Resective surgery for medically intractable epilepsy associated with schizencephaly

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Four adults with unilateral (three cases) or bilateral (one case) closed schizencephaly, medically intractable epilepsy, and otherwise normal neurological examinations are presented. Three were examined preoperatively with magnetic resonance imaging and one with computerized tomography. Scalp electroencephalographic (EEG) studies in all four patients and electrocorticography via intracranial electrodes in two showed seizure origin in the cleft regions in two patients and in the ipsilateral temporal lobe in the other two. Temporal lobectomy was performed in the two patients with temporal lobe foci. Resection of superficial pachygryria around the cleft was performed in one patient. The authors conclude that the abnormal cortical mantle lining schizencephalic clefts may be epileptogenic. Alternatively, temporal allocortex may become the source of seizures. Therefore, these patients require careful EEG monitoring of the entire ipsilateral hemisphere as well as the cleft region.

KEY WORDS • epilepsy • embryogenesis • porencephaly • schizencephaly

Schizencephaly is a developmental disorder of cortical migration that was first described in 1946,16,17 and is often associated with epilepsy. It develops before the end of the second month of gestation and consists of unilateral or bilateral clefts, which may be close-lipped (fused) or open-lipped (separated) with direct connection to the ventricular system. The clefts are lined with thickened, four-layered gray matter oriented parallel to a major sulcus. Other cortical areas may also show disordered migration with pachgyria, polymicrogyria, and heterotopias.26 Past reports have stressed that most patients with this disorder have significant neurological impairment and often paresis and subnormal intelligence.9,10,16,17 With the advent of magnetic resonance (MR) imaging, recognition of schizencephaly in neurologically normal subjects has become common.7,8,10 Furthermore, unilateral clefts seem to occur more frequently than the bilateral form initially described.9,16,17

To investigate the role of resective surgery for epilepsy in these patients and identify the relationship between the region of epileptogenesis and the schizencephalic cleft, we describe four adult patients referred to the Washington University Epilepsy Program for management of medically intractable seizures.

Clinical Material and Methods

Once a patient's seizures were proved to be medically intractable, closed-circuit television (CCTV)-
electroencephalographic (EEG) monitoring with scalp electrodes was performed. If a patient was determined to be a potential surgical candidate11,12 but scalp CCTV-EEG studies failed to demonstrate a consistent and well-localized discharge preceding the onset of clinical seizures, then subdural14 or epidural1 electrodes were placed for further monitoring. Following Wada examination of language and memory,3,15 cortical stimulation mapping14 to identify areas of Rolandic cortex and speech cortex was conducted extraoperatively in two patients and intraoperatively under local anesthesia in one.

Resected tissues were fixed in 10% formalin, embedded in paraffin, and sectioned. Sections were stained with hematoxylin and eosin and, when indicated, for glial fibrillary acidic protein.

Case Reports

Case 1

This 51-year-old left-handed man had a cluster of generalized tonic-clonic seizures at 24 years of age. He then began having occasional complex partial seizures, which in the 2 years prior to evaluation became medically refractory, increasing to three or four per week. The seizures consisted of speech arrest followed by automatism (lip smacking and pulling at his clothes with both hands), then loss of responsiveness, with 15 to 20 minutes of aphasia and confusion afterward. The
patient had completed high school and had worked full time since.

Examination. Physical examination was normal. Magnetic resonance imaging showed left-sided closed schizencephaly in the region of the rolandic cortex (Fig. 1 left and center). Wada examination demonstrated left-sided language and bilateral memory function, with normal vascular anatomy except for a slight paucity of vessels in the superior division of the left middle cerebral artery in the region of the cleft. Positron emission tomography (PET) showed decreased glucose metabolism in the region of the cleft and in both medial temporal lobes, with the most striking decrease in the left medial temporal lobe.

