TABLE 1: Summary of preoperative characteristics in 8 patients who underwent resection of deep brain structures*

Case No.	Sex	Age at Seizure Onset (mos)	Age at Last Surgery (yrs)	Frontal Region of Focus	No. of Past Resections	Past Callosotomy	Seizure Frequency Before Last Surgery	Preop Abnormal Findings on Neuroimaging			
									Deep Brain Structures		
								Frontal Lobe Ipsilat to Lesion Side	Nucleus Accumbens	Head of Caudate Nucleus	Periventricular White Matter
1	F	11	13	lt	1	–	daily	blurring of GM-WM	ictal HP, SD	SD	
2	M	4	7	lt	1	+	daily	blurring of GM-WM			ictal HP, SD
3	M	11	10	lt	1	–	monthly	abnormal gyration, hypometabolism, low IMZ	low IMZ, SD	low IMZ, SD	low IMZ
4	F	10	5	lt	2	–	daily	blurring of GM-WM	ictal HP	SD	ictal HP, SD
5	M	22	5	rt	1	+	daily	maldevelopmental gyration, blurring of GM-WM			SD
6	F	49	6	rt	0	–	hourly	low IMZ			ictal HP & low IMZ of deep WM of transmantle sign
7	M	12	1	rt	0	–	daily	transmantle sign, hypometabolism		transmantle sign	ictal HP of subcortical WM of transmantle sign
8	M	4	8	lt	0	+	daily	abnormal gyration, ictal HP	ictal HP	ictal HP	ictal HP of deep WM of transmantle sign, SD

* GM = gray matter; HP = hyperperfusion; IMZ = iomazenil uptake; SD = spike dipole; WM = white matter.

refractory status epilepticus lasting for 2 months before surgery. Corpus callosotomy was performed in 3 cases (Cases 2, 5, and 8) as palliative surgery before the last resections. Five patients (Cases 1–5) had to undergo multiple resections to treat seizure recurrence after previous surgical treatment.

Neuroimaging of the deep structures revealed the transmantle sign in 3 patients (Cases 6–8), ictal hyperperfusion in 6 (Cases 1, 2, 4, and 6–8), reduced iomazenil uptake in 2 (Cases 3 and 6), and spike dipole clustering in 6 (Cases 1–5 and 8). Abnormal neuroimaging findings were demonstrated in the nucleus accumbens in 4 patients (Cases 1, 3, 4, and 8), the head of the caudate nucleus in 5 (Cases 1, 3, 4, 7, and 8), and the periventricular white matter in 7 (Cases 2–8). In 3 cases, the regions of ictal hyperperfusion in the deep (Cases 6 and 8) and subcortical (Case 7) white matter were superimposed on the regions where MRI demonstrated the transmantle sign. From these findings, we interpreted these deep brain structures as epileptogenic zones.

Surgical Treatment

All 8 patients underwent the resection of assumed epileptogenic lesions in the periventricular white matter. Furthermore, the anterior striatum, including the head of the caudate nucleus (Cases 1, 3, 4, and 7) and the nucleus accumbens (Cases 1 and 4), was partially resected in 4 patients (Cases 1, 3, 4, and 7; Table 2). In most of the patients, resected brain tissues, including deep brain structures, were very solid as compared with normal tissues. Neuroimages of typical cases (Cases 4 and 6) are featured in Figs. 1 and 2, respectively.

Intraoperative Subdural EEG

Subdural EEG activity was recorded during resection in all patients. We identified epileptic spike discharges on the brain surface of the assumed epileptogenic lesions. In Case 1, depth electrodes in the nucleus accumbens detected epileptic discharges in detail, as previously reported.[11] After resection, the epileptic discharges disappeared.

