A case of sudden unexpected death of a patient with epilepsy: Continuous electrocardiographic monitoring and autopsy results

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Introduction

Epilepsy is one of the most common neurologic disorders in both adults and children. About 1% of the population (ie, almost 65 million people worldwide) suffer from this disease. Compared to the general population, the risk of death in patients with epilepsy is almost 3 times greater, and half of these patients die suddenly.[1] The most probable mechanisms of sudden unexpected death in epilepsy (SUDEP) include breathing disorders such as airway obstruction, central apnea, and neurogenic pulmonary edema.[2] Recent data show that one of the main reasons for sudden death in patients with epilepsy is arrhythmia and cardiac conduction disorder. Here we present the case of sudden unexpected death of a patient with epilepsy.

KEY TEACHING POINTS

- Sudden unexpected death in epilepsy (SUDEP) is a major cause of mortality in patients with epilepsy, particularly in those with refractory and poorly controlled epilepsy.
- Seizures commonly produce sinus tachycardia and occasionally may cause sinus bradycardia, asystole, and other rhythm disturbances.
- A variety of factors have been associated with SUDEP, including uncontrolled seizures, young age, generalized tonic–clonic seizures, and poor antiepileptic medication compliance.

Case report

Patient L, a 31-year-old man diagnosed with epilepsy, was hospitalized for implantation of a subcutaneous Reveal XT electrocardiographic (ECG) recorder (Medtronic, Minneapolis, MN) to detect arrhythmias and cardiac conduction disorders during ictal and postictal periods. Upon admission, the patient complained of episodes of loss of consciousness, with tongue biting, urine and fecal incontinence up to 3–5 times monthly (mainly at night), and episodes of absence, déjà vu, hypersalivation and subsequent amnesia during daytime.

Based on his medical history, the patient had suffered a traumatic brain injury at age 24 and 1 year later developed the complaint symptoms. He was diagnosed with epilepsy, and treatment with valproic acid (Depakine Chrono) 1200 mg/d and carbamazepine 400 mg/day was initiated. Antiepileptic treatment seizures occurred with the same frequency, but the patient had not taken the drugs regularly. The patient had episodes of alcohol abuse. He had no epilepsy or sudden death in the family medical history.

Upon admission, the patient's status was satisfactory, pulse was regular, and blood pressure was within 120/80 mmHg. ECG showed sinus rhythm with heart rate of 75 bpm, QTc duration of 382 ms, and signs of type 3 early ventricular repolarization syndrome (Figure 1). Echocardiography showed no enlargement of the cardiac cavities, no areas of local left ventricular contractility disorders, and no valve pathology. Ejection fraction was within the normal range. Daily Holter ECG monitoring did not show significant supraventricular and ventricular arrhythmia, ischemic changes of ST segment, or conductivity disorder.

Neurologic examination showed right-sided pyramidal insufficiency (anisoreflexia, change of muscle tone) and coordination disorders. Brain magnetic resonance imaging showed posttraumatic changes with residual hemosiderin in the left frontal lobe. Electroencephalography during an

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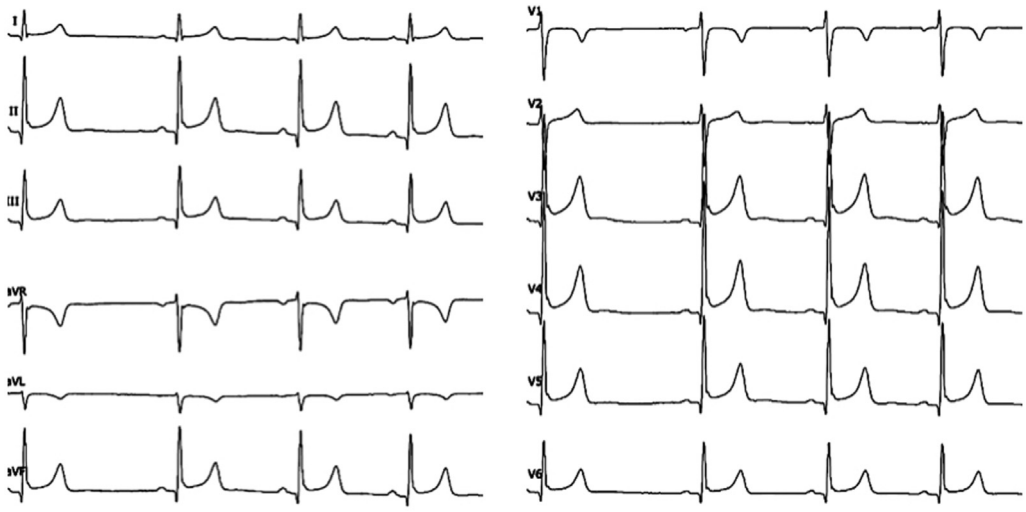

Figure 1 Baseline electrocardiogram (paper speed 25mm/s) showing sinus rhythm with heart rate of 75 bpm, QTc duration of 382 ms, and signs of type 3 early ventricular repolarization syndrome.

interictal period did not show epileptic activity. Continuous electroencephalographic monitoring was not performed.