Scalp CCTV-EEG monitoring demonstrated left temporal interictal spikes and suggested ictal onset from the same area. Bilateral subtemporal strip electrodes and a left-sided 64-contact electrode grid were placed subdurally under general anesthesia. Intraoperative cortical stimulation motor mapping and median nerve somatosensory evoked potential (SSEP) studies were performed. The somatosensory gyrus was narrow and split by a cleft (Fig. 1 right), corresponding to the schizencephalic seen on MR imaging. The sulci and gyri in the left temporal lobe were oriented vertically rather than in the normal horizontal arrangement.

Extraoperative electrocorticographic (ECoG) studies and language mapping were also performed. Temporal language was located far inferiorly in the temporal lobe, just above the floor of the middle cranial fossa, 4 cm posterior to the temporal pole. Interictal and ictal ECoG changes arose from the left subtemporal strip electrode, corresponding to the region of the hippocampal sulcus (as determined by postoperative computerized tomography (CT) for grid and strip localization), with rapid propagation to the region of the cleft (Fig. 2).

Operation and Postoperative Course. The patient underwent a left temporal lobectomy under general anesthesia, with resection of 3 cm of lateral (neocortical) tissue and 2 cm of mesial (allocortical) tissue. Histopathological evaluation showed hippocampal gliosis and neuronal dropout. One month after resection, the patient had a brief seizure with speech arrest but without amnesia. He has been seizure-free in the subsequent 3 months.

Case 2

This 20-year-old left-handed man presented with a 4-year history of seizures which typically consisted of pain in the left hand followed by 15 to 20 seconds of hand numbness and occasional tonic-clonic movements. There was no associated aura and no postictal changes were noted. The seizures occurred once or twice per week despite multiple medications. The patient worked full time and had completed high school without difficulty. Physical examination was normal. An MR image showed a right-sided unilateral closed schizencephalic cleft in the rolandic cortex region (Fig. 3). A scalp EEG study showed an interictal focus in the region of the cleft. Because the seizures were not disabling and originated in or near motor cortex, further evaluation was not undertaken.

Case 3

This 31-year-old right-handed woman had suffered complex partial seizures since the age of 11 years. At seizure onset she would abruptly stop responding and then her right arm would slowly fall. If she was sitting up, she would slowly lie back in the bed and her legs would stiffen; if she was standing, she would usually fall. Despite trials of multiple antiepileptic medications, she continued to have several clusters of seizures per week. In high school, she had completed 10th
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Fig. 3. Case 2. Sagittal T1-weighted magnetic resonance image showing a schizencephalic cleft (arrows) lined with thickened gray matter.

Fig. 4. Case 3. Coronal T1-weighted magnetic resonance image showing bilateral schizencephalic clefts (arrows) lined with thickened gray matter and extending toward the occipital horns of the lateral ventricles.

grade. The Wechsler Adult Intelligence Scale indicated general ability in the low average range (intelligence quotient (IQ) 88), with no discrepancy between verbal (IQ 88) and nonverbal (IQ 89) abilities.

Examination. Physical examination was normal. Magnetic resonance imaging showed bilaterally symmetrical closed schizencephalic clefts in the rolandic cortex region (Fig. 4). A PET scan showed increased glucose metabolism in the region of the clefts with a patchy decrease in both temporal lobes. Wada examination revealed left-sided speech dominance and bilateral memory function. Scalp CCTV-EEG monitoring recorded 12 seizures arising from the left temporal lobe (Fig. 5).

Operation. The patient underwent a temporal lobectomy while awake, tailored via intraoperative ECoG recording and speech and motor mapping. The cleft region was not exposed during surgery. Speech areas were typical in location, with the temporal lobe speech region approximately 8 cm posterior to the temporal pole in the superior temporal gyrus. Interictal discharges extended throughout the lateral temporal neocortex. Resection included 35 mm of superior temporal gyrus, 45 mm of middle and inferior temporal gyrus, and 20 mm of mesial tissue. Histopathological studies showed mesial temporal sclerosis without other abnormality. Surgery was recent, and follow-up data are not yet available.

