



Case Report

The ictal bradycardia syndrome: A case report[☆]Ilaria Fava^a, Salvatore Del Gaudio^b, Enrico Volpe^b, Giuseppe Paolisso^a, Maria Rosaria Rizzo^{a,*}^a Department of Medical, Surgical, Neurological, Metabolic and Geriatric Sciences, Second University of Naples, Piazza Miraglia 2, 80138 Naples, Italy^b Department of Emergency Medicine, Pineta Grande Hospital, Castel Volturno, Caserta, Italy

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ABSTRACT

We report a case of a 56-year-old man affected by frontal lobe seizures who has developed bradycardia followed by asystole. The patient had a positive family history for epilepsy. In fact, the mother, brothers, and one sister had epilepsy. Furthermore, the patient's two brothers suddenly died of unspecified heart disease at the ages of 26 and 53, respectively. The patient also experienced syncope once or twice a year. Three similar epileptic seizures, without the recurrence of asystole, were registered after pacemaker implantation.

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1. Introduction

Cardiac arrhythmias are frequently reported during epileptic seizures. In particular, increased heart rate has been reported to occur in 64–100% of temporal lobe seizures, while bradycardia (heart rate below 60 beats per min) has been reported to occur in only a small percentage of cases (less than 6%) [1]. Patients with seizure-related bradyarrhythmias, labeled ictal bradycardia syndrome [2], suffer mainly from temporal lobe epilepsy or from extratemporal seizures or from other brain regions, independently of the laterality of the epileptogenic focus [1].

To date, the physiologic mechanism involved in the association between epileptic seizures and cardiac arrhythmias is poorly understood. It is likely that several different mechanisms exist. Indeed, many studies have been focused on seizure-related cardiac arrhythmias as bradyarrhythmia, cerebral depression, and autonomic dysfunction [3]. An abnormal neuronal activity during an epileptic seizure in the center of the central autonomic nervous system has been demonstrated, resulting in changes of cardiac rhythm [3].

Diagnosis of ictal bradycardia syndrome is underestimated probably because patients with bradyarrhythmias are usually admitted to

cardiology services whereas patients with epileptic seizures are admitted to neurologic services. Therefore, both the electroencephalogram (EEG) and electrocardiogram (ECG) are exams not routinely performed simultaneously. Nevertheless, getting the diagnosis of ictal bradycardia syndrome can be of critical relevance since bradyarrhythmias play an important role in Sudden Unexpected Death in Epilepsy (SUDEP) [3]. Indeed, asystole followed by syncope and sudden death could be the consequence of bradyarrhythmias. At the moment, no guidelines for the management of patients with ictal bradycardia syndrome exist.

Here, we report the case of a patient with frontal lobe seizures who developed bradycardia followed by asystole.

2. Case presentation

A 56-year-old Caucasian man, with epilepsy from adolescence, treated with phenobarbital 100 mg/day, was hospitalized for pneumonia complicated by acute respiratory failure. He had also experienced syncope once or twice a year. The patient did not have any history of cardiovascular disease or diabetes, but he had a positive family history for epilepsy. His family consisted of his mother and father, two brothers, and one sister. Except for the father, all members of the family had epilepsy. His two brothers with epilepsy both suddenly died of unspecified heart disease at the ages of 26 and 53, respectively.

During hospitalization, when pneumonia had resolved and the complete hematological examination showed normal parameters, several episodes of bradycardia and one episode of asystole occurred after the onset of the epileptic seizures. Immediately after the epileptic seizure, the ECG revealed sinus bradycardia (<30 beats/min) (Figs. 1A and B) followed by asystole lasting 8 s and hypotension (70/40 mm Hg) (Fig. 1C), spontaneously returning to normal sinus rhythm

