

# Focal Cortical Resection for Complex Partial Status Epilepticus Due to a Paraneoplastic Encephalitis

Fadi Nahab, MD, Adam Heller, MD, and Suzette M. LaRoche, MD

**Abstract:** We report a 57-year-old female who presented with epilepsy partialis continua and rapidly progressed to refractory complex partial status epilepticus (CPSE) with brain magnetic resonance imaging revealing a focal cortical lesion on T2 sequences corresponding to the seizure focus on ictal electroencephalographic recordings. The patient underwent focal cortical resection of the seizure focus. Though clinical and electrographic seizure activity ceased, the patient remained unresponsive with repeat neuroimaging showing diffuse limbic and brainstem involvement. Serological tests revealed anti-Hu antibodies suggesting a paraneoplastic encephalitis. Chest computed tomography showed a 5-mm pulmonary nodule and resection of the pulmonary nodule confirmed the diagnosis of small cell lung cancer. Plasmapheresis was performed without clinical improvement. Focal resection can be effective in terminating refractory CPSE but evaluation for a paraneoplastic syndrome must be considered early in the diagnosis of epilepsy partialis continua and CPSE as these patients have a poor prognosis.

**Key Words:** epilepsy partialis continua, paraneoplastic encephalitis, anti-Hu antibodies, complex partial status epilepticus, focal resection

(*The Neurologist* 2008;14: 56–59)

Epilepsy partialis continua (EPC) is a clinical syndrome defined by continuous focal motor seizures of cortical origin often with minimal or no electrographic changes seen on scalp electroencephalograph (EEG). EPC in adults is most often caused by focal structural lesions as a result of vascular disease, neoplasm, trauma, or infection.<sup>1</sup> We present an adult with EPC who progressed to medically refractory complex partial status epilepticus. The patient underwent successful focal cortical resection of the seizure focus with cessation of clinical and electrographic seizure activity. The presence of anti-Hu antibodies and pathologic confirmation of small cell lung cancer led to the diagnosis of paraneoplastic encephalitis.

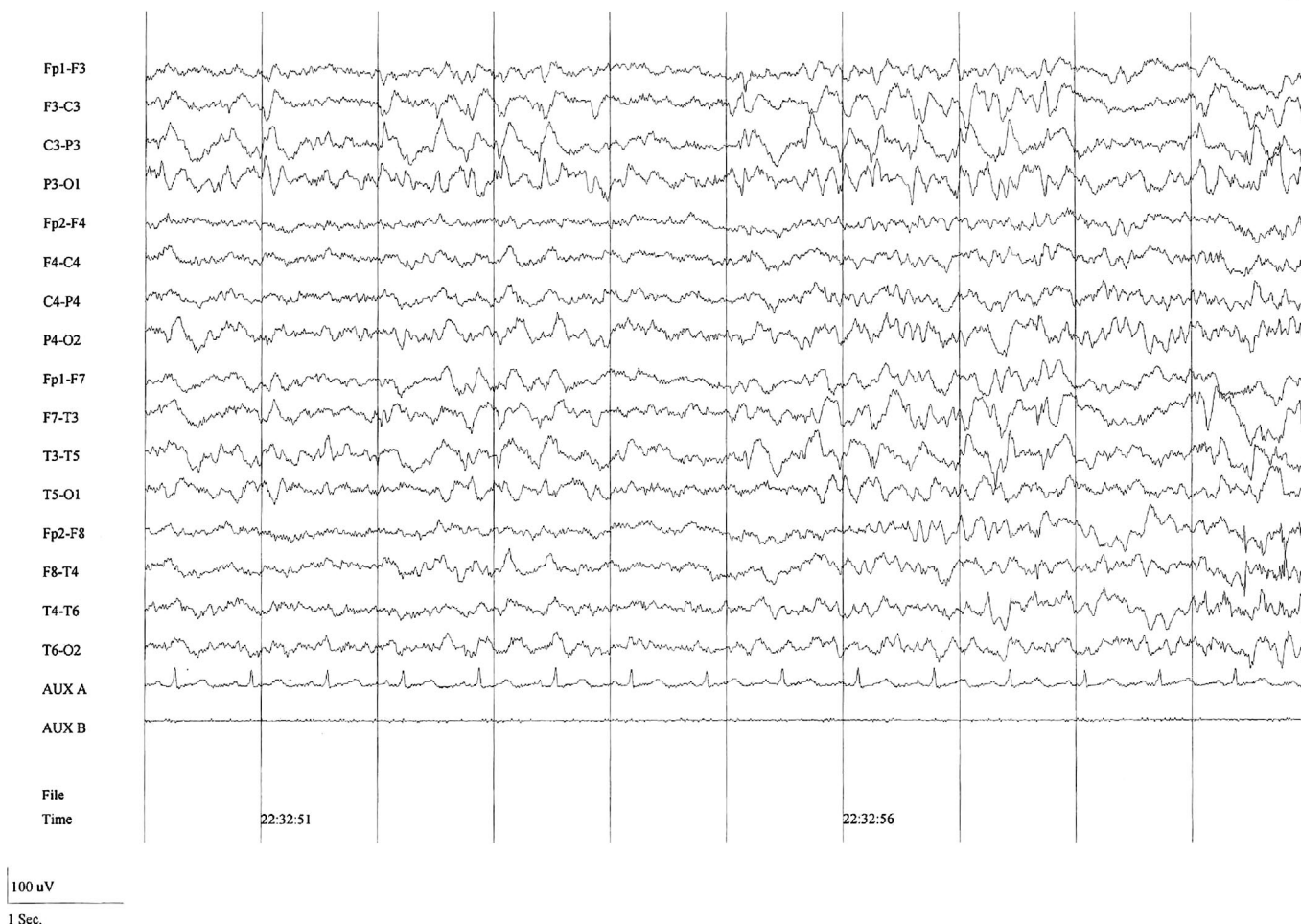
From the Department of Neurology, Emory University, Atlanta, GA.  
Reprints: Fadi Nahab, MD, 1001 Garden View Drive NE, #711, Atlanta, GA 30319. E-mail: fnahab@emory.edu or fadinahab@rocketmail.com.  
Copyright © 2008 by Lippincott Williams & Wilkins  
ISSN: 1074-7931/08/1401-0056  
DOI: 10.1097/NRL.0b013e3181578952

