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Epilepsy

Control of refractory status epilepticus precipitated by anticonvulsant withdrawal using left vagal nerve stimulation: a case report

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Abstract

Objective: To describe a case of left vagal nerve stimulation (VNS) resulting in immediate cessation of status epilepticus (SE) with good neurological outcome.

Case Description: A 30-year-old man with medically intractable seizures including episodes of SE was successfully treated using left VNS. After requiring discontinuation of phenytoin, valproic acid, carbamazepine, and topiramate because of severe allergic reactions resembling Stevens-Johnson syndrome, the patient required pentobarbital coma along with phenobarbital, tiagabine, and levetiracetam for seizure frequency reduction. He underwent left vagal nerve stimulator placement after nearly 9 days of barbiturate-induced coma, with stimulation initiated in the operating room. On the following day, electroencephalography revealed resolution of previously observed periodic lateral epileptiform discharges and the patient was free of seizures. Prestimulation seizure frequency was recorded at 59 times a day, with some seizures enduring 45 minutes despite barbiturate coma. Poststimulation, the patient has been free of seizures for 19 days and is presently taking only levetiracetam and phenobarbital, from which he continues to be successfully weaned without seizures. He is awake, alert, and can recall events leading up to his seizures, with good long-term memory and residual left upper extremity and lower extremity weakness.

Conclusion: This case illustrates the role of left vagal stimulation in the treatment of SE and otherwise medically intractable seizures caused by allergic reactions. To our knowledge, this is the first case in the world literature for adults reporting cessation of SE after VNS. Another case with a similar improvement has been reported in the pediatric population.

Keywords: Intractable seizures; Status epilepticus; Vagal nerve stimulation

1. Introduction

Status epilepticus (SE) occurs in approximately 50 000 individuals annually in the United States [5]. Mortality has been estimated at 22% [16]. The armamentarium of therapy available for control of SE includes multiple medications such as benzodiazepines, barbiturates, and propofol [1,4]. Despite initial treatment measures, refractory status epilepticus (rSE, defined as SE unresponsive to treatment with a benzodiazepine and first-line antiepileptic such as phenytoin [PHT]) was noted in 30% of patients with SE diagnosed at a large academic teaching hospital [8].

Options remaining in the treatment of rSE are few. Case reports of topiramate (TPM) [15], continuous midazolam infusion [3], and even focal cortical resection [11] have noted control of rSE anecdotally. A recent article describes the use of left vagal nerve stimulation (VNS) in control of rSE in a pediatric patient [18]. We found no such documented attempts at controlling rSE in adult patients using VNS in a PubMed literature search done on May 27, 2003.

The patient described in the present report developed severe allergy to multiple medications, a crescendo pattern

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of increasingly frequent seizures, and subsequent evolution into SE, which required induction of pentobarbital coma (PBC). Pentobarbital coma was prolonged because of the induction of new anticonvulsant medication allergies that led to the implantation of the vagal nerve stimulator.

2. Case report

A 30-year-old man was diagnosed with seizure activity at the age of 24 years, at which time he suffered a generalized tonic-clonic (GTC) seizure. At that time, results of a workup, which included computed tomography and magnetic resonance imaging, were negative for a structural lesion. Despite initial treatment with PHT, he had occasional GTC seizures without an aura at a frequency of approximately once every 4 months. Over the next 2 years, the seizure frequency increased to a rate of approximately 4 times a day with complex partial seizures (CPS) and GTC seizures. Complex partial seizures were associated with an aura of "burning in the feet," followed by a listless stare. Video-electroencephalograph (EEG) monitoring in July 2000 demonstrated independent bifrontal slowing and rare right-greater-than-left frontal spikes. He also had a single CPS with secondary generalization, with right frontal onset. Carbamazepine was initiated and then substituted by oxycarbamazepine, but the patient experienced severe mood depression and increased seizure frequency. After self-withdrawal from anticonvulsants because of these side effects, the patient experienced combinations of simple partial seizures, CPS, gelastic seizures, and secondary GTC seizures. Seizure frequency increased to 30 times per day with induction of SE. This was unresponsive to maximized doses of PHT and valproic acid (VPA) and required midazolam-induced coma for resolution. The hospital course was complicated by deep venous thrombosis, pulmonary embolism, and methicillin-resistant *Staphylococcus aureus* pneumonia. After his recovery, he was discharged free of seizures on a combined regimen of high-dose VPA and levetiracetam (LEV) with maintenance levels of 125 and 4 g/d, respectively. He was maintained free of seizures on this regimen for the next 1 1/2 years, except for rare seizures if he missed a dose of anticonvulsant medications.

