Temporal lobectomy for refractory status epilepticus in a case of limbic encephalitis

Case report

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The authors report a case of status epilepticus secondary to limbic encephalitis that was successfully treated with temporal lobectomy. A 45-year-old woman presented in status epilepticus refractory to high-dose suppressive medical therapy. Magnetic resonance imaging of the brain showed T2- and FLAIR-weighted hyperintensities in the right temporal lobe, left and right frontal lobes, and pons. A lumbar puncture revealed normal findings. Continuous electroencephalography monitoring showed continued right temporal seizure activity. A paraneoplastic panel was positive for N-type voltage-gated calcium channels. Subsequent bronchial biopsy revealed small cell carcinoma of the lung. A right temporal lobectomy was performed due to refractory status, resulting in resolution of seizure activity and recovery of good neurological function. The authors describe their case and review the literature on surgical therapy for refractory status epilepticus and limbic encephalitis. (DOI: 10.3171/JNS/2008/109/10/0742)

Key Words • nonlesional status epilepticus • paraneoplastic limbic encephalitis • temporal lobectomy

Nonconvulsive status epilepticus is a life-threatening condition with a mortality rate of ~59% in cases refractory to medical therapy.14 Death is linked to the duration of seizure activity.22 In addition to death, there is a significant risk of morbidity associated with refractory seizures, including profound memory deficits and deterioration of intellectual function.5 Standard therapy consists of high-dose suppressive medications as well as intubation and monitoring in an intensive care setting, sometimes for weeks. This significantly increases the incidence of complications associated with hospitalization. Successful surgical treatment of refractory status epilepticus has been reported, primarily in a pediatric population. Previously reported procedures include hemispherectomies, multiple subpial transections, frontal lobectomies, focal frontal lobe resections, and insertion of vagal nerve stimulators.2,6,10,18,19,21 The majority of these procedures were performed after clear identification of an epileptogenic lesion on neuroimaging. Surgical therapy for nonlesional status epilepticus has been rarely documented.6,15,16 Surgical outcome in patients with chronic, nonlesional epilepsy has traditionally been worse than in comparable cases with clearly defined lesions. It is not known if this also holds true for nonlesional surgery performed for intractable status epilepticus.

Seizures are a frequent symptom of paraneoplastic limbic encephalitis and may take the form of refractory status.3,8,13,20 Successful treatment of limbic encephalitis usually involves antineoplastics to treat the tumor or immunosuppressive therapy. Surgical therapy of seizures resulting from limbic encephalitis is not well characterized and has been only briefly reported.13 We report a case of temporal lobectomy undertaken in a patient with paraneoplastic limbic encephalitis and nonlesional status epilepticus that resulted in good neurological outcome.

Case Report

History and Examination. This 45-year-old woman in whom new onset seizures had been diagnosed 2 months earlier presented to an outside facility after suffering a seizure. She reported having 8 brief seizures in 2 months. At the time of admission, she had missed her maintenance doses of phenytoin and clonazepam for 2 days. She was treated with intravenous phenytoin and clonazepam at the outside facility but despite this, had 14 seizures over a 24-hour admission period. She was then
transferred to our facility. At presentation, she was disoriented and unable to follow complex commands. Cranial nerve, motor, and sensory examinations revealed normal findings.

Magnetic resonance imaging performed at the outside facility showed T2 white matter lesions in the pons and cerebral hemispheric white matter. Repeated MR imaging at our facility was performed 8 days after admission and showed the previously seen abnormalities as well as increased signal in the right temporal lobe on T2- and FLAIR-weighted images (Fig. 1). Findings on MR angiography and digital subtraction angiography were unremarkable. Analysis of cerebrospinal fluid obtained from an initial lumbar puncture revealed a red blood cell count of 900/μl, a white blood cell count of 35/μl (90% lymphocytes), a glucose level of 70 mg/dl, and a protein level of 58/μl. A repeated study showed a red blood cell count of 23/μl, a white blood cell count of 1/μl, a glucose level of 79 mg/dl, and a protein level of 22. The cerebrospinal fluid cultures and herpes polymerase chain reaction were negative.

A paraneoplastic panel returned positive for N-type calcium channel binding antibody (331 nmol/L [reference rate < 20 nmol/L]). As a result of this finding, a total body CT/PET scan was obtained, which showed areas of hypermetabolism in the mediastinum. A needle biopsy of the lung showed small cell carcinoma.