## CASE PRESENTATION

A 57-year-old female was evaluated for a 2 month history of refractory simple partial seizures. Her first seizure consisted of right upper extremity clonic movements that progressed to a generalized tonic-clonic seizure. These developed into frequent episodes of clonic right face, arm, and occasionally leg movements without alteration of awareness. She had no significant medical history other than an 80 pack-year smoking history. Despite trials of phenytoin, valproic acid, and levetiracetam titrated to toxic doses, she continued to have these persistent movements. Our clinical diagnosis was EPC of unclear etiology. Previous evaluation had included 2 normal brain magnetic resonance imaging (MRIs) and an ambulatory electroencephalograph (EEG) that demonstrated frequent epileptiform discharges over the left fronto-central region correlating with clinical seizure activity (Fig. 1). Inpatient admission for further evaluation was declined by the patient and topiramate was added to her AED regimen of phenytoin, valproic acid, and levetiracetam.

Four days later the patient was brought to the hospital by family after they noticed some speech difficulty. Examination was notable for expressive aphasia with persistent clonic movements of the right face and arm. The patient was admitted to the hospital and on hospital day 1, scalp EEG showed brief runs of epileptiform discharges over the left fronto-central region similar to those seen on ambulatory EEG, which correlated with clinical seizures. Brain MRI on day 1 revealed a T2 hyperintensity in the left fronto-parietal region (Fig. 2A–C). The seizures continued despite titration of topiramate and the addition of clonazepam. On hospital day 2 a computed tomography (CT) scan of her chest, abdomen, and pelvis was done to evaluate for possible malignancy and revealed a single 5-mm noncalcified nodule in the left lower lobe of the lung. The pulmonary team was consulted and given its small size serial imaging was recommended. Lumbar puncture was performed with cerebrospinal fluid (CSF) showing an elevated protein of 70 mg/dL but normal WBC count (2 cells/uL) and glucose (47 mg/dL). CSF cytology was negative for malignant cells. A serum and CSF paraneoplastic panel was sent.

On hospital day 8, the neurosurgery team performed a brain biopsy of the lesion seen on MRI. Pathology revealed reactive gliosis and no evidence of metastatic or primary brain neoplasm. The patient's seizures continued despite multiple antiepileptic medications and progressed to complex partial status epilepticus. She was placed in a burst-suppres-



**FIGURE 1.** Ambulatory EEG showing seizure onset over the left fronto-central region.

sion coma with intravenous diprivan and phenobarbital while continuing phenytoin, valproic acid, levetiracetam, and topiramate. The patient failed attempts to wean off the anesthetic coma with regression back to electrographic status epilepticus.

The patient was evaluated for surgical resection of the seizure focus though functional imaging of the presumed focus was limited by the patient now being intubated and therefore ineligible for SPECT and PET scans. On day 16, intracranial grids were placed over the left fronto-parietal region for detailed localization; prolonged seizures occurred over the left frontal region. Motor mapping was completed on day 18 and the patient was taken for surgical resection on day 22. Pathology on the resected area showed mild-moderate chronic inflammatory infiltrate involving the leptomeninges, perivascular spaces of the cortex, and white matter blood vessels. The pathologist's differential diagnosis included autoimmune disease, paraneoplastic disease, and Rasmussen's encephalitis.

