Posterior Disconnection in Early Infancy to Treat Intractable Epilepsy With Multilobar Cortical Dysplasia—Three Case Reports—

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Abstract

Extensive multilobar cortical dysplasias occasionally occur in children and can induce seizure onset in early infancy, causing severe epileptic encephalopathy. Surgical interventions in early infancy, such as disconnection of large parts of the brain, are challenging because of the degree of invasiveness and carry greater risks in infants compared with older children. Here we report the successful treatment of intractable epilepsy with multilobar cortical dysplasias in the posterior cortex by posterior disconnection in three infants (age 3 months). The patients showed good postoperative recovery and exhibited excellent seizure control at follow-up evaluation within a year after surgery. Developmental catch-up was also achieved and no early complications have been detected to date. Use of the posterior disconnection technique for early-stage extensive multilobar cortical dysplasias can result in good seizure control and developmental progress with little perioperative morbidity. However, the efficacy of this surgical technique needs to be verified with long-term follow up after surgery.

Key words: epilepsy, cortical dysplasia, posterior disconnection

Introduction

Children with extensive multilobar cortical dysplasias (MCDs) frequently present with seizure onset in early infancy, ultimately resulting in severe epileptic encephalopathy.5,13 Although early surgical intervention is necessary to control epilepsy and allow normal brain development, conventional resective surgery, which involves the removal of large parts of the cerebral hemisphere, is challenging and carries substantial operative risks in infants compared with older children.17,20 Similar to the evolution of hemispherectomy, surgical techniques for epilepsy with MCDs have advanced toward more disconnection and less resection to minimize perioperative complications.4,5 In addition to minimizing complications, maximizing the suppression of epileptic seizures is a primary goal of surgical intervention. We report here the successful treatment of three infants with intractable epilepsy resulting from MCDs in the posterior cortex by posterior disconnection with an optimal therapeutic strategy based on multimodal examinations.

Case Reports

Case 1: A 3-month-old boy born at term after an uneventful pregnancy presented with generalized tonic seizures with eye deviation to the left side, beginning 6 days after birth. The frequency of seizures was 10–40/day. Seizures were intractable to multiple anticonvulsants (phenobarbital 35 mg/day, clonazepam 0.24 mg/day). His development was significantly delayed with a developmental quotient (DQ) of 60. Magnetic resonance (MR) imaging showed an increase in the volume of the right temporal, parietal, and occipital lobes compared with the contralateral side. In addition, poor differentiation was observed between gray and white matter in the right temporal, parietal, and occipital lobes. These radiological findings suggested temporo-parieto-occipital cortical dysplasia (Fig. 1A, B).

Interictal single photon emission computed tomography (SPECT) showed decreased cerebral blood flow (CBF) in the right temporal, parietal, and occipital lobes. Ictal SPECT showed relative hyperperfusion in the right temporal, parietal, and occipital lobes (Fig. 1C). Subtraction ictal SPECT coregistered with MR imaging (SISCOM) showed that significant ictal hyperperfusion was

predominantly observed in the lateral part of right temporal lobe. Magnetoencephalography (MEG) revealed spike dipoles in the occipital lobe and the transitional area between the occipital and temporal lobes (Fig. 1D). Interictal electroencephalography (EEG) showed bilateral occipital-dominant large δ waves and θ waves and frequent spikes over the right occipital, temporal, and posterior temporal areas. The ictal EEG was characterized by bilateral occipital dominant polyspike spreading over the right cerebral hemisphere (F8, T6, P4, O2).

The aim of the surgery was to eliminate the influence of the large dysplastic epileptogenic zone comprising the temporal, parietal, and occipital lobes. The patient underwent right parieto-occipital disconnection and temporal lobectomy with no postoperative complications. Postoperative EEG (2 months after operation) showed localized epileptic waves in the disconnected right temporal lobe. At the latest follow-up review, a year after surgery, the patient was seizure free and had achieved developmental catch-up with a DQ of 73.

Case 2: A 3-month-old girl born at term after an uneventful pregnancy presented with tonic seizures and epileptic spasms with asymmetric tonic posture and eye blink and deviation to the left side, beginning 13 days after birth. The frequency of seizures was 10–40/day. Seizures were intractable to multiple anticonvulsants (zonisamide 120 mg/day, phenobarbital 56 mg/day). Her development was significantly delayed with a DQ of 44. MR imaging showed a diffuse lesion in the left temporo-parieto-occipital lobe. Axial images revealed that abnormal gray matter extended from the trigone of the lateral ventricle to the occipital cortex and extended anterior to the central sulcus and insular cortex (Fig. 1G). Ictal SPECT revealed relative hyperperfusion in the transitional area between right temporal, parietal, and occipital lobes (Fig. 1I). MEG showed spike dipoles in the area around the angular gyrus (Fig. 1J). Interictal EEG revealed lateralized epileptic discharges on the left. Ictal EEG was characterized by unilateral spike-wave activities spreading over the left hemisphere (P3, O1, T5, T3).