Despite the ongoing episodes, the patient refused further treatment correction. Because of persistent epileptic seizures and to detect life-threatening arrhythmias and cardiac conduction disorders, a subcutaneous ECG recorder was implanted. The device was programmed to automatically register arrhythmic events and heart pauses, including atrial tachyarrhythmia/atrial fibrillation, ventricular tachycardia, bradycardia, and asystole. The durations of the episodes saved in the ECG recorder were 30 seconds before and 30 seconds after activation; in case of atrial tachyarrhythmia, the duration was 2 minutes before autoactivation. In addition, the patient could manually activate detection using the external device immediately after the end of an epileptic seizure. In this case, 3 ECG fragments that lasted 6.5 minutes before and 1 minute after the activation were saved in the device.

Data saved in the loop ECG recorder were complemented by information from a diary in which the patient recorded the type of episode, the time of onset, and drug intake regimen.

The patient was discharged, with recommendations to visit the clinic for neurologic examination and analysis of ECG recorder data saved after 3 manual record activations.

During the first follow-up visit, the interview showed that the frequency of generalized seizures had remained unchanged and the seizures occurred mainly during sleep, despite the intake of combination antiepileptic treatment with valproic acid 1200 mg/d and carbamazepine 400 mg/d.

Three ECG fragments were extracted from the loop recorder memory. In all instances, the patient activated recording immediately after the end of a generalized epileptic seizure. All the ECG fragments were identical and were characterized by the presence of sinus rhythm with heart rate of 66 bpm followed by increase up to 100 bpm and then decrease down to 48 bpm, and a singular ventricular extrasystole, supraventricular extrasystole, followed by the artifacts common for skeletal muscle contraction during tonic and later clonic phase of seizures, followed by sinus tachycardia with heart rate of 130 bpm (Figure 2). The ECG fragments are shown in Supplemental Figure 1.

Because of the absence of life-threatening arrhythmias and cardiac conduction disorders, antiarrhythmic treatment was not prescribed, and the patient was discharged with a recommendation for dynamic follow-up.

Before the patient's next visit to the clinic, his relatives informed the clinic that the patient had been found dead in the forest several days earlier. The medical forensic examination agency submitted the medical forensic autopsy report, and the subcutaneous loop ECG recorder was removed from the patient's body. Autopsy showed signs of acute death: diffuse intensive blue postmortem lividities, facial cyanosis, acute venous congestion of all internal organs, liquid venous blood type in the cardiac cavities and major vessels, and presence of subserous, subpleural, and subendocardial hemorrhages.

Major pathologic changes were detected during examination of the brain and meninges, cardiovascular system, and lungs. Cerebral examination showed morphologic signs of edema, such as smooth relief, flattening of gyri in all segments, and increased weight. No signs of cerebral herniation were seen. Sagittal and frontal sections showed moist white matter and significant congestion of brain tissue without structural focal pathologies. The most significant pathologic changes, including diffuse thickening with vascular congestion more expressed in frontal and parietal lobes, were present in the pia matter. These pathomorphologic signs reflect brain tissue atrophy.

Lung examination showed focal pale-red hemorrhages under the pulmonary pleura. The lungs were inflated, emphysematous, and marblelike. Pulmonary tissue sections were dark red, congested, and edematous, with large amounts of

