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Clinical Observations

Vagus Nerve Stimulation for Electrographic Status Epilepticus in Slow-Wave Sleep

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ABSTRACT

BACKGROUND: Electrographic status epilepticus in slow sleep or continuous spike and waves during slow-wave sleep is an epileptic encephalopathy characterized by seizures, neurocognitive regression, and significant activation of epileptiform discharges during nonrapid eye movement sleep. There is no consensus on the diagnostic criteria and evidence-based optimal treatment algorithm for children with electrographic status epilepticus in slow sleep. **PATIENT DESCRIPTION:** We describe a 12-year-old girl with drug-resistant electrographic status epilepticus in slow wave sleep that was successfully treated with vagus nerve stimulation. Her clinical presentation, presurgical evaluation, decision-making, and course after vagus nerve stimulator implantation are described in detail. **FINDINGS:** After vagus nerve stimulator implantation, the girl remained seizure free for more than a year, resolved the electrographic status epilepticus in slow sleep pattern on electroencephalography, and exhibited significant cognitive improvement. **CONCLUSION:** Vagus nerve stimulation may be considered for electrographic status epilepticus in slow sleep.

Keywords: electrographic status epilepticus in slow sleep, continuous spike and waves during slow-wave sleep (CSWS), vagus nerve stimulation (VNS), epilepsy surgery

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Introduction

Electrographic status epilepticus in slow sleep or continuous spike and waves during slow-wave sleep (CSWS) is a poorly understood epileptic encephalopathy characterized by seizures, neurocognitive regression, and significant activation of epileptiform discharges during nonrapid eye movement (NREM) sleep.[1,2] In spite of recognition of electrographic status epilepticus in slow sleep/CSWS as a distinct clinical entity since 1971, there is a lack of well-defined diagnostic criteria and evidence-based therapeutic algorithm.[1,3] There are few data regarding nonpharmacologic treatment options for patients with suboptimal response to medications. We describe a girl with drug-resistant electrographic status epilepticus in slow sleep, who was not a suitable candidate for epilepsy surgery and achieved long-term seizure freedom and substantial cognitive improvement with vagus nerve stimulation (VNS).

Patient Description

This 12-year-old right-handed girl presented with seizures at 4.5 years of age. Her seizures consisted of stereotypic heavy breathing, unintelligible vocalizations, right facial twitching, head deviation toward

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the right, and right arm twitching, lasting for two to three minutes. Postictal manifestations included headache, somnolence, and vomiting. Around the age of ten years, she developed another seizure type characterized by staring without any motor automatisms or postictal manifestations. Seizures occurred once or twice every month. An overwhelming majority of seizures occurred during sleep and were identified by video monitoring instituted by parents. Her past history was noteworthy for vacuum extraction at 37 weeks gestation, neonatal hyperbilirubinemia at age seven days, and diagnosis of congenital hypothyroidism at age 19 days. She was reported to be otherwise healthy and developing age appropriately until four years of age.

After the onset of seizures, parents and teachers recognized progressively worsening focus, attention, acquisition of new memories, word finding, verbal recall, and general information retention. She presented to us having failed adequate trials of oxcarbazepine, levetiracetam, and lamotrigine. She had a normal physical and neurological examination. Although she was attending seventh grade, her reading comprehension was at fourth grade level. Serial neuropsychologic evaluations between the ages of seven and 12 years revealed a pattern of global intellectual decline. At the ages seven and ten years, she had a full-scale intelligence quotient of 89 and 87, respectively. At age 12 years, she had an intelligence quotient of 72 and Wechsler Intelligence Scale for Children IV scores of 69 (verbal), 71 (perceptual), and 97 (working memory).

Along with initiating a noninvasive presurgical evaluation, modification of antiepileptic drug (AED) regimen was recommended. Zonisamide and valproic acid were offered, with zonisamide being prescribed because of parental preference. Her electroencephalographic (EEG) monitoring demonstrated bilateral multifocal discharges most frequently in the left temporal region and generalized discharges, which activated during NREM sleep stages 2 and 3. These bilateral frontal-prominent discharges occurred in evolving bursts lasting up to several minutes during NREM sleep stages 2 and 3 and were classified as electrographic seizures. There was no normal sleep architecture, and her spike-wave index was estimated to be approximately 85%. On amplitude integration of C3 and C4 referential channels, there was a distinct elevation of lower boundary of power envelope above 50 μV^2 during NREM sleep stages 2 and 3 (Fig 1). Magnetic resonance imaging of the brain illustrated an area of encephalomalacia in the posteromedial aspect of the left thalamus, along with mild left-sided periventricular white-matter volume loss (Fig 2). Functional magnetic resonance imaging for language lateralization depicted an atypical pattern with frontal–temporal diaschisis. Verb generation paradigm depicted left-sided frontal lateralization but symmetric temporal activation. Other paradigms (story processing and picture encoding) revealed right lateralizing activation. Interictal fluorodeoxyglucose positron emission tomography showed left hemispheric hypometabolism with left temporal localization on statistical parametric mapping. Interictal single photon emission tomography suggested relative left temporal hypoperfusion. On magnetic source imaging of diffuse bilateral spike-wave discharges using multiple algorithms, widely varying bilateral or midline sources were estimated.

