Epilepsi 2(2): 51-54, 1996

Surgically Remediable Epileptic Syndromes

Jerome ENGEL, JR.

It has been estimated that there are approximately 100,000 patients with medically refractory epilepsy in the United States who are potential candidates for surgical treatment, with an additonal 5,000 to 10,000 added to this pool each year; while the latest data indicate that only 1,500 surgical procedures for epilepsy were performed in 1991[1]. There has been an increasing interest in surgical treatment for epilepsy over the past 5 to 10 years, as evidenced by the number of recent books published on this subject[2-8]. Many new epilepsy surgery facilities are being developed, and surgical intervention has now become an option for a larger number of patients who suffer from epileptic seizures that cannot be controlled by standard antiepileptic drugs. In order to take advantage of this alternative mode of therapy, referring physicians must know how to identify surgical candidates, which requires an understanding of the term "medical intractability"[9].

With the recent additonal of several new antiepileptic drugs to our pharmacological armamentarium, and the promise of more in the near future, assessment of medical intractability can become a lengthy process. Is it really necessary to try every antiepileptic drug, alone and in combination, before concluding that a patient is a surgical candidate? A major conclusion deriving from the last major international conference on surgical treatment of epilepsy, held in Palm Desert, California, in 1992[4,10], was that surgical treatment should not necessarily be considered always a therapy of last resort. Rather, a number of surgically remediable epileptic syndromes have been identified which are associated with an invariably poor response to pharmacotherapy, but a predictably excellent response to surgical intervention[1].

UCLA School of Medicine, Reed Neurological Research Center
Los Angeles, California 90024 - 1769 USA

MESIAL TEMPORAL LOBE EPILEPSY

The prototype of a surgically remediable syndrome is *mesial temporal lobe epilepsy*, a condition of medically refractory temporal lobe seizures associated with hippocampal sclerosis that usually begins in the first decade of life and can have disastrous psychosocial consequences [11,12]. The characteristic features of this syndrome are shown in Table 1. The presurgical evaluation of mesial temporal lobe epilepsy can usually be accomplished noninvasively with long-term EEG and video monitoring, high resolution magnetic resonance imaging (MRI), neuropsychological testing, and perhaps functional imaging such as positron emission tomography (PET) or single photon emission computed tomography (SPECT). Seventy-to 80% of patients so identified can expect to become seizure free following a relatively limited anteromedial temporal lobe resection, and the remainder experience a marked reduction in seizure frequency. The prognosis with respect to epileptic seizures, and perhaps more importantly, the degree of psychosocial rehabilitation, however, depends upon the age at surgery and the duration of epilepsy prior to operation[13]. Because early surgical intervention provides the greatest opportunity to return the patient to a completely normal lifestyle, prolonged trials with second line drugs and drug combinations can be counterproductive. Once this syndrome has been identified, and it has been ascertained that the primary pharmacologic agents, carbamazepine and phenytoin, are unable to control the habitual seizures, patients should be referred directly to an epilepsy center and considered for surgical treatment.

Table 1: The Syndrome of Mesial Temporal Lobe Epilepsy (MTLE)

A. History

1. Increased incidence of complicated febrile convulsions.
2. Increased incidence of a family history of epilepsy.
3. Onset in latter half of first decade of life.
4. Auras common and occur in isolation.
5. Secondarily generalized seizures occur infrequently.
6. Seizures often remit for several years until adolescence or early adulthood.
7. Seizures often become medically intractable.
8. Interictal behavioral disturbances can occur (most commonly depression)

B. Clinical Seizure

1. *Aura* is usually present - most common is epigastric rising, often other autonomic or psychic symptoms, with emotion (e.g., fear), can be olfactory or gustatory sensation (several seconds).
2. *Complex partial seizure* - often begins with arrest and stare, oroalimentary automatisms and complex automatisms common. Posturing of one upper extremity may occur contralateral to the ictal discharge (one to two minutes).
3. *Postictal phase* - usually includes disorientation, recent memory deficit, amnesia for the event, and dysphasia if seizures begin in the language dominant hemisphere (several minutes).