**Treatment.** The patient was initially treated medically with fosphenytoin, valproic acid, and acyclovir. She was admitted to the video-EEG monitoring unit where continuous EEG revealed right temporal seizures (Fig. 2). She was transferred to the medical intensive care unit when these seizures continued despite appropriate levels of valproic acid, fosphenytoin, and 9 mg of lorazepam in divided doses. After intubation, continuous propofol and midazolam infusions were started, along with the subsequent addition of phenobarbital and leviteracetam. The patient’s seizures continued, however, and after 8 days, intravenous pentobarbital was introduced. Electroencephalography then showed long bursts of activity consisting of generalized pseudoperiodic epileptiform discharges. Tapering of the pentobarbital dose brought about recurrence of the partial epileptic activity.

**Operation.** On hospital Day 11, the patient underwent a right corticoamygdalohippocampectomy with resection of the superior, middle, and inferior temporal gyri extending ~ 5 cm posterior from the temporal tip, and including the mesial temporal structures. A postsurgical pathological examination showed only nonspecific inflammatory changes consistent with encephalitis in the hippocampus and temporal cortex.

**Postoperative Course.** Propofol and pentobarbital were slowly tapered, and the patient did not have any further electrographic seizures. The patient’s neurological examination revealed steady recovery over the course of 12 days postoperatively. On postoperative Day 19 she began chemotherapy with etoposide and cisplatin. On postoperative Day 55, the patient was discharged to a rehabilitation facility for physical therapy. At this point, she was very interactive with an essentially intact neurological examination. Her seizures remained completely controlled on leviteracetam and clonazepam. She died 6 months later of metastatic lung cancer but had no further seizures. Her mental status remained intact until the time of her death.

**Discussion**

Limbic encephalitis is characterized by inflammatory infiltration of the hippocampal and medial temporal lobe regions of the brain. It is frequently a paraneoplastic phenomenon associated with small cell carcinoma of the lung. It may occur in isolation or as part of a multifocal paraneoplastic encephalomyelitis. The characteristic clinical findings include a relatively acute onset of personality changes, memory loss, and seizures that may be refractory to medical therapy. Symptoms frequently present well before the diagnosis of cancer is made. Temporal lobe seizures are most frequently noted; however, generalized seizures and combinations of seizures have been identified.

Treatment of paraneoplastic limbic encephalitis has traditionally included treatment of the underlying malignancy, pharmacological treatment of symptoms, and immunosuppressive therapy. The clinical course is highly variable, and patients may progress to a level of severe neurological disability despite treatment. Status epilepticus in cases of paraneoplastic limbic encephalitis...
may be especially refractory to pharmacological treatment. There is potential for rapid generalization and progression of seizures. Resection as therapy for seizures associated with limbic encephalitis has not been previously well characterized.

There are no clear guidelines for the treatment of refractory status epilepticus. Generally, high-dose suppressive therapy is used, and the choice of therapeutics is guided by physician preference. Often, therapy is ineffective even after weeks of intensive adjustments. This increases the rate of complications associated with intensive care such as pneumonia, deep venous thrombosis, hypotension, and line sepsis. Successful surgical treatment of refractory status epilepticus has been previously reported but traditionally has been reserved for severely refractory cases after prolonged treatment with high-dose suppressive therapy. Few cases have been attempted early in the course of management.

It has been proposed that criteria for surgical therapy of refractory status epilepticus should include failure of usual treatment protocols, the presence of a clearly defined lesion on structural and functional neuroimaging, and congruent abnormalities on EEG. Surgery for nonlesional epilepsy has traditionally had a worse outcome with regard to seizure control. Nonlesional resections for ameliorating status epilepticus have been rarely performed. Our patient had no clearly defined epileptic lesion on neuroimaging. The increased signal on T2- and FLAIR-weighted sequences noted in the temporal lobe are frequently seen in cases of limbic encephalitis but do not necessarily correlate with increased seizure frequency. It is unclear if the hyperintensities in this case were a result of prolonged seizure activity. Our patient also had extratemporal neuroimaging abnormalities, which are frequently seen in limbic encephalitis and paraneoplastic encephalomyelitis. In previous cases of limbic encephalitis presenting with epilepsy partialis continua, seizures initially abated after chemotherapeutic treatment of the underlying malignancy, but neurological symptoms recurred. Our patient did well from a neurological standpoint until the time of her death.

**Conclusions**

Our case reinforces the efficacy of surgical intervention for refractory status epilepticus even in patients with nonlesional epilepsy, particularly in regard to treatment of limbic encephalitis. Despite the traditionally worse outcome of surgery in nonlesional chronic epilepsy, the high morbidity and mortality rates associated with status epilepticus may make surgical intervention an attractive option even in cases of status epilepticus in which clearly defined lesions are not present. Consideration of this condition relatively early in the course of refractory seizures may result in fewer iatrogenic complications and better neurological outcome.

**Disclaimer**

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.
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References