Pathological Diagnosis

The histological features of our cases are summarized in Table 2, and characteristic histology is featured in Fig. 3. Resected cortex exhibited noticeable architectural abnormalities in all cases and cellular abnormalities in a large proportion of cases, corresponding to FCD Type IA in 1 patient, IB in 1, IIA in 3, and IIB in 1.[11] Cortex in Cases 4 and 5 revealed a polymicrogyric configuration in which the cortical ribbon was abnormally undulated and excessively folded and the molecular layers of adjacent gyri appeared to be fused (Fig. 3A). Therefore, focal cortical abnormalities were diagnosed in the polymicrogyric cortex. In Cases 1, 3, 4, and 6, numerous dysmorphic neurons (Fig. 3B and I) were scattered, and in Case 7, both dysmorphic neurons and balloon cells were widely distributed. In Case 2, several giant neurons were seen in the cortex. Resected white matter also showed abnormalities in all cases. In Cases 1, 3, 4, 6, and 7, a large number of cortical and dysmorphic neurons were scattered con-

TABLE 2: Summary of pathological diagnoses and postoperative findings in 8 patients who underwent resection of deep brain structures*

Case No.	Partially Resected Regions of Deep Brain Structures	Pathological Abnormality				FU (mos)	Engel Class Postsurgery
		Diagnosis	Ac	CN	PWM		
1	Ac, CN, PWM	FCD IIA	DN	DN	DN, RA	53	IA
2	PWM	FCD IB			RA	49	IA
3	CN, PWM	FCD IIA		NA	RA	37	IA
4	Ac, CN, PWM	FCA, polymicrogyria	DN	DN	DN, RA	23	IC
5	PWM	FCA, polymicrogyria			RA	19	IA
6	PWM	FCD IIA			DN, RA	12	IA
7	CN, PWM	FCD IIB		DN	RA	11	IA
8	PWM	FCD IA			RA	10	IA

* Ac = nucleus accumbens; CN = head of caudate nucleus; DN = dysmorphic neuron; FCA = focal cortical abnormality; FU = follow-up; NA = not available; PWM = periventricular white matter; RA = reactive astrocytosis.