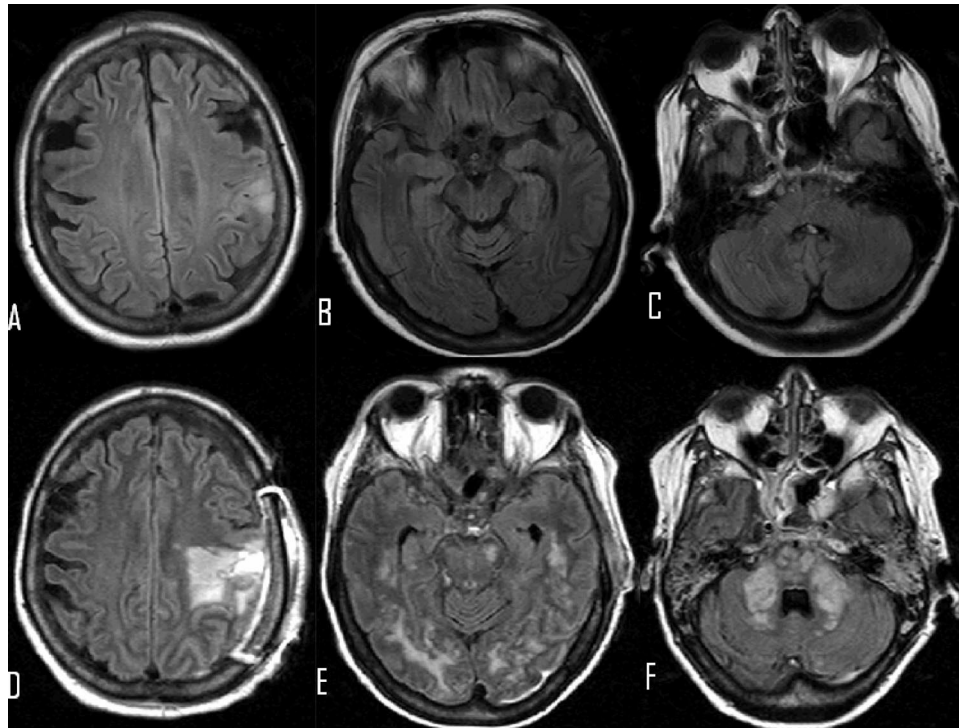
Postoperatively, the patient's seizures resolved both clinically and electrographically. Despite resolution of seizures and weaning of anesthetic agents, the patient remained comatose and ventilator dependent. A follow-up brain MRI

was performed on day 29 (Figs. 2D–F). Diffuse T2 hyperintensities were seen throughout the subcortical white matter and brainstem, consistent with limbic encephalitis. The following day, results of previously obtained serum testing for anti-Hu antibodies were positive. The patient was taken for resection of the 5-mm lung nodule and pathologic diagnosis was consistent with small cell lung carcinoma.

The patient underwent a 5-day course of plasmapheresis in an attempt to treat the paraneoplastic limbic encephalitis. The patient remained comatose without recurrence of seizures. Repeat MRI after plasmapheresis remained unchanged. The patient developed a ventilator-acquired pneumonia in the ICU and the family agreed on comfort care measures. The patient died on hospital day 54.

## DISCUSSION

The present case highlights an adult with paraneoplastic encephalitis (PE) presenting as EPC who underwent cortical resection to treat medically refractory complex partial status epilepticus (CPSE). Our patient clearly had medically intractable CPSE with failure of multiple medical therapies, includ-



**FIGURE 2.** (A,B,C) Brain MRI on hospital day 1, with FLAIR images showing an area of T2 hyperintensity in the left frontoparietal, peri-rolandic distribution, which involves the postcentral gyrus to a greater extent than the precentral gyrus with minimal mass-effect. (D,E,F) Brain MRI on hospital day 29 with FLAIR images showing diffuse T2 hyperintensity of the bilateral occipital and temporal lobes, corpus callosum, middle cerebellar peduncles, pons, and left cerebellar hemisphere.

ing anesthetic-induced coma. The patient provided a unique situation in which the rapidly declining neurologic status after admission warranted aggressive treatment before the diagnosis of PE was definitive.

