence of primary seizure activity on VEM. Hence, it is reasonable to conclude that our patients developed cardiac asystole due to a severe form of cardioinhibitory vasovagal syncope.

The aetiopathogeneis of vasovagal asystole arising from NREM sleep and supine posture in our patients is unclear. Exaggerated basal vagal tone is considered to be a potential mechanism for "malignant vasovagal syncope" (Nakagawa *et al*., 2000). We extend upon the hypothesis proposed by Krediet *et al*. (2004) that these patients have an increased baseline vagal tone, which is exaggerated during NREM sleep. The preceding "aura" of butterfly sensation in the chest and nausea were likely to be secondary to excessive vagal activity, culminating in prolonged cardiac asystole in our patients.

Treatment options for reflex syncope include physical counterpressure manoeuvres, tilt training, and drug therapy (Moya *et al*., 2009). Cardiac pacemaker implantation in reflex syncope is controversial. Both American and European guidelines list recurrent reflex syncope with prominent cardioinhibitory response as a class IIa indication for cardiac pacing (Epstein *et al*., 2008; Moya *et al*., 2009).

We acknowledge some limitations in the diagnostic workup. Intracardiac electrophysiological studies were not performed to exclude a primary cardiac dysrhythmia. The possibility of sick sinus syndrome is not completely excluded in the older patient (Case 2).

Convulsive activity in sleep, particularly when accompanied by tongue biting, is generally considered to be an epileptic seizure. Convulsive syncope is not usually recognised as a sleep-related phenomenon. However, these two cases illustrate that severe cardioinhibitory vasovagal syncope with cardiac asystole, which could easily be misdiagnosed as epileptic seizures, may rarely occur in sleep and supine posture. □

Disclosures.
None of the authors has any conflict of interests or financial support to disclose.

Legends for video sequences

Video sequence 1

Video-EEG of Case 1. A 16-channel EEG was used with the associated ECG strip demonstrating sinus arrest and asystole lasting for 47 seconds. During asystole, brief convulsive movements and tonic posturing of her body are observed and myoclonic activity is seen with restoration of sinus rhythm. Note "slow-flat-slow" pattern of EEG (generalised slowing, followed by generalised suppression and generalised slowing again). The sound has been muted as requested by the patient.

Video sequence 2

Video-EEG of Case 2. A 16-channel EEG was used with the associated ECG strip demonstrating sinus arrest and asystole. Brief generalised myoclonus is seen during asystole. Generalised hyperkinetic and clonic movements of the extremities are seen upon return of normal sinus rhythm.

Key words for video research on www.epilepticdisorders.com

Syndrome: non epileptic paroxysmal disorder
Etiology: syncope (vagal); syncope (cardiac)
Phenomenology: tonic posture; non epileptic paroxysmal event; clonic (non epileptic)
Localization: not applicable

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