A left temporal hypothesis was formulated in cognizance of semiology, most common interictal focus on EEG, and imaging evidence. A left-sided craniotomy was performed with placement of subdural electrodes covering dorsolateral and orbital frontal regions; lateral and basal temporal surfaces; and adjacent anterior parietal lobe. Nonlocalizing nature of ictal onsets and magnetic source imaging prompted placement of dual-sided interhemispheric strips. Intracranial EEG monitoring documented evolving runs of epileptiform activity independently from multiple locations in left frontal, left temporal, and contralateral (right) frontal lobes. During NREM sleep stages 2 and 3, the epileptiform activity occurred nearly continuously which was thought to correspond with electrographic status epilepticus in slow sleep pattern observed on scalp EEG. A consensus was reached that she is not an optimal surgical candidate, and a left VNS was implanted after the removal of the subdural electrodes.

VNS was initially started at: output current 0.5 mA, frequency 20 Hz, pulse width 250 μs, on time 30 s, off time 5 min (duty cycle 10%), and magnet strength 0.75 mA. VNS settings were sequentially adjusted to: output current 1 mA, frequency 20 Hz, pulse width 250 μs, on time 21 s, off time 3 min (duty cycle 12%), and magnet strength 1.25 mA. Starting at 1-month follow-up, improved cognition and academic performance, decreased difficulty with expressive and receptive language, decreased irritability and mood disturbances, and reduced headaches, nausea, and vomiting were reported. The last reported seizure occurred 5 months after implantation. This seizure was not actually observed and inferred by parents based on typical postictal manifestations in the morning. Follow-up EEG 8 months after implantation showed normal NREM sleep architecture. Electrographic status epilepticus in slow sleep pattern was not observed, although rare bilateral independent epileptiform discharges were observed (Fig 1). Presently, she has been seizure-free for over a year, successfully weaned off AEDs, and attends age-appropriate grade in school.

Discussion

Electrographic status epilepticus in slow sleep is an enigmatic entity with lack of uniform evidence-based guidelines for diagnosis and treatment.[2] AEDs including valproic acid, ethosuximide, levetiracetam, and high-dose benzodiazepines have anecdotal evidence for efficacy, although there is no consensus about optimal therapeutic strategy.[1,4] Corticosteroids, adrenocorticotrophin, and immunoglobulins have also been used, but there is similar lack of evidence for best practice.[5,6] Electroclinical resolution of electrographic status epilepticus in slow sleep with drug therapy has varied from 17% to 41%.[1,6] There is a paucity of evidence to support nonpharmacologic management of patients who do not respond to AEDs or immunotherapy.[1] Ketogenic diet may improve the EEG in some patients, but not the neuropsychologic outcomes.[7] Multiple subpial transections may be efficacious in some patients with Landau–Kleffner syndrome, but the results have been inconsistent.[1,8] Epilepsy surgery has some documented efficacy, particularly in patients with an actual or potential epileptogenic substrate.[9,10]

VNS is a recognized therapeutic option for patients with drug-resistant epilepsy (DRE), particularly if they are not suitable candidates for resective and/or disconnection procedures. VNS is known to decrease seizure frequency by 32% to 67% at one-year follow-up in adults with DRE.[11] In children with focal DRE, it has a 50% responder rate of about 55%.[12] In addition, in children with primary generalized epilepsies, seizure frequency has been reported to decrease by 43% to 61% after one or more years of follow-up with 50% responder rate being 44% to 67%.[13] However, there are few data about the use of VNS for disorders on the electrographic status epilepticus in slow sleep/CSWS spectrum. One report of six patients with Landau–Kleffner syndrome documented at least a 50% decrease in seizure frequency and improved quality of life at six months in three of six (50%) patients with no reduction in the number of AEDs.[14]

Our report documents the efficacy of VNS in one child with typical electroclinical syndrome of electrographic status epilepticus in slow sleep. Although this should prompt consideration of VNS use in electrographic status epilepticus in slow sleep patients with suboptimal response to other treatments, it is difficult to attribute resolution of electrographic status epilepticus in slow sleep and clinical improvement in our patient conclusively to VNS alone. It is known that electrographic status epilepticus in slow sleep spontaneously resolves with progressive return of physiologic NREM sleep markers, typically after the age of eight to ten years. However, the period of EEG improvement can be