

FOCAL CORTICAL DYSPLASIA: A CLEARER VIEW OF SURGICAL OUTCOME

Long-term Outcome after Epilepsy Surgery for Focal Cortical Dysplasia

Cohen-Gadol AA, Ozduman K, Bronen RA, Kim JH, Spencer DD

J Neurosurg 2004;101:55–65

PURPOSE: Reports of outcomes for surgical treatment of cortical dysplasia associated with epilepsy are conflicting because of the inclusion of patients with a wide range of malformations of cortical development. The authors report their experience and the long-term outcome for a subgroup of patients with the histopathological diagnosis of focal cortical dysplasia of Taylor.

METHODS: The records of 22 patients with focal cortical dysplasia of Taylor (15 with the balloon-cell type and seven with the non-balloon-cell type) were reviewed. There were 11 female and 11 male patients whose mean age was 26 ± 17.6 years [mean \pm standard deviation (SD)] at surgery. The details of their epilepsy evaluation and resection were analyzed. Extent of resection was preoperatively planned by using information obtained from long-term intracranial monitoring (15 patients) or more definitively determined by histopathologically proven clear margins during resection when feasible (12 patients) or both. The mean duration of follow-up was 6.3 ± 5.1 years (mean \pm SD; range, 0.5–15.6 years). Risk factors for epilepsy were trauma (seven patients) or meningoencephalitis (one patient); 14 (64%) patients had no obvious risk factors. The mean age at seizure onset was 9.2 years, and the mean duration of their epilepsy was 16.1 ± 9 years. In two patients, there were no adverse findings on magnetic resonance (MR) imaging. In 15 (68%) patients, the epileptogenic zone identified on long-term intracranial monitoring extended beyond the abnormality observed on MR images. Focal resection (lesion plus margins) was performed in 14 (64%) patients, whereas eight (36%) underwent partial/tailored lobectomy. Two pa-

tients underwent multiple subpial transections in addition to partial lesionectomy because their lesions involved the sensorimotor cortex. In these two, functional MR imaging confirmed a normal functional anatomy despite the presence of the cortical dysplasia. Eleven (92%) of 12 patients who underwent resection guided by histopathologically proven clear margins and three (43%) of seven patients who underwent histopathologically proven subtotal resection have remained seizure free. Evidence of clear margins was significantly associated with an improved seizure outcome ($P = 0.003$). Postoperatively, expected deficits included nondisabling visual field defects, which occurred in three (14%) patients, and transient sensorimotor deficits, which appeared in five (23%). Two patients had meningitis, which was successfully treated with antibiotics. Overall, 16 patients (73%) are either seizure free (13 patients), have rare nondisabling partial seizures (one patient), or had one seizure after their medication was changed (two patients). Thirteen (59%) patients have discontinued anticonvulsant medications or are being maintained on monotherapy. Of five (23%) patients, two have had rare disabling seizures or significant reduction in their seizure frequency (three patients). One patient's seizures have remained the same.

CONCLUSIONS: Focal cortical dysplasias are a distinct subgroup of malformations of cortical development and have a favorable outcome after resection. The epileptogenic zone often extends beyond the abnormality found on neuroimaging. Resection of the epileptogenic zone guided by histopathologically proven clear margins is associated with an improved seizure outcome.

COMMENTARY

Malformations of cortical development are now recognized to be an important epileptogenic substrate for many patients with pharmacoresistant epilepsy. Of these, focal cortical dysplasia of Taylor—defined histopathologically by loss of a distinct gray–white matter junction and dyslamination of cerebral cortex, with or without the presence of balloon cells in cortical and subcortical areas—is among the most common category of these malformations. Focal cortical dysplasia also is potentially

a surgically remediable syndrome for patients with associated intractable seizures, although reported outcomes concerning postoperative seizure control have been mixed.

The present report by Cohen-Gadol and colleagues describes 22 consecutive patients with pathologically confirmed focal cortical dysplasia, who underwent epilepsy surgery at a single center. These patients typically had onset of seizures in childhood and had many years of intractable epilepsy before undergoing multimodal evaluation and surgical treatment. Follow-up was lengthy for some, but not all, patients (mean, 6 years; range, 0.5–16 years).