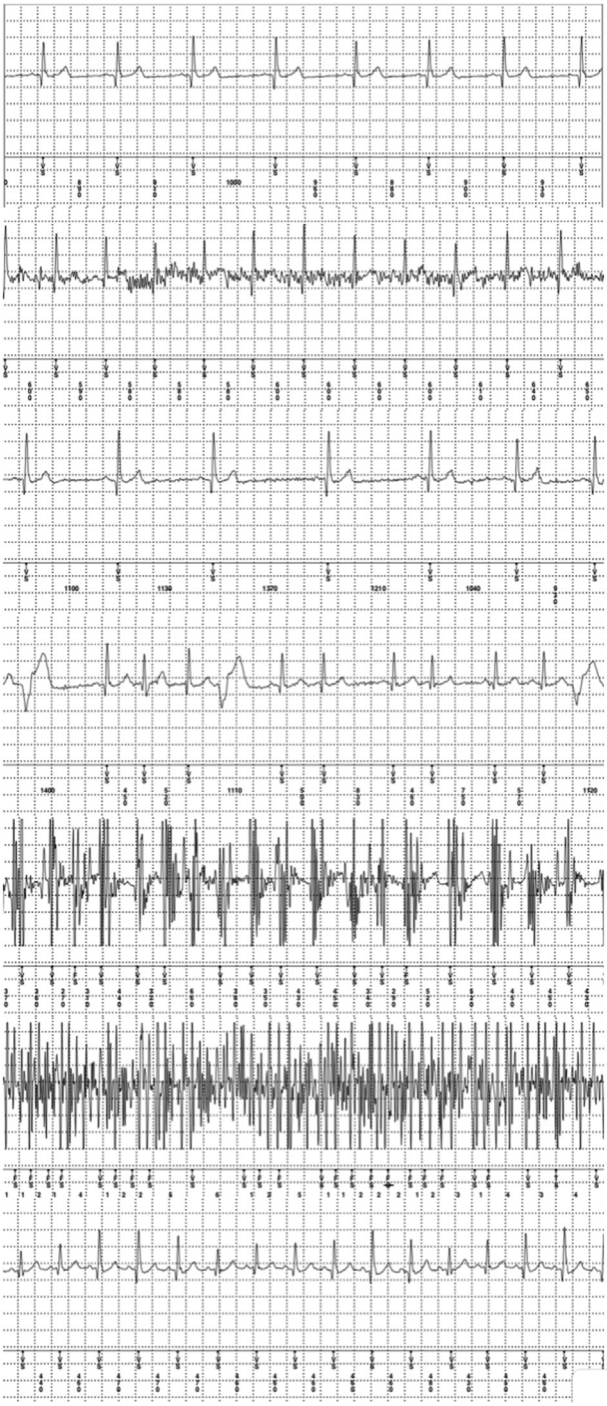

Figure 2 Electrocardiographic recording (paper speed 25mm/s) during an epileptic seizure showing sinus rhythm with heart rate of 66 bpm followed by increase up to 100 bpm and then decrease down to 48 bpm, and a singular ventricular extrasystole, supraventricular extrasystole, followed by the artifacts common for skeletal muscle contraction during tonic and later clonic phase of seizures, followed by sinus tachycardia with heart rate of 130 bpm.

liquid dark-red blood and foamy fluid exuding from the surface of the sections.

Cardiac examination showed signs of cardiodystrophy but no myocardial hypertrophy. The myocardium was flaccid and faded, with uneven blood filling; the cavities were not dilated. Cardiac weight was not increased. No signs of coronary atherosclerosis were seen. Pathohistologic examination was not performed.

Chemical forensic testing showed an ethanol concentration of 0.7%, which corresponds to mild alcohol intoxication.

Data extracted from the loop ECG recorder included information of termination of physical activity and cardiac activity corresponding to the date of the patient's death (Figure 3A). On the day of the patient's death, episodes of idioventricular rhythm with ventricular contraction rate about 17 bpm were registered for 26 minutes, from 18:17 to 18:43, followed by heart arrest (Figure 3B). Postmortem ECG fragments are shown in Supplemental Figure 2.

Discussion

We present a case of sudden unexpected death of a young man with epilepsy, whose subcutaneous ECG recorder registered heart arrest at the moment of his death, and autopsy results excluded any comorbidity that could cause it.

According to the literature, the most significant risk factor of SUDEP is generalized tonic–clonic seizures, which increase the risk of sudden death in patients with epilepsy by almost 10 times. Lack of epileptic seizure control is another important risk factor that results from treatment insusceptibility and lack of compliance to treatment, as in our patient. Combination antiepileptic treatment increases the probability of SUDEP. Alcohol abuse increases sudden death risk in patients with epilepsy by increasing the rate of epileptic seizures, stress-induced catecholamine release, and cardiac arrhythmias.[3]

Sudden unexpected death in patients with epilepsy is verified mostly by autopsy. The most common autopsy finding is cerebral edema, which induces an increase of intracranial pressure that can be associated with bradycardia and apnea. The cerebral atrophy detected in our patient is not a common finding and can be explained by cerebral hypoxia, ischemia, edema, and continuous anticonvulsant treatment. According to various investigators, lung edema and alveolar hemorrhages, which according to experimental data result from induced epileptic seizures, asystole, or ventricular fibrillation, were revealed by autopsy in 62%–84% of patients who died of SUDEP.[4]

Continuous ECG monitoring using a subcutaneous loop recorder not only provided information about the patient's cardiac rhythm type during the epileptic seizure but also revealed bradycardia and asystole as the cause of death. It is known that long episodes of heart arrest (from 10 seconds to minutes), which usually occur secondary to apnea during generalized seizures, may lead to a lethal decrease of cerebral circulation and sudden death. The main mechanism leading to SUDEP begins with early, centrally mediated, severe alterations of both respiratory and cardiac function after generalized tonic–clonic seizures, a pattern referred to as early postictal neurovegetative breakdown. Depending on its intensity, this mechanism might lead to immediate death or delayed terminal cardiorespiratory arrest after several minutes of