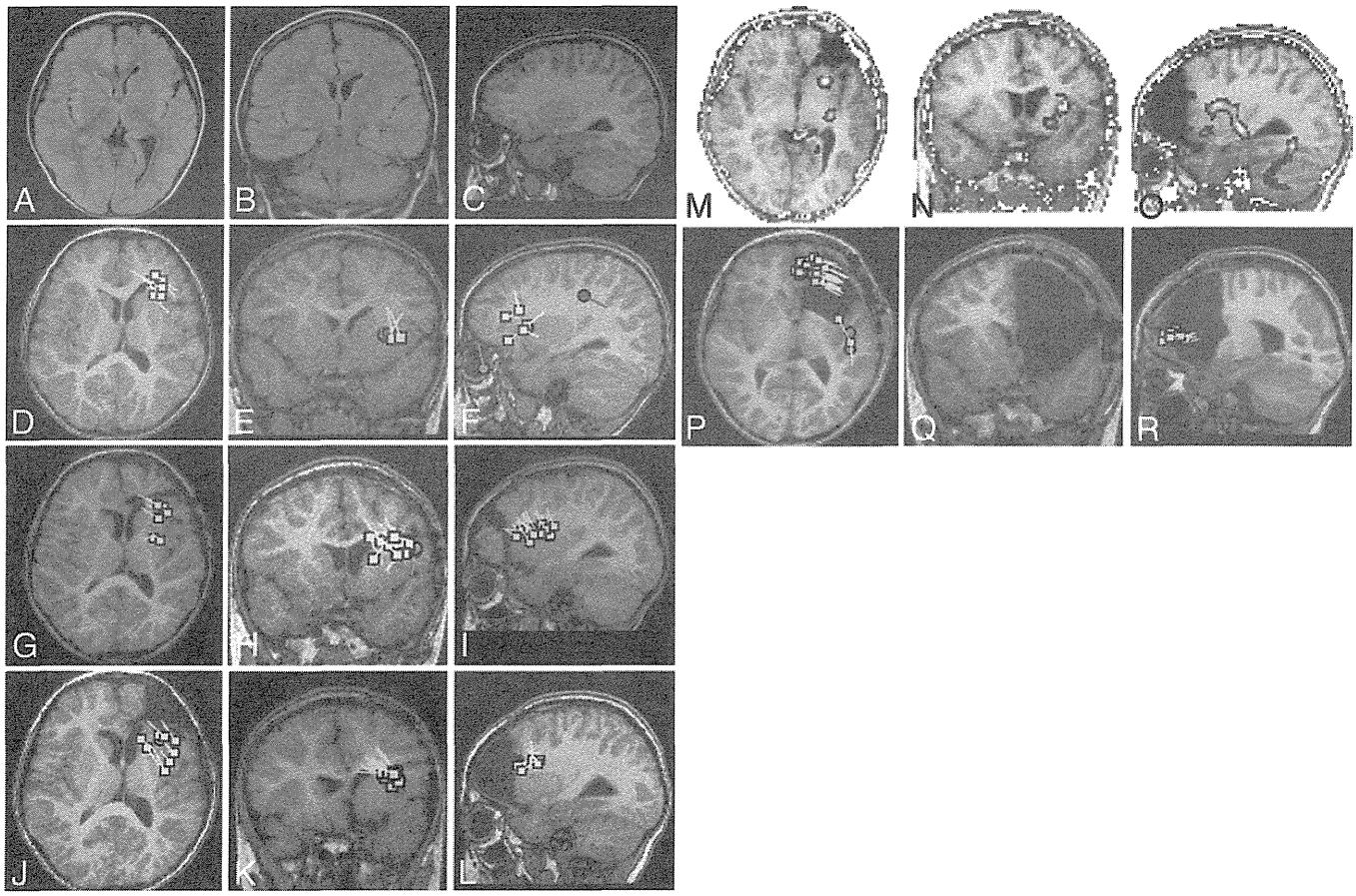

Fig. 1. Case 4. **A–C:** Preoperative MR images showing blurring of gray matter–white matter in the left frontal lobe. **D–F:** Preoperative magnetoencephalograms showing a cluster of spike dipoles in the deep white matter of the left frontal lobe. Dipole sources with a goodness-of-fit better than 90% *(yellow squares)* and 80% *(green circles)* were accepted and overlaid on the MRI results. A somatosensory evoked magnetic field was obtained on stimulation of the right median nerve *(red circle)*. **G–I:** Magnetoencephalograms obtained after the first frontal lobe disconnection surgery, revealing a cluster of spike dipoles in the deep white matter of the residual frontal lobe. **J–L:** Magnetoencephalograms obtained after a second partial frontal lobectomy, revealing a cluster of spike dipoles in the head of the caudate nucleus and the deep white matter of the residual frontal lobe. **M–O:** Subtraction ictal SPECT coregistered with structural MRI (SISCOM) revealing hyperperfusion of the nucleus accumbens and the deep white matter of the left frontal lobe. **P–R:** Magnetoencephalograms obtained after the third surgery, a partial resection of the anterior striatum and residual frontal lobe, showing a cluster of spike dipoles mostly in the disconnected frontal lobe and slightly in the margin of the residual brain tissue.