The patient initially underwent right posterior disconnection. After the first surgery, seizures persisted. Judging from the postoperative MEG and SISCOM findings, the seizures were considered to arise from the residual parieto-temporal operculum, the posterior insular cortex, and temporal lobe. Additional resection of those cortices were performed 40 days later. There were no postoperative complications. Postoperative EEG (2 months after operation) revealed localized epileptic waves in the right temporal lobe. At a follow-up evaluation 5 months after surgery, the patient was seizure-free and had made developmental progress with a DQ of 50.

Case 3: A 3-month-old boy born at term after an uneventful pregnancy presented with seizures consisting of epileptic spasms with eye deviation to the left side, beginning 10 days after birth. The frequency of seizures was 20–30/day. Seizures were intractable to multiple anticonvulsants (carbamazepine 120 mg/day, lamotrigine 4 mg/day, zonisamide 60 mg/day). His development was normal with a DQ of 117. MR imaging showed an increase in the volume of the transitional area of the right temporal, parietal, and occipital lobes. Poor differentiation was observed between gray and white matter in the abnormal area (Fig. 1M, N). Interictal SPECT revealed increased CBF in the right occipital lobe (Fig. 1O). MEG showed dipoles in the right occipital and temporal lobes (Fig. 1P). Interictal EEG showed lateralized epileptic discharges on the right. Ictal EEG was characterized by unilateral spike-wave activity spreading over the right hemisphere (C4, P4, C3, P3).
The patient underwent posterior disconnection with no postoperative complications. Postoperative EEG (one month after operation) revealed localized epileptic waves in the disconnected right temporal lobe. At a follow-up evaluation 6 months after surgery, the patient was seizure-free with normal development.

**Surgical Procedure and Outcome**

During the operations, electrocorticography was performed over the exposed cortices and the locations of the central and postcentral sulci were identified in relation to known anatomic landmarks on MR imaging. Anterior temporal lobectomy was carried out, including resection of the amygdala and the anterior hippocampus up to the level of the choroid fissure (Fig. 2B). The temporal and parietal opercular cortices were removed to make the perinsular window (Fig. 2A). The opening of the ventricle was extended in the posterior direction to the trigone of the lateral ventricle. Parenchymal resection was performed from the posterior limit of the temporal cortical resection to the postcentral sulcus, upward along the parietal lobe, and finally, to the corpus callosum (Fig. 2C–E). Transventricular posterior callosotomy was carried out in an intraventricular parasagittal plane posterior to the intraparietal disconnection line (Fig. 2C). This procedure would interrupt all the parieto-occipital commissural fibers as they reach the corpus callosum. After the splenial disconnection, incision reached the fornix. The fornix is then incised to disconnect the posterior hippocampus. Finally, the electrocorticography was re-recorded and no spikes were observed in the remaining temporal, occipital, and parietal lobes.

The brain tissues harvested from surgery revealed structural abnormalities consistent with MCDs. The cerebral cortex did not achieve its normal architecture. Accumulation of numerous balloon cells was present throughout the whole cerebral cortex and in the underlying white matter.

**Discussion**

Children undergoing epilepsy surgery more often exhibit extratemporal lesions compared with temporal lesions, which are more common in adults. In addition, cortical dysplasia is the most frequent etiology. Extratemporal and multilobar cortical resections for intractable epilepsy are much more common in pediatric patients compared with adult patients. In some cases of medically intractable pediatric epilepsy, the extent of the underlying cortical abnormality requires hemispherectomy; however, in others, the epileptogenic focus is more limited, involving one or more lobes of one hemisphere. The pathological profile in the cases presented here involved malformations of cortical development, and all patients were diagnosed with catastrophic epilepsy, characterized by seizure onset within 2 weeks of birth and high frequency of seizures (10–40/day). The concept of “intrinsic epileptogenicity” may account for the medical intractability, incidence of status epilepticus, and the persistence of epilepsy after incomplete removal of the dysplastic zone. It may be that the extent of the malformation explains the high association between MCDs and catastrophic epilepsy. These ideas support the diagnoses of catastrophic epilepsy in our cases, because of the huge cortical dysplasias observed and because the patients were seizure-free after complete disconnection of MCDs.

