Late-onset asystolic episodes in a patient with a vagal nerve stimulator

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Introduction

Insertion of a vagal nerve stimulator is an option to control partial complex seizures in patients with refractory epilepsy. The therapy is reported to be safe and is generally well tolerated by patients. We present a patient with periodic asystolic episodes causing syncopal events, thought to be caused by a previously placed vagal nerve stimulator. The patient was successfully treated with a pacemaker implantation.

Case report

A 46-year-old woman with a past medical history significant for intractable complex partial seizures underwent implantation of a LINQ rhythm recorder (Medtronic, Minneapolis, MN) for suspicion of cardiac syncope. The patient had established care with our neurology clinic 4 years prior and had an extensive history of epilepsy, having been diagnosed at the age of 21. She experienced breakthrough seizures at least once a month despite being on optimal antiepileptic medical therapy. Medications consisted of maximally tolerated doses of levetiracetam 1000 mg in the morning and 1500 mg in the afternoon, topiramate 200 mg twice daily, and carbamazepine 400 mg 3 times a day. A vagus nerve stimulator (Cyberonics, Houston, TX) was placed in 2004 as she was not considered to be a surgical candidate. A generator change was performed in 2012.

The patient described her seizures as a tonic-clonic activity but also experienced episodes of feeling weak with blanking and staring. In the past 2 years, the patient noted a change in her seizure pattern. She began to experience significant falls with injuries requiring sutures and staples, resulting in multiple admissions to the hospital for further monitoring. No changes to her medications were made. She reported increased frequency of spells, which occurred randomly, were not related to changes in position, and were without a prodromal or postictal period. There was no associated urinary or bowel incontinence. She experienced loss of consciousness for a brief period of time with an average of 2 falls a month. This was different from her prior episodes of staring and unresponsiveness, with gradual automatic behaviors.

On physical examination, the patient had a normal pulse rate and was normotensive. Cardiopulmonary auscultation was unremarkable. There were no symptoms of heart failure. Magnetic resonance imaging of the brain revealed left mesial temporal sclerosis as well as increased signal in the posterior right frontal region near the central sulcus. Three separate prolonged electroencephalogram evaluations consistently revealed a spike in the sharp waves in the F7–T3 distribution, suggestive of hemispheric epileptiform activity. A Ziopatch (iRhythm, San Francisco, CA) monitor was performed and did not reveal any abnormal rhythm. An electrocardiogram demonstrated normal sinus rhythm. An echocardiogram was performed, which was unrevealing. A myocardial perfusion stress test was also performed to rule out ischemia and was normal. No specific cause could be found to explain the appearance of these episodes.

Review of the vagal nerve stimulator settings showed that the output current strength on the stimulator was gradually increased over the past 2 years in order to control the patient's frequent seizures. She initially showed improvement with these changes; however, she then started falling and experiencing this new seizure pattern. The description of her spells was felt to be most consistent with cardiac syncope; however, differential diagnosis included drop attacks and complex partial seizures. The vagal nerve stimulator settings were changed in order to decrease the vagal stimulation with reduction of current strength and increasing current time off.

Owing to the infrequent nature of events, a LINQ recorder was implanted with periodic interrogation performed in the cardiology clinic. During interrogation it was noted that the patient had several sinus pauses of 10 to 12 seconds in duration. Review of medical records showed that these episodes correlated with date and time of recent falls and injuries as

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KEY TEACHING POINTS

- Late-onset asystole is a rare but significant complication in patients with a vagal nerve stimulator of which the clinician needs to be aware. A good clinical suspicion, thorough history, and physical examination are key to help discern cardiac vs neurogenic causes of syncope.
- Autonomic neural input to the heart exhibits some "sidedness," with the left vagal nerve having more influence on the atrioventricular node and right vagal nerve having more influence on the sinus node, which is why the stimulator is placed on the left side of the chest. This is thought to be secondary to the embryonic rotation of the body during development. However, it is important to know that there is some degree of overlap between the left and right vagal nerve innervation.
- Very few cases of late-onset syncopal events associated with vagal nerve stimulation therapy have been reported that were treated with removal or deactivation of the device. Another approach could be to implant a permanent pacemaker in a patient who would not tolerate removal of the stimulator owing to intractable epilepsy.

reported in her primary care provider's note (Figures 1 and 2). The leading diagnosis was that the excessive vagal nerve stimulation caused depression of the sinus node and led to profound bradycardia and asystole. The diagnosis of ictal bradycardia syndrome was also considered, as it can cause epileptic discharges that slow the cardiac function and lead to asystole in patients with temporal lobe epilepsy. The close relationship of worsening episodes and change of seizure pattern with increasing vagal nerve stimulation was more suggestive of syncope.