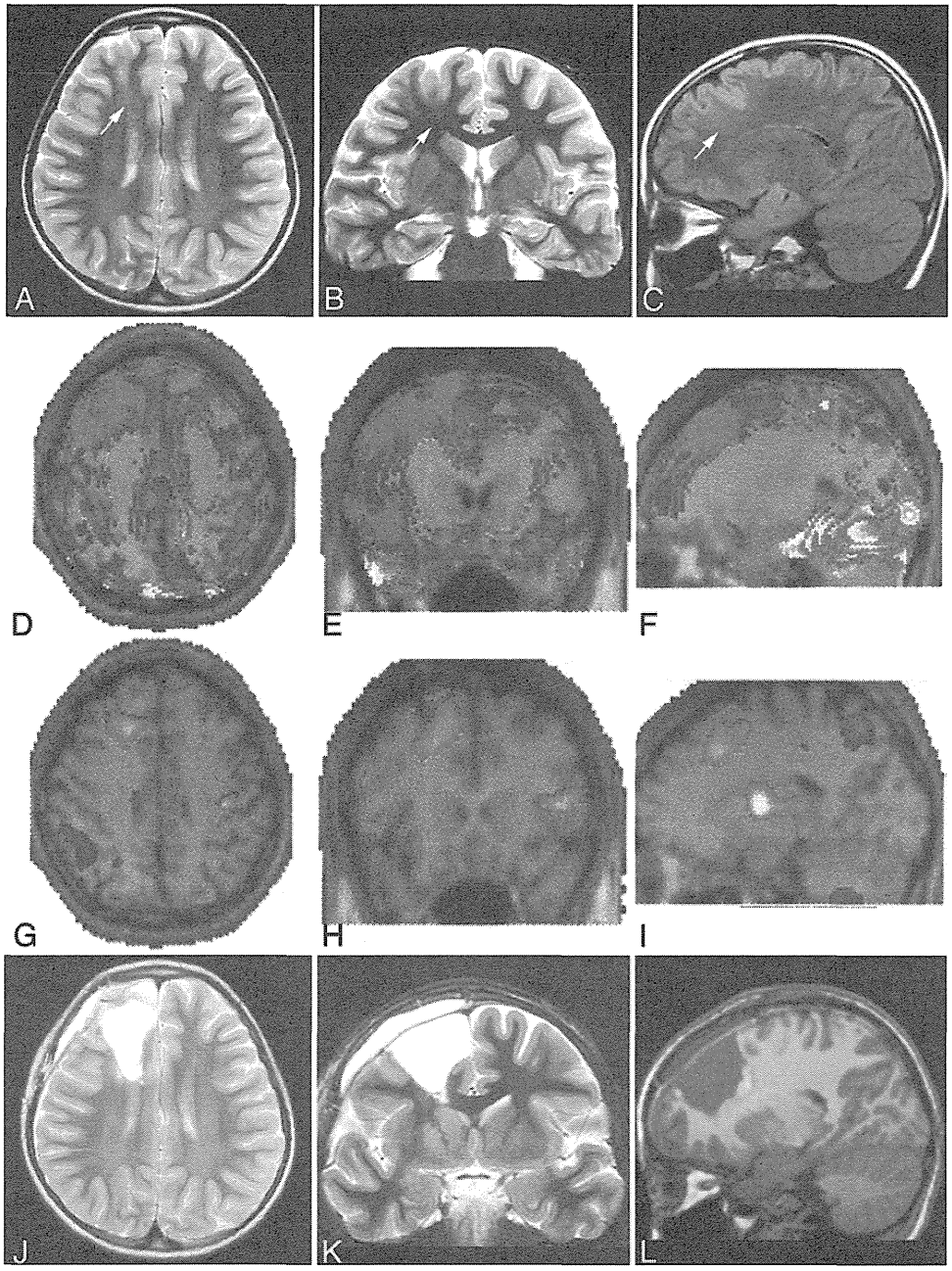

Fig. 2. Case 6. **A–C:** Preoperative MR images showing blurring of gray matter–white matter in the right frontal lobe and the transmantle sign, that is, signal abnormalities extending radially inward toward the lateral ventricle from the cortical surface *(arrows)*. **D–F:** ^{123}I-iomazenil SPECT scans revealing low uptake at the right frontal lobe. **G–I:** Ictal SPECT scans showing significant hyperperfusion in the white matter of the right frontal lobe. **J–L:** Postoperative MR images obtained after resection of the right frontal lobe and the periventricular white matter.

tinuously in the subcortical white matter (Fig. 3C and J), occasionally forming ectopic nests within the white matter (Fig. 3D). All cases showed a high concentration of neurons (Fig. 3K), and prominent astrocytosis in the subcortical white matter[12,17] was evident. In Cases 1 and 4, dysmorphic neurons were also observed in the resected insular cortex (Fig. 3E). Histological verification of the resected anterior striatum was successful (Fig. 3F) with a small number of dysmorphic neurons (Fig. 3G). In the periventricular white matter, some dysmorphic neurons (Fig. 3H) were found in Cases 1, 4, and 6. Marked reactive astrocytosis (Fig. 3L) was recognized in all 8 cases.