The patient developed a severe rash resembling Stevens-Johnson syndrome. Erythema multiforme with severe blistering was noted on both upper and lower extremities with spread to the trunk and face mucosa, which progressed over 1 week before it was brought to medical attention. Valproic acid was reduced in half with some sequent clearing of the rash. Gabapentin (GPN) was initiated quickly. After 3 days, however, the patient developed an increased seizure frequency (of up to 10 GTC seizures per day that lasted approximately 1 to 4 minutes each) because of VPA withdrawal. Because LEV and GPN were not controlling the seizures and because he had been taking PHT in the past, he was bloused with PHT. Because of a continued increase in seizure frequency over the next 24 hours, TPM was added and increased quickly to 400 mg/d over 1 week with subsequent good improvement. Gabapentin was discontinued and he was maintained on PHT, LEV, and TPM. The patient was discharged after 4 days of seizure freedom.

He returned only 2 days after discharge with another severe allergic reaction, which cleared upon reduction of TPM. Phenobarbital (PB) was then added and TPM was discontinued but, after several days, an acute increase in seizure frequency again occurred because of TPM withdrawal. This seizure increase did not respond to very high doses of PHT, PB, and LEV and evolved into refractory SE, with approximately 30 to 60 discrete seizures per day. In addition, this seizure increase did not respond to propofol or intravenous lorazepam and subsequently required PBC induction. Pentobarbital was slowly titrated to a burst-suppression pattern on continuous video-EEG monitoring. Subsequently, the patient developed a third hypersensitivity rash to PHT, despite having taken this medication twice in the past. The rash improved with discontinuation of PHT. However, in an effort to avoid further drug withdrawal seizures, this discontinuation extended his time in PBC regimen because he was now only taking barbiturates and LEV. After having 3 hypersensitivity drug reactions, further anticonvulsant treatment was limited. The patient's mother had an allergy to sulfonamides, so zonisimide was not considered. Very low-dose tiagabine (TGB) was instituted, with the plan of a very slow titration to aid in long-term management. In addition, a dose-dependent central erythema was noted to PB. Because the patient had failed multiple anticonvulsants, either due to severe allergic reactions or to inefficacy in controlling the seizures, left VNS was considered as an option. Because the patient had previously expressed desire for the device, the patient's family consented to the procedure. In preparation for VNS implantation, pentobarbital was weaned beginning 48 hours before implantation of the VNS. Periodic epileptiform discharges emerged on the EEG. This further evolved into rhythmic sharp and wave complexes waxing and waning with semirhythmic high-voltage δ activity, which at times had a notched appearance. The evening before implantation, the background began to improve with intermixed α and β activities and less organized δ activity. Clinically, by 3:00 AM on the day of implantation, the patient began arousing but remained obtunded.

A left vagal nerve stimulator (Neurocybernetics Prosthesis System, Cyberonics, Webster, TX) was implanted on the 12th hospital day, in the standard manner for this procedure [7]. The stimulator was activated in the operating suite, with parameters of 0.25 mA, 30 seconds on/5 minutes off, frequency 20 Hz, pulse width 250 microseconds. The patient remained on his PB (150 mg IV q 6 hours, levels maintained at 38-40), LEV, and TGB regimen. On the morning of