A collaborative risk-and-benefit discussion took place with the patient and Neurology and Cardiology teams. Deactivation and removal of the vagal nerve stimulator was entertained; however, the patient's epilepsy was very hard to control with just the use of antiepileptic medications. A permanent pacemaker was recommended and implanted via a right subclavian vein approach (Figure 3). There was consideration of a leadless pacemaker placement; however, the device was relatively new at the time and not available in our institution. The implantable loop recorder was removed prior to the procedure. The device representatives for the pacemaker and the vagal nerve stimulator were both present onsite during implantation. No interference between the vagal nerve stimulator and the pacemaker was noted. The patient has been seen in follow-up several times and has been doing well, without any further syncopal episodes. She has been followed every 3 months for the past year.

Discussion

The vagus nerve is a parasympathetic nerve with efferent and afferent function. Through its motor efferent fibers, it regulates the autonomic tone of various organs such as the heart. Through its afferent sensory fibers, it transmits information to the brain from the head, neck, thorax, and abdomen.[1] Autonomic neural input to the heart exhibits a degree of "sidedness," with studies suggesting that this is perhaps owing to rotation of the body during embryonic development.[1] The right sympathetic and vagal nerves affect the sinus node more than the atrioventricular (AV) node. The left sympathetic and vagal nerves have more influence on the AV

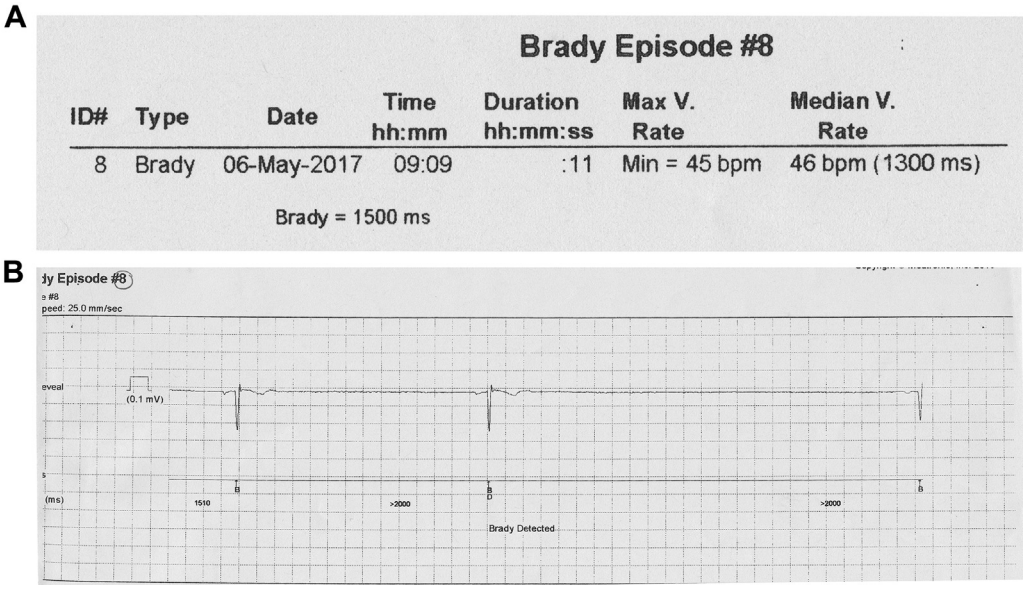

Figure 1 Severe symptomatic bradycardia with heart rate of 46 beats per minute, which coincided with a syncopal episode as stated in patient's primary care note. **A:** LINQ report of severe bradycardia. **B:** LINQ tracing of severe bradycardia.