Successful Treatment of Refractory Status Epilepticus Using Anterior Thalamic Nuclei Deep Brain Stimulation

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BACKGROUND: **Refractory status epilepticus (RSE) is considered a medical emergency in neurology and is related to high mortality. We report a successfully treated case of RSE using deep brain stimulation (DBS) at the anterior thalamic nuclei (ATN) in a 17-year-old woman.**

RESULTS: **This patient developed RSE as a result of progressive seizure activity. RSE with generalized tonic-clonic seizures was noted 2 weeks before admission. Video electroencephalography monitoring showed continuous 3-Hz generalized spike-and-wave complexes with higher amplitude over bilateral frontal. Four weeks after RSE onset, bilateral DBS of the ATN was started. This treatment was immediately followed by the disappearance of tonic-clonic seizures and spike-and-wave complexes, suggesting resolution of the RSE. Significant clinical improvement was noted 1 week after DBS implantation.**

CONCLUSIONS: **DBS at the ATN significantly improved both the electroencephalography and clinical presentation in the patient with RSE. DBS at the ATN should be considered as a possible treatment choice once a patient develops RSE.**

INTRODUCTION

Status epilepticus (SE) is a frequent neurologic emergency associated with an annual incidence of between 8[1] and 41[2] cases per 100,000 individuals.[1,2] Although conventional antiepileptic drugs (AEDs) can terminate SE in most cases, some patients develop medically refractory SE (RSE).[3,4] Surgical treatments for RSE include destructive open surgery,[5] transcranial magnetic stimulation,[6] vagal nerve stimulation (VNS),[7] and centromedian thalamic nuclei deep brain stimulation (DBS).[8] We report the first patient with RSE to be treated using DBS of the anterior thalamic nucleus (ATN).

CLINICAL REPORT

A 17-year-old woman visited our clinic because of an increased frequency of alteration of consciousness over 6 months. She was noted to have slow reaction, associated with episodic brief staring, head nodding, and myoclonic jerk. These episodes had worsened during the previous 2 weeks and occurred 2 or 3 times a minute, each lasting for 10–20 seconds. Consequently, her daily activities were almost completely interrupted. A detailed examination of the patient's history showed that she had delayed speech development and a moderate intellectual disability. She experienced her first seizure with generalized tonic-clonic seizures (GTCS) when she was 12 years old. Episodic absentmindedness and myoclonic jerk developed several months later. Multiple AEDs in different combinations were tried, and at baseline, the patient had 1 or 2 GTCS monthly and 2 or 3 absence/myoclonic seizures daily. The AEDs that she had taken before admission included lamotrigine 400 mg/day, clobazam 30 mg/day, topiramate 200 mg/day, and levetiracetam 500 mg/day.

Under the impression of absence status SE in juvenile absence epilepsy, the patient was admitted for AED adjustment under long-term video electroencephalography (EEG) monitoring. There was no history of recent illness, head trauma, sleep deprivation, or missing dosage of AEDs. Hematologic estimations and serum biochemical analyses were all normal. Brain magnetic resonance imaging was unremarkable. Video EEG monitoring showed

Key words
- Anterior thalamic nucleus
- Deep brain stimulation
- Refractory status epilepticus

Abbreviations and Acronyms
AED: Antiepileptic drug
ATN: Anterior thalamic nucleus
DBS: Deep brain stimulation
EEG: Electroencephalography
GTCS: Generalized tonic-clonic seizures
RSE: Refractory status epilepticus
SE: Status epilepticus
SWC: Spike-and-wave complexes
VNS: Vagal nerve stimulation

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continuous 3-Hz generalized spike-and-wave complexes (SWCs) with higher bilateral frontal amplitude (Figure 1). Intravenous benzodiazepines (lorazepam 4 mg), levetiracetam (2000 mg/day) and valproic acid (1800 mg/day) were given immediately after admission, but both her clinical and her EEG seizures persisted. Topiramate 400 mg/day and perampanel 4 mg/day were administered on the following days. On day 4 of admission, she developed nearly continuous generalized or focal myoclonic jerks over the face and limbs. She was confused and failed to recognize her family, and 2 GTCS lasting for 1–3 minutes occurred. Because first-line AEDs were not able to achieve remission of the SE, intubation and administration of a continuous midazolam infusion were used to maintain the patient in an electrographic burst-suppression pattern. Induced coma was maintained sequentially with midazolam, and enteral AEDs were titrated to a higher dose (i.e., levetiracetam 3000 mg/day, valproic acid 1800 mg/day, topiramate 800 mg/day, and perampanel 12 mg/day). Despite this treatment, the EEG continued to show generalized 1-Hz to 3-Hz SWCs and convulsions consistent with ongoing SE occurred whenever attempts were made to wean her off intravenous drips. Propofol and pentobarbital were offered to control the RSE but were not administered because of adverse event concerns of the family. A ketogenic diet was initiated via nasogastric tube feeding 3 weeks after admission; however no clear clinical or EEG improvements were seen despite the patient becoming ketotic.