Patients in this series underwent an extensive presurgical evaluation. This evaluation included structural imaging with magnetic resonance imaging (MRI), which in several cases involved imaging with phased-array surface coils for enhanced ability to resolve subtle structural changes produced by the dysplasia; functional imaging with ictal or interictal single-photon emission computed tomography (SPECT) or positron emission tomography (PET); and ictal physiological recordings (two thirds with intracranial studies).

All but three patients had at least one MRI finding typical of cortical dysplasia (i.e., cortical thickening, a radial band extending from the ventricle to the cortex, or subcortical hyperintensity. Perfusion abnormalities colocalizing to the MRI lesion were seen in five of the 12 patients who underwent subtraction SPECT studies. Seven of nine patients who were studied with interictal PET had evidence for hypometabolism in the region defined by MRI to be abnormal; indeed, the area of PET hypometabolism extended beyond the boundaries of the MRI abnormality—suggesting a broader zone of dysfunctional tissue than that delineated by structural disruption. Similarly, in the 15 patients monitored by using intracranial electrodes, the epileptogenic zone extended beyond the area of MRI abnormality in all cases.

Surgical resection was guided by intraoperative image-based navigation of the MRI abnormality, physiological delineation of the epileptogenic zone (as determined by extraoperative ictal recordings and intraoperative electrocorticography), and identification of functionally important areas based on extra- and intraoperative cortical stimulation mapping. Borrowing from strategies used in tumor-resection procedures, the surgeons in this report took multiple biopsy samples of all resection margins and used immediate histopathologic analysis to determine when margins were free from dysplasia and thus when no further resection was deemed necessary. In this series of 22 patients, focal resection (lesion plus margins) was performed in 14 (with multiple subpial transection additionally performed in two of these patients to treat lesions extending into sensorimotor cortex), whereas partial lobectomy occurred in eight. Notably, five patients required a second operation, when the first failed to provide sufficient seizure control.

With this meticulous approach to surgical resection, 16 patients (nearly three fourths) achieved an excellent (class I) outcome, and five patients had a good outcome (rare seizures or worthwhile reduction in seizures). Only one patient had an insignificant response to surgery. Of the six patients who did not achieve a class I outcome, the authors note that resection was limited in four because of extension of the epileptogenic region into functional cortex. Patients in this study experienced no permanent neurologic deficits, other than expected nondisabling visual deficits after occipital resection.

The most important conclusion that can be drawn from this report is that the specific entity of focal cortical dysplasia is a surgically treatable epileptogenic substrate. With thorough presurgical evaluation and thoughtful surgical technique, the overwhelming majority of properly selected patients realize meaningful benefit, and many achieve complete seizure control. The authors highlight a very practical issue, as well. Although MRI can delineate characteristic structural abnormalities in many patients, it is clear from the functional imaging findings and physiological recordings documented in this report that the epileptogenic region is more widespread than that evident on MRI. This conclusion has important consequences from the standpoint of surgical planning.

Technically, the authors' use of intraoperative histopathologic evaluation of the resection margins provides a novel, yet practical, method for determining the boundaries for the surgical excision. This strategy appears to be effective: histopathologically clear margins were significantly associated with a favorable seizure-control outcome. Whether this approach is superior to simply using intraoperative electrocorticography alone to guide surgical resection, with those regions displaying continuous or frequent epileptiform abnormalities defining the volume of resection, is difficult to assess from this report. It is worth noting that in the present study, electrocorticography was performed in eight of the patients, and the initial resection was, indeed, guided by the areas of electrophysiologic abnormality. After such resection, intraoperative biopsies were then performed at the edges of the resection, and when histopathologic analysis revealed evidence for remaining dysplasia, further resection was performed (although the authors do not report the number of patients in whom this was the case). This suggests that, at least in some patients, the extent of electrocorticographic abnormality underestimates the scope of pathologic abnormality. Certainly, it seems reasonable on a clinical basis to use all techniques readily available to ascertain the extent of both electrophysiologic and structural abnormality and to use both parameters for delineation of the tissue to be potentially removed, qualified ultimately by functional eloquence of those areas.

For each pathogenetic entity underlying pharmacoresistant epilepsy, it is crucial to establish effective approaches to presurgical evaluation and operative technique that will lead to consistently successful outcomes. Malformations of cortical development can be a challenging epileptogenic substrate to evaluate and treat, but the present report adds clarity to methods for effectively managing intractable epilepsy caused by one specific type of malformation—focal cortical dysplasia.

by William J. Marks, Jr., M.D.