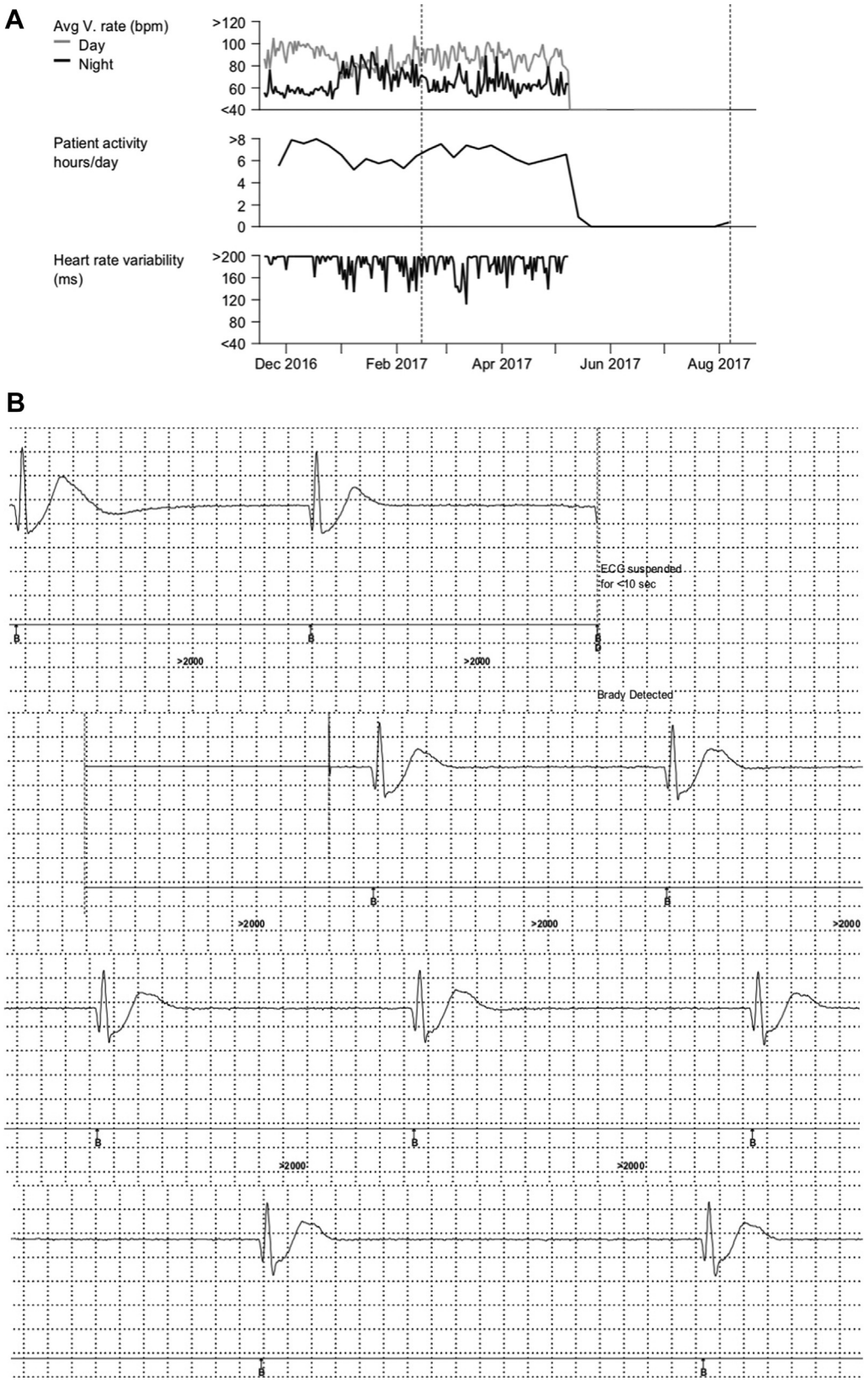

Figure 3 **A:** Heart rate trends and physical activity graphs showing termination of physical activity and cardiac activity corresponding to the patient's date of death. **B:** Postmortem electrocardiographic recording (paper speed 25mm/s) showing episodes of idioventricular rhythm with ventricular contraction rate about 17 bpm followed by heart arrest.

altered cardiorespiratory function, most likely aggravated by profound hypoxia.[5]

Appendix

Supplementary data

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.hrcr.2018.11.014.

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