Postoperative Outcome

The postoperative outcomes are summarized in Table 2. The follow-up period was 10–53 months (mean 27 months). All patients were free from seizures postsurgery, except 1 who had transient postoperative seizures (Case 4). Therefore, 7 patients had Engel Class IA out-

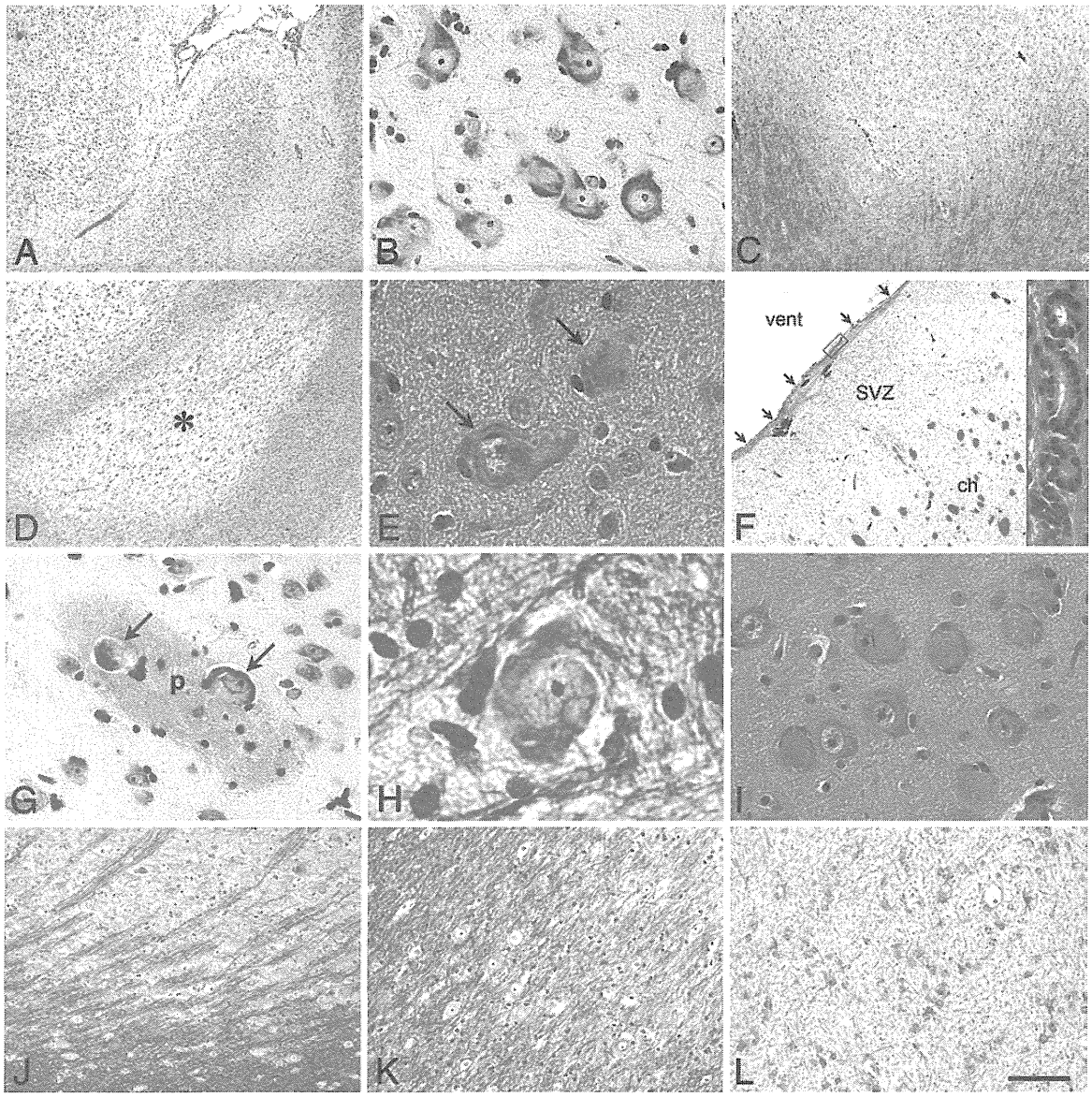

Fig. 3. Photomicrographs showing histopathological features of resected tissue. Case 4. **A:** Low-magnification view of cortex demonstrating the polymicrogyric cortical ribbon. **B:** High-magnification view of cortex showing several dysmorphic neurons. **C:** Area with abnormally blurred transition from the cortex (upper) to the subcortical white matter (lower). **D:** A heterotopic neuronal nest *(asterisk)* within the white matter **E:** Two dysmorphic neurons *(arrows)* in the insular cortex. **F:** Low-magnification view of the area close to the ventricle (vent) demonstrating orientation of the subventricular zone (SVZ) and the anterior caudate head (ch). *Arrows* indicate the ependymal cell lining. **Inset:** Higher magnification of the area indicated by a *square* in F, showing small ependymal canals (forking). **G:** Two dysmorphic neurons *(arrows)* within or adjacent to the axon bundles (pencil fibers [p]) in the striatum. **H:** A dysmorphic neuron in the periventricular white matter. Case 6. **I:** Dysmorphic neurons in the cortex. **J:** Many neurons are scattered in the deeper layers of the cortex (upper) and underlying white matter (lower). **K:** Dysmorphic neurons distributing parallel to the direction of myelinated fibers in the deep white matter. **L:** Prominent reactive astrocytosis in the periventricular white matter. Klüver-Barrera stain (A–D, F–H, J, and K), H & E (E, Inset, and I), and glial fibrillary acidic protein immunostaining with diaminobenzidine as the chromogen (L). Bar (all in μm) = 770 (A), 40 (B, G, and I), 385 (C), 520 (D), 25 (E), 800 (F), 30 (Inset), 15 (H), 155 (J), 100 (K), and 75 (L).