Case 4

This 20-year-old right-handed man began having complex partial seizures at the age of 11 years. The seizures consisted of staring and repetitive picking movements of the hands for 1 to 2 minutes and were sometimes preceded by micropsia. After a seizure he was usually confused for 5 to 10 minutes.

Examination. A CT scan was interpreted as normal, but postoperative MR imaging demonstrated right-sided closed schizencephaly (Fig. 6). Wada examination revealed left-sided language dominance.

Operation and Postoperative Course. Bilateral epidural electrode strips and a right-sided epidural electrode grid were placed. Pale and hypovascular pachygyria surrounded the schizencephaly. Extraoperative CCTV-EEG monitoring revealed ictal and interictal abnormalities arising from the lips of the cleft, in the region of the widened gyri. The patient was then returned to surgery for resection of the abnormal pachygyric cortical mantle surrounding the schizencephaly; cortical stimulation motor mapping was performed and SSEP's were measured intraoperatively. Histopathological study revealed malformed cortex with neural and glial elements haphazardly arranged without normal cortical lamination. Nodules of gray matter were scattered throughout the underlying bands of white matter. This patient has been seizure-free for over 5 years.

Discussion

This study demonstrates that patients with schizencephaly may have seizures originating either in the vicinity of the cleft or in the temporal lobe, and if seizures are medically intractable neurosurgical treatment may be an option. It is possible that seizures originate in the temporal lobe because maldeveloped gray matter may exist there in addition to the abnormal cortex lining the schizencephalic clefts.1,10,16,17 For example, the patient in Case 1, who had a temporal lobe focus, had an abnormal sulcal/gyral pattern in the temporal lobe which was apparent at surgery but not on MR imaging. This cannot be the sole explanation for the occurrence of temporal lobe seizures in these patients, however; Case 3 had no gross or histological evidence of abnormal cortical migration in the resected temporal lobe, although there was mesial temporal sclerosis. A more subtle developmental abnormality of synaptic organization could exist in the temporal lobe, or perhaps
some schizencephalic patients may initially have extratemporal seizures but through a kindling-like process develop intractable temporal lobe seizures.

Porencephaly has traditionally been divided into two types, on the grounds that bilaterally symmetrical lesions are unlikely to be due to a destructive process. Type I, encephaloclastic porencephaly, is acquired from an insult to the brain. Type II, true schizencephaly, is an ontogenic process of dysgenesis of the cortical mantle, with migrational abnormalities in the cleft and elsewhere. Characteristically, both types have been associated with early childhood presentation due to poor neurological function and delayed development. We have evaluated several patients under the age of 2 years with true schizencephaly. These patients tend not to develop seizures until later in life.

Schizencephaly is often difficult to diagnose with CT (as in our Case 4), whereas MR imaging makes its identification straightforward. Typically, clefts in the cerebral hemispheres paralleling adjacent major sulci, extending to the ipsilateral ventricle, and lined with thickened gray matter can be identified. All five cases...
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Presented by Yakovlev and Wadsworth\textsuperscript{16,17} were bilateral, while three of the four cases in the present series had unilateral defects with the seizure focus ipsilateral to the cleft. This preponderance is typical, even with cases that become symptomatic early in life.

Although MR imaging increases the ability to visualize schizencephalic clefts and provides clues for focus localization, the pathological cleft does not always coincide with the location of the seizure onset. The existence of several potential sites of seizure origination means that these patients require extensive presurgical evaluation, and that postoperative seizure control may be more difficult than in other patients. Nevertheless, resection of tissue in the cleft or in the temporal lobe is an appropriate and effective treatment for selected schizencephalic patients.

References

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Fig. 6. Case 4. Coronal T\textsubscript{1}-weighted magnetic resonance image showing a schizencephalic cleft (open arrows) extending to, but not opening into, the ventricle (black arrow).

Manuscript received July 6, 1993.
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