Posterior disconnection is indicated when the epileptogenic zone encompasses large areas of the temporal,
<table>
<thead>
<tr>
<th>Author (Year)</th>
<th>No. of patients</th>
<th>Age group</th>
<th>Seizure type (no. of patients)</th>
<th>MR imaging findings (no. of patients)</th>
<th>PET metabolism</th>
<th>Ictal SPECT</th>
<th>Scalp EEG</th>
<th>Operation</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chugani et al. (1993)</td>
<td>11</td>
<td>infant</td>
<td>ES (7), other (4)</td>
<td>HM (1), MCDs (1), pachygyria (1), normal (9)</td>
<td>i in 9/11,</td>
<td>not done</td>
<td>concordant in 11/11</td>
<td>all resection</td>
<td>10/11 SF (91%)</td>
</tr>
<tr>
<td>Wyllie et al. (1996)</td>
<td>2</td>
<td>child</td>
<td>tonic (1), ES (1)</td>
<td>MCDs (2)</td>
<td>i in 2/2</td>
<td>not done</td>
<td>concordant in 1/2</td>
<td>all resection</td>
<td>2/2 SF (100%)</td>
</tr>
<tr>
<td>Leiphart et al. (2001)</td>
<td>24</td>
<td>child</td>
<td>no details</td>
<td>CD (15), gliosis (6), TS (1), encephalomalacia (1), angioma (1)</td>
<td>no details</td>
<td>not done</td>
<td>no details</td>
<td>all resection</td>
<td>no details</td>
</tr>
<tr>
<td>Fogarasi et al. (2003)</td>
<td>12</td>
<td>child</td>
<td>PS (9), tonic (5), myo (6), ES (1)</td>
<td>MCDs (10), TS (1), abscess (1)</td>
<td>i in 7/8,</td>
<td>↑ in 1/1</td>
<td>concordant in 11/12</td>
<td>all resection</td>
<td>6/12 SF (50%)</td>
</tr>
<tr>
<td>Olavarria and Petronio (2003)</td>
<td>1</td>
<td>infant</td>
<td>GTS</td>
<td>MCDs</td>
<td>i in 1/1</td>
<td>not done</td>
<td>concordant all resection</td>
<td>Engel class II</td>
<td></td>
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<tr>
<td>D’Agostino et al. (2004)</td>
<td>10</td>
<td>child</td>
<td>partial (9), ES (5), myo/drops (2)</td>
<td>CDs (14 HM, 5 MCDs)</td>
<td>i in 5/5,</td>
<td>↑ in 3/5,</td>
<td>concordant in 9/10</td>
<td>4 disconnect, 6 resection</td>
<td>5/10 SF (50%)</td>
</tr>
<tr>
<td>Daniel et al. (2007)</td>
<td>13</td>
<td>adult/child</td>
<td>partial (12), ES (1), GC (1)</td>
<td>porencephaly (4), MCDs (3), atrophy (3), Sturge-Webber (2), AVM (1)</td>
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<td>no details</td>
<td>concordant in 12/13</td>
<td>7 disconnect, 6 resection</td>
<td>12/13 SF (92%)</td>
</tr>
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<td>Novegno et al. (2011)</td>
<td>4</td>
<td>infant</td>
<td>partial (4)</td>
<td>MCDs (4)</td>
<td>no details</td>
<td>no details</td>
<td>concordant in 4/4</td>
<td>4 resection</td>
<td>1/4 SF (25%)</td>
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<tr>
<td>Mohamed et al. (2011)</td>
<td>16</td>
<td>infant/child</td>
<td>partial (7), ES (10), tonic (7), myo (1)</td>
<td>MCDs (6), angioma (3), cystic encephalomalacia (1), subtle WM signal abnormality (5), subtle sulcus irregularity (1)</td>
<td>i in 9/16,</td>
<td>↑ in 6/16,</td>
<td>concordant in 4/4</td>
<td>14 disconnect, 2 resection</td>
<td>9/16 SF (56%)</td>
</tr>
</tbody>
</table>