EPC has been previously reported as a rare manifestation of an anti-Hu-associated PE.<sup>2-6</sup> EPC was the initial presentation of an underlying small cell lung cancer in 5 of 7 reported cases. Our patient was unique in that at presentation there was no evidence of limbic involvement by clinical, EEG, or radiographic testing. Initial limbic involvement was seen in all but one previous report of patients with an anti-Hu-associated PE.<sup>2</sup>

Our patient demonstrated an atypical evolution of MRI findings from a focal nonenhancing lesion on T2-weighted imaging in the sensorimotor area to multifocal involvement of both limbic and brainstem structures on repeat imaging after surgical and immunologic therapy. Previous studies of PE have suggested that MRI represents an important tool in the diagnosis. The presence of a nonenhancing T2-weighted abnormality on our patient's initial MRI is consistent with previous reports of PE in which up to 83% of patients had T2-weighted abnormalities.<sup>7</sup> However, in our patient, the T2 abnormality may represent the sequelae of recurrent focal seizures rather than a specific paraneoplastic phenomenon given that similar T2 abnormalities have been reported in EPC secondary to nonketotic hyperglycemia.<sup>8</sup> Evolution from focal to multifocal involvement of both limbic and brainstem structures on our patient's repeat imaging has not

been reported previously though patients with PE who undergo repeat neuroimaging often have new abnormalities.<sup>9</sup> Our patient's repeat imaging is similar to that seen in the majority of paraneoplastic limbic and brainstem encephalitides, including those associated with anti-Hu, anti-Ri, and anti-Ma2 antibodies.<sup>10</sup>

Only one other case report has described a patient with anti-Hu-associated PE who progressed from EPC to a medically refractory CPSE and this patient succumbed to medical complications as a result of anesthetic coma.<sup>4</sup> Our patient underwent successful focal cortical resection with complete cessation of clinical and electrographic seizures as in previous reports of successful focal resective surgery of patients with medically refractory status epilepticus.<sup>11,12</sup>

There is no definitive treatment for anti-Hu-associated PE and the prognosis of these patients is poor. The median survival was 11.8 months in an analysis of 200 patients with anti-Hu-associated PE.<sup>13</sup> Previous treatments have included the use of antineoplastic therapy with or without immunotherapy and immunotherapy alone, with some evidence of improvement or stabilization of the PE, though 3-year survival remains 20%.<sup>13</sup>

EPC that evolves into CPSE can be difficult to treat and patients with medically refractory CPSE should be considered for focal resective surgery when a seizure focus can be found. Given the poor prognosis of patients with anti-Hu-associated PE, aggressive surgical intervention in these patients is likely to increase short-term morbidity without extending survival. Thus,

evaluation for a paraneoplastic syndrome must be considered early in the diagnosis of EPC and CPSE.

### REFERENCES

1. Cockerell OC, Rothwell J, Thompson PD, et al. Clinical and physiological features of epilepsy partialis continua. *Brain*. 1996;119:393–407.
2. Shavit YB, Graus F, Probst A, et al. Epilepsia partialis continua: a new manifestation of anti-Hu-associated paraneoplastic encephalomyelitis. *Ann Neurol*. 1999;45:255–258.
3. Porta-Etessam J, Ruiz-Morales J, Millan JM, et al. Epilepsia partialis continua and frontal features as a debut of anti-Hu paraneoplastic encephalomyelitis with focal frontal encephalitis. *Eur J Neurol*. 2001;8:359–360.
4. Jacobs DA, Fung KM, Cook NM, et al. Complex partial status epilepticus associated with anti-Hu paraneoplastic syndrome. *J Neurol Sci*. 2003;213:77–82.
5. Mut M, Schiff D, Dalmau J. Paraneoplastic recurrent multifocal encephalitis presenting with epilepsy partialis continua. *J Neurooncol*. 2005;72:63–66.
6. Kinirons P, O'Dwyer JP, Connolly S, et al. Paraneoplastic limbic encephalitis presenting as lingual epilepsy partialis continua. *J Neurol*. 2006;253:256–257.
7. Lawn ND, Westmoreland BF, Kiely MJ, et al. Clinical, magnetic resonance imaging, and electroencephalographic findings in paraneoplastic limbic encephalitis. *Mayo Clin Proc*. 2003;78:1363–1368.
8. Singh BM, Strobos RJ. Epilepsia partialis continua associated with nonketotic hyperglycemia: clinical and biochemical profile of 21 patients. *Ann Neurol*. 1980;8:155–160.
9. Bataller L, Dalmau J. Paraneoplastic disorders of the central nervous system: update on diagnostic criteria and treatment. *Semin Neurol*. 2004;24:461–471.
10. Dalmau J, Graus F, Villarejo A, et al. Clinical analysis of anti-Ma2-associated encephalitis. *Brain*. 2004;127:1831–1844.
11. Desbiens R, Berkovic SF, Dubeau F, et al. Life-threatening focal status epilepticus due to occult cortical dysplasia. *Arch Neurol*. 1993;50:695–700.
12. Ma X, Liporace J, O'Connor JM, et al. Neurosurgical treatment of medically intractable status epilepticus. *Epilepsy Res*. 2001;46:33–38.
13. Graus F, Keime-Guibert F, Rene R, et al. Anti-Hu-associated paraneoplastic encephalomyelitis: analysis of 200 patients. *Brain*. 2001;124:1138–1148.