Case Report

A 25-year-old previously healthy man was hospitalized due to a recent history of syncope with a generalized tonic clonic seizure (GTC). He had experienced prodromes consisting of chest discomfort and flashbacks of visual memory. He was currently receiving carbamazepine (CBZ, 400 mg/day), as prescribed by another medical facility. No abnormal physical findings were noted except for skin rashes on his trunk. His initial electrocardiogram (ECG) and electroencephalogram (EEG) were normal; magnetic resonance imaging (MRI) of the brain also showed no abnormalities. A laboratory examination revealed moderate liver injury along with mild eosinophilia. At this time, CBZ was discontinued due to potential allergic reactions. After 21 days of admission, while standing beside his bed and talking to his physician, he felt prodromes and suddenly lost consciousness, followed by a GTC that lasted for approximately 30 s. He recovered spontaneously without resuscitation. ECG monitoring at this time demonstrated asystole (5 s and 9 s, respectively, Fig. 1A). On the next day, asystole occurred twice along with prodromes (Fig. 1B). However, he did not lose consciousness and no GTC was observed. He was then transferred to the cardiology department for an evaluation of bradyarrhythmia. Results from Holter ECG monitoring, a signal-averaged ECG, and the head-up tilting test were normal. No cardiac abnormalities were detected on the echocardiogram, cardiac MRI with gadolinium contrast agent, fluorodeoxyglucose positron emission tomography/computed tomography, or coronary angiogram. An electrophysiological study showed normal sinus node and atrioventricular node function. An electroencephalogram revealed small spike waves in the fronto-temporal region. Brain MRI demonstrated a left-sided amygdala enlargement. To the best of our knowledge, this is the first case of temporal lobe epilepsy with an amygdala enlargement that induced cardiac asystole.

Key words: asystole, epilepsy, sudden unexpected death in epilepsy

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Figure 1. ECG monitoring findings demonstrating asystole with syncope and a generalized tonic clonic seizure (A); syncope was not observed the following day (B).

Figure 2. An electroencephalogram showing small spike waves at the fronto-temporal region.

(Fig. 3), which was the potential focus of temporal lobe epilepsy. Although no repeat episodes of loss of consciousness and/or asystole have been documented thus far, combination antiepileptic treatment with ZNS (400 mg/day) and levetiracetam (1,000 mg/day) has not eliminated the prodromes. Therefore, neurosurgical intervention is being discussed.

**Discussion**

Although sudden unexpected death in epilepsy (SUDEP) is a rare complication in patients with seizures (3.5-9.3 per 1,000 person-years in refractory epilepsy), the efficacy of adjunctive antiepileptic drugs remains unclear since inadequate poly-drug therapy cannot prevent SUDEP (1). Epilepsy-induced cardiac asystole, also termed “ictal asystole,” was previously described in patients with temporal lobe epilepsy (2, 3) and has been proposed as one of the potential mechanisms causing SUDEP (4). However, epilepsy-induced cardiac asystole can be difficult to diagnose due to its underrecognition and appearance only during seizures.

In our patient, with the support of the EEG findings after the attacks, we reached the diagnosis of temporal lobe epilepsy according to the presence of a complex partial seizure, which evolved to generalized seizures afterward and was composed of somatosensory symptoms (chest discomfort), psychic symptoms (flashbacks of visual memory), and loss of consciousness. In temporal lobe epilepsy, a secondary generalized seizure is atypical but has been reported to have
A positive association with hippocampal sclerosis (5). In addition, our patient had prodromes and loss of consciousness before the GTC. Therefore, we speculate that the patient’s GTC was secondary. Because video-EEG/ECG monitoring was not available, the initiation of the epileptiform discharge on EEG and asystole on ECG could not be documented simultaneously. However, the entire episode was witnessed by a neurologist and recorded on ambulatory ECG monitoring. In addition, comprehensive cardiac assessments, including a cardiac electrophysiological study of the sinus and atrial ventricular node, denied any existence of organic heart disease and conduction system disease. The above-mentioned facts contributed significantly to the establishment of our diagnosis.

At present, the cause of epilepsy-induced cardiac asystole is not clear. The time delays between seizure onset and cardiac asystole development suggest that an activation of a certain brain region may be the first trigger, which subsequently alters the cardiac function through efferent pathways. The central autonomic network, including the insula, cortex and amygdala, is a possible candidate of this mechanism (6). Indeed, the stimulation of the left hippocampus, amygdala, and insula induce asystole in humans (7). Recently, unilateral amygdala enlargements have been found in patients with temporal lobe epilepsy (8), and its pathophysiological roles are currently being investigated.

In patients with epilepsy-induced cardiac asystole, no specific treatment regimen has been established, and the efficacy of cardiac pacing may have a role, but remains controversial (9). In such patients with refractory epileptic symptoms, a surgical approach could be an option in the future (10).

To the best of our knowledge, this is the first case of temporal lobe epilepsy with an amygdala enlargement that induced cardiac asystole. Further studies are necessary to uncover the main mechanism of epilepsy-induced cardiac asystole, especially in regard to the central autonomic network, including the amygdala.

The authors state that they have no Conflict of Interest (COI).

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