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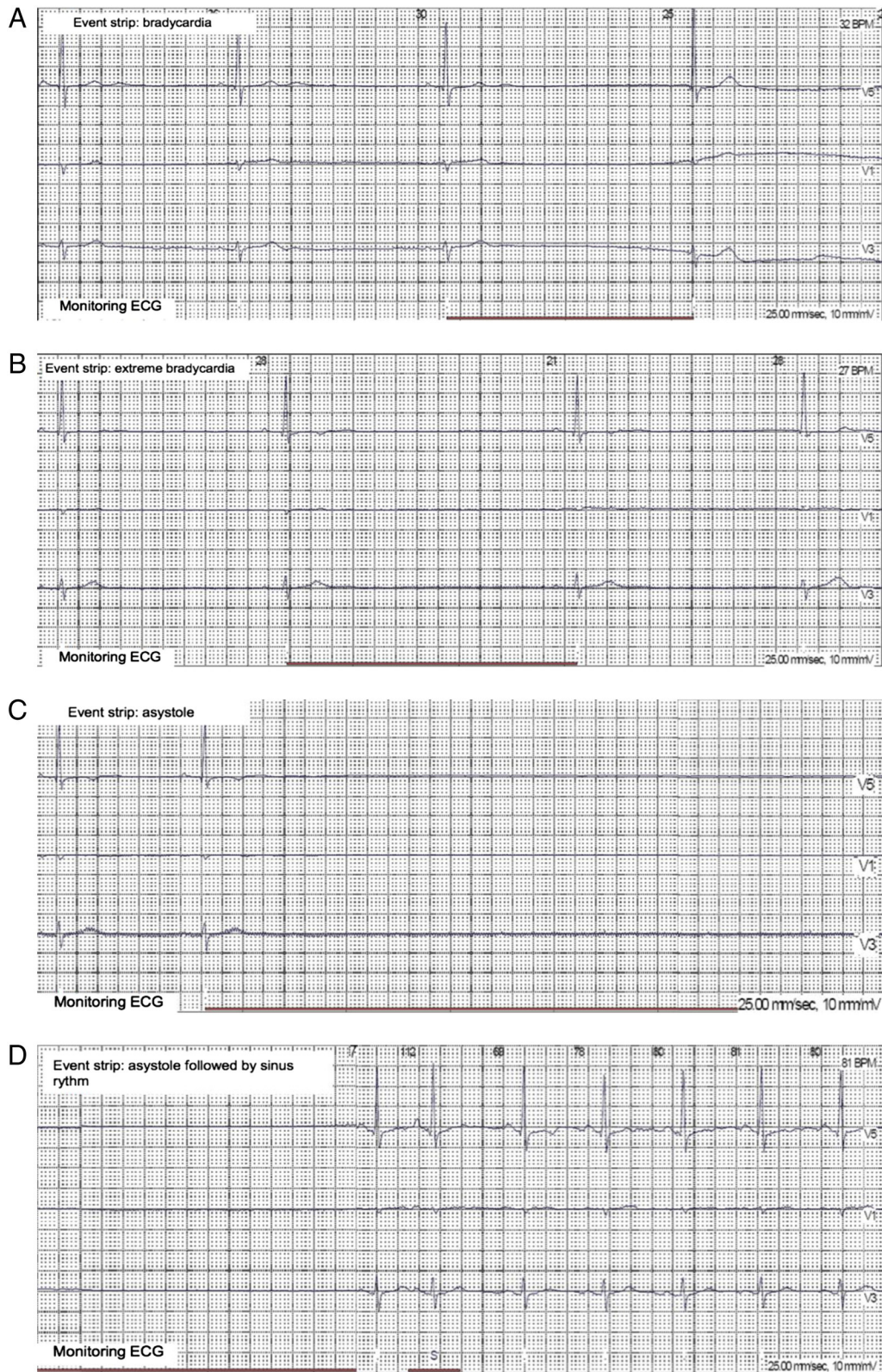


Fig. 1. ECG monitoring during and after the epileptic seizures showed a progressive prolongation of RR intervals (A) with a subsequent sinus bradycardia (<30 beats/min) (B) followed by asystole lasting 8 s (C), spontaneously returned to normal sinus rhythm of 80 beats/min (D).

of 80 beats/min (Fig. 1D) with normalization of blood pressure. The physical examination revealed no specific findings, while he reported symptoms of confusion, anxiety, and nausea. The computerized tomography imaging results were normal. Although the patient had been treated

with oxcarbazepine, four episodes of epileptic seizures and sustained bradycardia developed 48 h later.

Unfortunately, during the epileptic seizures, only ECG monitoring and respirogram were available. Baseline EEG, performed a few days

later, was abnormal, showing dominant 7 Hz sub-alpha activity admixed with slower elements (theta rhythm: 4–6 Hz) prevailing in frontocentral right regions, sometimes with spike morphologies (Fig. 2).