C. Neurological Examination

1. Usually normal.
2. May have recent memory deficit.

D. EEG

1. Unilateral or bilateral independent anterior temporal spikes, maximum amplitude in basal electrodes.
2. May be intermittent or continuous rhythmic slowing in one mesial temporal area.
3. Extracranial ictal activity appears only with complex partial symptoms, usually initial or delayed focal onset pattern of 5-7/sec rhythmic activity, maximum amplitude in one basal temporal derivation.
4. Depth electrode ictal onset most often high amplitude rhythmic spikes or sharp waves, less commonly low voltage fast or supression.
5. Propagation to contralateral side is slow (>5 sec, but may be minutes), or does not occur at all.

E. Focal Functional Deficits

1. Usually temporal lobe hypometabolism on interictal FDG-PET, often involves ipsilateral thalamus and basal ganglia.
2. Usually temporal lobe hypoperfusion on interictal SPECT and characteristic pattern of hyper- and hypoperfusion on ictal SPECT.
3. Usually material specific memory disturbances on neuropsychological testing and amnesia with contralateral intracarotid sodium amobarbital injection.
4. Mesial temporal EEG slowing and attenuation of normal rhythms can be seen with scalp/sphenoidal electrodes, but more common with depth electrodes; exarcerbated by iv pentothal test.

F. Structural Imaging

1. May have small hippocampus on one side (on MRI).
2. May have small temporal lobe on one side.
3. May have enlarged temporal horn on one side.

G. Pathophysiology

1. Hippocampal sclerosis (>30% cell loss with specific patterns).
2. Sprouting of dentate granule cell mossy fibers.
3. Selective loss of certain hilar neurons (somatostatin and NPY-containing cells).
4. Hamartomas and heterotopias may occur as "dual pathology".
5. Microdysgenesis common.
6. Seizures may originate in sclerotic hippocampus but much larger area appears to be included in the epileptogenic region.

H. Features That Place Diagnosis in Doubt

1. History of severe head trauma, encephalitis or other specific causal events.
2. Focal motor or specific sensory symptoms at seizure onset or postictally.
3. Interictal focal neurological deficits.
4. Marked cognitive impairment on neurophsychological testing.
5. Bilaterally synchronous, generalized or extratemporal focal EEG spikes.
6. Diffuse or extratemporal focal EEG slowing.
7. Cerebral lesion other than hippocampal sclerosis on MRI.

From Engel, 1993[10]

PARTIAL EPILEPSY DUE TO A DISCRETE STRUCTURAL LESION

A second surgically remediable epileptic syndrome is *partial epilepsy due to a discrete structural lesion that can be easily resected without causing additional neurologic deficit*[14]. Such lesions include small neoplasms, hamartomas, vascular malformations, traumatic scars, and congenital disturbances including migration defects such as focal cortical dysplasia. Most of these lesions can now be readily demonstrated with high resolution MRI; however, a more detailed presurgical evaluation is necessary to ascertain that the observed lesion is in fact responsible for the habitual epileptic events. In some cases, the structural disturbance is multifocal and the epileptogenic lesion is missed. In others, the observed lesion is a fortuitous finding unrelated to localize ictal and interictal epileptiform discharges to the area of the lesion, and removal of epileptogenic cortex adjacent to the lesion provides the best chance of a seizure free outcome[15]. Results of limited surgical resection in this patient population are as good as those for anteromedial temporal resection in patients with mesial temporal lobe epilepsy. Consequently, there is no need to pursue lengthy drug trials in these patients once the first line antiepileptic medications fail.