come and 1 had Class IC outcome. There were no cases of transient or permanent morbidity. All patients showed postoperative EEG improvement especially in terms of the frequency of abnormal discharges except in Case 5 (Table 3). Electroencephalography records of 2 cases (Cases 6 and 7) were normalized and revealed the disappearance of epileptic discharges.

Discussion

After resection of the epileptogenic cortices along with a portion of the anterior striatum and periventricular white matter, medically refractory epilepsy was cured, and all 8 patients were free from seizures. Pathological abnormalities were observed in the surgical specimens

TABLE 3: Preoperative and postoperative findings of interictal EEG*

Case No.	Preop	Postop
1	lt Fp, F, aT continuous q wave	sporadic lt C small spike & wave
2	frequent bilat synchronous spike & wave	sporadic lt aT spike
3	frequent continuous lt F spike	sporadic lt aT spike
4	frequent lt Fp, F, aT spike	rare lt Fp, aT small spike
5	frequent rt Fp, F, aT spike & wave	frequent rt C sharp wave
6	frequent bilat F spike & wave	no spike
7	frequent rt Fp, F, P spike & wave	no spike
8	frequent lt F, C polyspike burst	sporadic rt Fp, F spike & wave

* aT = anterior temporal; C = central; F = frontal; Fp = frontopolar; P = parietal.

of the anterior striatum and periventricular white matter. These findings suggested that dysplastic deep brain structures, such as the anterior striatum and periventricular white matter, may participate in epileptogenesis in some cases.