After 4 weeks of continuous absence SE, bilateral ATN DBS was suggested because other treatment options appeared exhausted. Intraoperative brain computed tomography image navigation with Brown-Roberts-Wells systems was used for localization of the bilateral ATN under mechanical ventilator support. After intraoperative microelectrode recording for confirmation of the location of the ATN, 2 standard 4-contact DBS electrodes were implanted (Activa system Model 3389s [Medtronics, Minneapolis, Minnesota, USA]) and externalized. Postoperative magnetic resonance imaging was performed to confirm the location of the

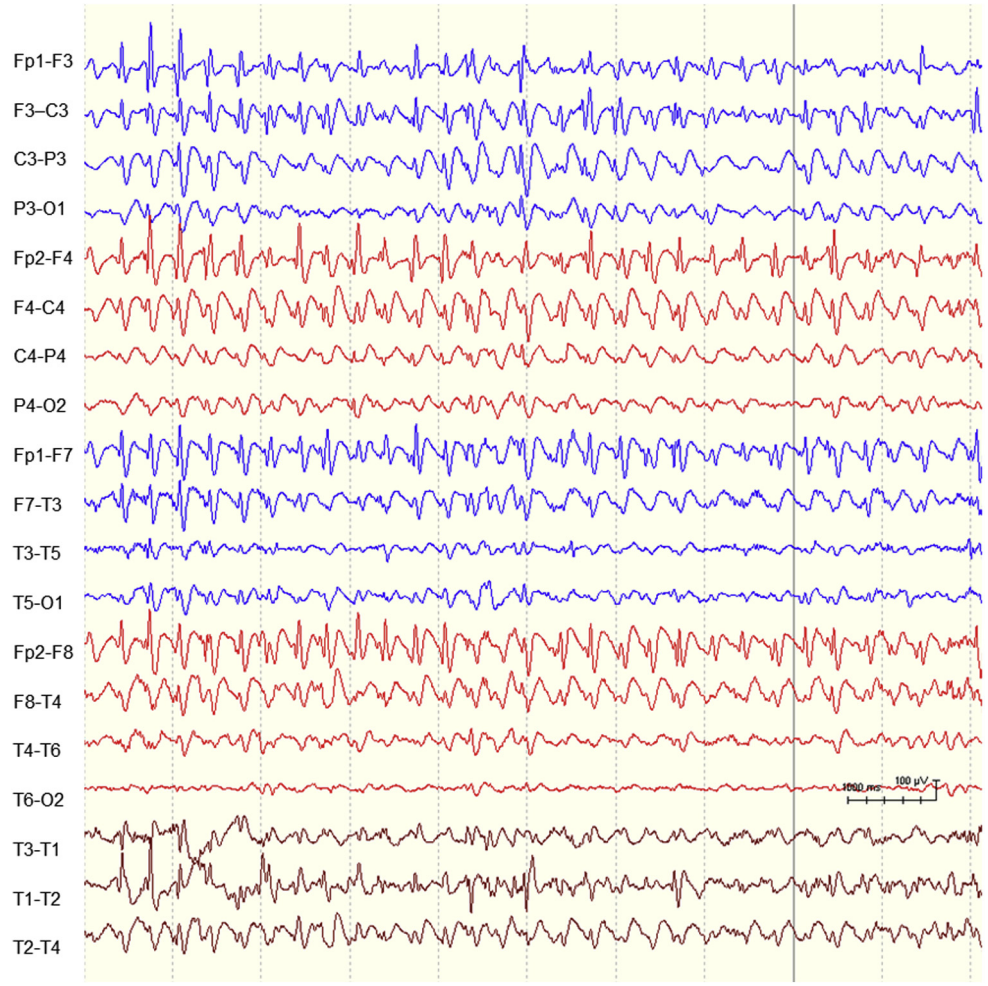

Figure 1. Initial scalp video electroencephalography showed continuous generalized 3-Hz spike-and wave activities with higher bilateral frontal amplitude.