UNILATERAL AND SECONDARY GENERALIZED EPILEPSY DUE TO A DIFFUSE HEMISPHERIC LESION

Other surgically remediable epilepsies include a variety of *unilaterally diffuse hemispheric disturbances in infants and small children that produce catastrophic seizures and profound developmental delay* (e.g., hemimegencephaly, Sturge-Weber syndrome and Rasmussen's encephalitis)[16]. There is also a subpopulation of patients who present with signs and symptoms of infantile spasms, who have extensive unilateral cortical dysplasia, usually confined to the posterior part of the hemisphere, that can be identified with PET[17], and in many cases now, MRI[18]. Because seizures are very frequent in these patients, the ineffectiveness of the most appropriate antiepileptic drugs can usually be ascertained relatively quickly. Where as these children have a dismal prognosis with medical therapy, 70- to 80% become seizure free following either hemispherectomy or a large multilobar hemispheric resection, and developmental delay can be largely reversed. Early surgical intervention is essential in this situation, not only because of the deleterious effect that the seizures appear to have on behavioral development, but also because the plasticity of the immature brain reduces the degree of neurological impairment resulting from removal of large cortical areas.

SECONDARY GENERALIZED EPILEPSY WITH DROP ATTACKS AS THE MOST DISABLING SEIZURE TYPE

A final class of surgically remediable syndromes are those associated with drop attacks as the most disabling seizure type. In most patients with drop attacks (for instance those with the Lennox-Gastaut syndrome), there are also other types of epileptic seizures which contribute to the disability, as well as mental retardation or other neurologic deficits. Drop attacks, however, are among the most medically refractory seizure types, often casue repeated serious injuries, and place a severe limitation on activities of daily living. Corpus callosotomy can be very effective in eliminating drop attacks; however, this is only a palliative procedure because it does not usually affect the other seizure types, nor does it reduce the associated cognitive neurological impairments[19]. Nevertheless, there is no need to consider extensive trials of antiepileptic drugs to control drop attacks that are severely disabling in patients who could be candidates for corpus callosotomy.

SURGICAL CONSIDERATIONS FOR OTHER INTRACTABLE EPILEPSIES

Patients with partial seizures associated with a symptomatic, rather than idiopathic form of epilepsy who have no demonstrable lesions on MRI, and no localizing functional deficit on PET or SPECT, are much less likely to benefit from surgical treatment than patients with surgically remediable syndromes[20]. Furthermore, when the boundaries of the surgical resection are defined only on the basis of electrophysiological recordings, this usually requires chronic intracranial recordings, using either depth or subdural grid electrodes. Such studies are expensive and associated with a small but not insignificant morbidity[21]. Consequently, decisions to proceed to surgery in this patient population are only justified after adults with extensive structural lesions, evidence of bilateral

independent ictal onset, or other discordant findings on presurgical evaluation, who also would require intracranial recording to determine whether surgical treatment is advisable and what should be removed, have a poorer extended trails of most of the available antiepileptic drugs might be appropriate before proceeding to invasive testing.

For patients with symptomatic or cryptogenic partial epilepsy who might be considered candidates for surgical treatment but who do not have an obvious surgically remediable syndrome, decisions concerning how far to pursue pharmacotherapy before referral to an epilepsy surgery center should be based, in part, on psychosocial considerations. For instance, patients who are not cognitively impaired, but who are experiencing increasing difficulties at school or work as a result of their seizures, should be referred relatively quickly. Examples might be a child who has been at the top of the class but is now receiving failing grades, either because of frequent seizures or drug side effects, or a young adult who is well-trained and capable but is in jeopardy of losing a job because of seizures or their consequences. Not only do the ictal events themselves interfere with quality of life, but they can be associated with progressive neurologic symptoms such as memory loss, or behavior problems such as depression, which are also an indication to consider surgical treatment sooner rather than later. When quality of life is not severely affected by epileptic seizures, either because they are relatively mild or because activities of daily living are more impaired as a result of other neurological disturbances or mental retardation, new drugs and drug combinations can be pursued for longer periods of time before considering referral, if at all.

ACKNOWLEDGMENTS

Original research reported by the author was supported in part by Grants NS-02808, NS-15654, NS-33310, and GM-24839, from the National Institutes of Health, and Contract DE-AC03-76-SF00012 from the Department of Energy.