parietal, and occipital lobes (posterior quadrant) and does not involve the central and frontal areas. In infants, the epileptogenic lesions may be difficult to image because of incomplete myelination. The indication relies on good concordance between the imaging studies (MR imaging, SPECT, and positron emission tomography), EEG, MEG, and clinical and neuropsychological evaluations, which collectively localize the lesion unilaterally to the posterior quadrant. We emphasize this concordance to select patients. In our cases, the preoperative investigations aimed at localizing the epileptogenic zone were concordant and therefore eliminated the need for chronic invasive recording. In addition, it is difficult to perform chronic intracranial electrocorticography on infants. During the operation, the disconnection is tailored to encompass the whole epileptogenic lesion and to avoid the central area, which is likely functional. Our surgical technique is similar to the functional posterior quadrantectomy. We used the postcentral sulcus to define the line of parietal disconnection anterolaterally, which was followed medially to the splenium of the corpus callosum. The identification of the postcentral sulcus in dysplastic hemispheres can be difficult. Prior to the dissection, the primary motor and sensory cortices and postcentral sulcus were identified from a preoperative scrupulous study of the three-dimensional surface rendering from the patient’s MR images (Fig. 2) and correlation with intraoperative surface anatomy, based on gyral pattern, superficial arteries, and veins. Electrophysiological localization of central sulcus is also useful using somatosensory evoked potentials or cortical stimulation for mapping of the motor cortex. The surgical accuracy facilitated by such techniques provides the best chance for complete seizure relief.

It is important to note that all three infants treated by our protocols exhibited total control of seizures at the follow-up evaluation (6–12 months after operation). However, the long-term efficacy is yet to be determined. Experience with surgical treatment of such lesions is limited and the results reported in the literature are not uniformly positive (Table 1). In a series of 5 patients with MCDs, 3 patients had satisfactory outcomes; 2 were seizure free, and 1 required monotherapy. The other 2 patients received no permanent benefit from the surgery. Early application of the disconnective technique for excisions associated with large brain excisions.

Of 5 patients with MCDs, 1 patient had Engel's class IIIB and 4 patients had Engel's class IIIA outcomes. In a report of 3 infants after surgeries for malformations of cortical development, Engel's class I outcome was obtained in 1 patient. Finally, of 4 infants with MCDs, only 1 patient had Engel's class I and 3 patients had Engel's class II, III, and IV outcomes, respectively. Our Case 1 and Case 2 presented with delayed development of infants. Both infants had excellent postoperative recovery and definite catch-up in their development, both motor and cognitive, at postoperative follow-up evaluation 5 months and 12 months, respectively. Previous studies have suggested similar results. For example, in a study of infants treated surgically for catastrophic epilepsy, marked catch-up development was observed in patients with at least 50% reduction in seizures. Previous studies have shown that the noxious effects of catastrophic epilepsy and antiepileptic medications (at high doses) on the developing brain have a deleterious psychomotor impact and usually result in severe epileptic encephalopathy, developmental delay, and mental retardation. In addition, the social implications of a debilitating disease and lost school time due to the encephalopathy are significant negatives. Early surgical intervention in patients who develop intractable epilepsy in infancy or childhood may improve quality of life and possibly cognitive outcomes in the developing child. Furthermore, the need for early surgical intervention after onset of medically refractory epilepsy is supported by studies demonstrating better seizure outcome and improved development in patients with shorter epilepsy duration. Thus, early surgical intervention is mandatory in cases of intractable epilepsy with extensive MCDs in infants.

All 3 cases reported here had excellent postoperative recovery and no complications have been detected to date. However, the long-term complications including an inevitable homonymous visual field deficit, if any, are yet to be determined. Epilepsy surgery in infants poses a higher risk of perioperative complications. In a series of 12 infants who underwent surgery for catastrophic epilepsy, 1 death and 2 postoperative complications (subdural hematoma and loculated temporal horn) occurred. Two of 13 patients under 3 years of age died (operative mortality of 6%). The disconnective technique is the logical evolution of the concept of an anatomically subtotal, but functionally complete resection in subhemispheric dysplasias. This procedure minimizes the size of the resection cavity and consequently reduces perioperative morbidity, in addition to preventing hydrocephalus. As the dysplastic cortex left behind is completely disconnected, seizure outcomes are identical to those for multilobar resection. Our cases show that intractable epilepsy was alleviated with a more limited resection using the disconnective technique.

Early application of the disconnective technique for extensive MCDs can result in good seizure control and developmental outcomes with little perioperative morbidity at follow-up within a year after surgery. Long-term follow-up evaluation will be required to verify the efficacy of this surgical technique. We believe that disconnective techniques will decrease the potential of long-term complications associated with large brain excisions.

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Conflicts of Interest Disclosure

The authors have no conflicts of interest to disclose. All authors who are members of The Japan Neurosurgical So-
society (JNS) have registered online Self-reported COI Disclosure Statement Forms through the website for JNS members.

References

9) Fish DR, Smith SJ, Quesney LF, Andermann F, Rasmussen T: Surgical treatment of children with medically intractable frontal or temporal lobe epilepsy: Results and highlights of 40 years’ experience. Epilepsia 34: 244–247, 1993

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