Given the clinical findings, a pacemaker was implanted without complications, and the patient was discharged home with antiepileptic therapy. After pacemaker implantation, three similar epileptic seizures were registered without the recurrence of asystole. During one of these epileptic seizures, the ECG Holter recording reported pacemaker rhythm. At four-month follow-up, the patient reported additional epileptic seizures but without syncope or traumatic falls.

3. Conclusion

We present a case of a patient affected by electric abnormalities of frontocentral areas associated with bradycardia and asystole and, consequently, treated with pacemaker implantation. In addition, this patient also had a strong family history of epilepsy and sudden death probably from heart disease.

Although the physiologic mechanism involved in the association between epileptic seizures and cardiac arrhythmias is poorly understood, notably, SUDEP is characterized by the absence of any identifiable structural cause of death at postmortem, suggesting that a hidden arrhythmogenic predisposition may exist [4]. In this light, the genetic susceptibility to the development of cardiac arrhythmias may represent a possible pathogenic mechanism responsible for the sudden death and the increased risk of cardiovascular disease in patients with epilepsy. Besides the cardiac channelopathies, such as familial long QT syndrome,

a common pathogenetic mechanism proposed is the heritable arrhythmogenic syndrome. Consequently, it is very important to identify early genes or genetic factors as screening biomarkers in families with at least two members affected by epilepsy and/or a heart condition that entails a risk of sudden death [4].

At the same time, we can also suspect that the presence of a brain injury may disrupt the autonomic system network, favoring a specific network for the production of bradycardia, thereby amplifying a possible sick sinus disease. In fact, it seems that epileptic activity might directly influence the autonomic nervous system, thereby producing heart rate changes [1,3].

Moreover, the diagnosis of ictal bradycardia is based on documentation of bradycardia/asystole produced by concomitant epileptic seizures recorded by both ECG and EEG, respectively [2]. However there are few cases described in the literature in which epileptic seizures associated with arrhythmias were detected by simultaneous EEG/ECG [1]. In our patient, bradycardia and asystole were documented by ECG monitoring which occurred after epileptic seizures that were only clinically observed. Due to the lack of EEG/ECG monitoring, ictal asystole can be underdiagnosed. Nevertheless, ictal bradycardia syndrome should still be considered in patients with unusual or refractory episodes of syncope or in patients with a history suggestive of both epilepsy and syncope because this syndrome could be a cause of SUDEP [3].

There are no guidelines for the management of patients with ictal bradycardia syndrome. Nevertheless, implantation of cardiac pacemaker along with the administration of antiepileptic drugs may be necessary

Fig. 2. Baseline electroencephalogram (EEG), performed a few days later, showed dominant 7 Hz sub-alpha activity admixed with slower elements (theta rhythm: 4–6 Hz) prevailing in frontocentral right regions, sometimes with spike morphologies. EEG conclusion: specific electrographic abnormalities in frontocentral areas, with basic activity deregulated and slowed.

in order to decrease the risk of death, making the patients free from ictal symptoms and preventing epileptic seizure-related falls [5].

In conclusion, there is no single risk factor common to all cases, and the pathogenic mechanism underlying sudden death in those with epilepsy still remains unclear. Unfortunately, a limitation of our study is represented by the lack of opportunity to contact the patient's brothers and sister and the consequent impossibility to perform genetic studies in other family members to assess disease coinheritance.

Finally, two factors can be of critical relevance in the diagnosis and risk stratification of the ictal bradycardia syndrome, such as the simultaneous EEG/ECG monitoring and the identification of genetic factors that predispose patients with epilepsy to the development of cardiac arrhythmias and/or syncope and/or sudden death.

Abbreviations

SUDEP	sudden unexplained death in epilepsy
ECG	electrocardiogram
EEG	electroencephalogram

Authors' contributions

MRR and IF contributed to manuscript writing and interpretation of the data. SDG and EV contributed to acquisition of the data. GP contributed to the critical revision of the manuscript for intellectual content. All authors read and approved the final manuscript.

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Competing interests

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The authors confirm that the manuscript has been read and approved by all named authors and that the order of authors listed in the manuscript has been approved by all.

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