REFERENCES

1. Engel J Jr, Shewmon DA. Overview: Who Should Be Considered a Surgical Candidate? In *Surgical Treatment of the Epilepsies, 2nd Edition.* J Engel Jr, ed. New York: Raven Press, 1993; 23-34

2. Apuzzo MLJ. *Neurosurgical Aspects of Epilepsy.* Park Ridge, Illinois: American Association of Neurological Surgeons, 1991.

3. Chauvel P, Delgado-Escueta AV, Bancaud J, Halgren E, eds. *Frontal Lobe Seizures and Epilepsies.* New York: Raven Press, 1992

4. Engel J Jr, ed. *Surgical Treatment of the Epilepsies, 2nd Edition.* New York: Raven Press, 1993

5. Lüders HO, ed. *Epilepsy Surgery.* New York: Raven Press, 1992.

6. Silbergeld DL, Ojemann GA. Neurosurgery Clinics of North America. *Epilepsy Surgery* 4, 1993

7. Spencer DD, Spencer SS, eds. *Epilepsy Surgery.* Cambridge: Blackwell, 1991

8. Theodore W, ed. Surgical Treatment of Epilepsy. Epilepsy Res (Suppl 5), 1992

9. Engel J Jr. Current concepts: Surgery for seizures. *N. Engl. J. Med.* 1996, 334: 647-652

10. Engel J Jr. Update on surgical treatment of the epilepsies. *Neurology* 1993; 43: 1612-1617

11. Engel J Jr. Recent Advances in Surgical Treatment of Temporal Lobe Epilepsy. *Acta Neurol Scand* 86 (Suppl 5): 1992; 71-80

12. Wieser HG, Engel J Jr, Williamson PD, Babb TL, Gloor P. Surgically remediable temporal lobe syndormes. In *Surgical Treatment of the Epilepsies, 2nd Edition.* J Engel Jr, ed. New York: Raven Press, 1993; 49-63.

13. Rausch R, Crandall PH. Psychological status related to surgical control of temporal lobe seizures. *Epilepsia* 1982;23:191-202

14. Cascino GD, Boon PAJM, Fish DR. Surgically remediable lesional syndromes. In *Surgical Treatment of the Epilepsies, 2nd Edition.* J Engel Jr, ed. New York: Raven Press, 1993, 77-86

15. Fried I, Cascino GD. Lesional surgery. In *Surgical Treatment of the Epilepsies, 2nd Edition.* J Engel Jr, ed. New York: Raven Press, 1993; 501-509.

16. Shields WD, Duchowny MS, Holmes GL. Surgically remediable syndromes of infancy and early childhood. In *Surgical Treatment of the Epilepsies, 2nd Edition.* J Engel Jr, ed. New York: Raven Press, 1993; 35-48.

17. Chugani HT, Shields WD, Shewmon DA, Olson DM, Phelps ME, Peacock WJ. Infantile spasms: I. PET identifies focal cortical dysgenesis in cryptogenic cases for surgical treatment. *Ann Neurol* 1990; 27: 406-413

18. Sankar R, Curran JG, Kevill JW, Rintahaka PJ, Shewmon DA, Vinters HV. Microscopic cortical dysplasia in infantile spasms: Evolution of white matter abnormalities. *AJNR* (in press).

19. Gates JR, Wada JA, Reeves A, Lassonde M, Papo I, Spencer SS, Andermann F, Risse G, Ritter FJ, Purves SJ. Re-evaluation of corpus callosotomy. In *Surgical Treatment of the Epilepsies, 2nd Edition.* J Engel Jr, ed. New York: Raven Press, 1993; 637-648.

20. Van Ness P. Surgical outcome for neocortical (extratemporal) focal epilepsy. In *Epilepsy Surgery.* Lüders HO, ed. New York: Raven Press, 1992; 613-624.

21. Pilcher WH, Roberts DW,Flanigin HF Crandall PH, Wieser HG, Ojemann GA, Peacock WJ. Complications of epilepsy surgery. In Surgical Treatment of the Epilepsies, 2nd Edition. J, Engel Jr, ed. New York: Raven Press, 1993; 565-581