Previously, we reported on a case of frontal lobe epilepsy with dysmorphic neurons in the striatum[11] (Case 1 in the present study) and a case of refractory frontal lobe epilepsy treated with multiple surgeries[15] (Case 2 in the present study). Interestingly, patients in these cases became completely seizure free, and resected tissues contained anterior striatum and periventricular white matter. These facts suggest that the resection of part of the deep structures would be curative. In addition, patients in the present study became seizure free or had a dramatic reduction in seizure frequency after the resection of deep structures. Importantly, they had never shown any permanent neurological deficits. In the present study, 1 patient (Case 4) underwent 3 repeated surgeries. We could identify definitive pathology in the deep structures at the third resection without any other abnormalities. The epileptogenic lesion would be confirmed at the anterior striatum and periventricular white matter. Based on this case, we thought that the deep cerebral structures could be epileptogenic.

A significant number of FCD lesions remain unidentified using current neuroimaging techniques.[23] Even if an FCD becomes evident on neuroimaging, it can be merely a small part of the FCD, similar to the tip of a huge iceberg. Therefore, recurrence of the epileptogenic lesion in the resected cortical margin may be unmasked latent epileptogenic lesions. It would resemble the unmasking process of cerebral plasticity.[9] In the process, disinhibition of redundant latent neural networks is induced after acute cerebral insult and results in functional representations. However, the hypothesis of unmasking cortical epileptogenicity is not enough to explain the existence of pathological abnormalities and the possibilities of epileptogenicity in deep brain structures.

Deep brain structures widely connect with cerebral cortices in a circular manner. Authors of a previous article reported that the giant ectopic neurons in the white matter of FCD cases were surrounded by hypertrophic basket formations, which formed symmetrical (inhibitory) synapses with both the somata and the proximal portion of the dendrites of these giant neurons.[2] Furthermore, the density of excitatory and inhibitory synapses was more or less than that of the normal adjacent cortex. Focal cortical dysplasia would lead to multiple changes in excitatory and inhibitory synaptic circuits. If only the cortical lesion is resected in a case with epileptogenicity in both the cortex and the adjacent deep brain structures, epileptic discharges may spread via the neural network between the epileptogenic deep structures and the cortical margin. The latent network between the epileptogenic deep brain structures and the resected cortical margin might be disinhibited after cortical resection and become active. Thus, the apparent epileptogenic area recurs in the resected margin, which for the surgeon is like pursuing a mirage.

Previous detailed histopathological and electrophysiological studies[1,8] about periventricular nodular heterotopia also support the epileptogenicity of the periventricular structures. Authors of a previous article[8] reported that the surgical specimen of the subependymal nodular heterotopia has sparse connections with the cortex. The nodules contain immature neurons of GABA production. These authors suggested that local disinhibition due to immature GABAergic neurons could also lead to synchronized multisynaptic excitatory interactions and generate prolonged bursts and afterdischarges. These findings are similar to one of the FCDs described above.

Another report[1] describes surgical cases of periventricular nodular heterotopia. Eight patients underwent stereo-EEG recordings. At least one heterotopion was involved at seizure onset in 6 patients. Four patients underwent removal of the nodules along with adjacent or connected tissues, and all of them showed improvement in seizure frequency. The surgical results of this study suggest the intrinsic epileptogenicity of the periventricular structures.

Previous studies[4,14] have shown radiological abnormalities of the striatum and periventricular white matter adjacent to the cortex in cases of FCD. Histological findings in resected tissues in patients with the transmantle sign, that is, signal abnormalities extending radially inward toward the lateral ventricle from the cortical surface, showed pathological abnormalities, such as abnormal cortical lamination, neuronal cytomegaly, neuronal disorientation, indistinct cortical–white matter junctions, scattered individual neurons in the white matter, hypomyelination with astrogliosis in the white matter, and subcortical balloon cells.[4] Results of the present study suggested that abnormal tissues can extend into the periventricular white matter in cases with cortical development malformations. Three patients (Cases 6, 7, and 8) in our study demonstrated the transmantle sign on preoperative MRI. This sign is a potent supportive trail to pursue an epileptogenic lesion to be resected; however, sensitivity of the signal is not always high enough to demonstrate the

lesion. The transmantle sign was observed in 37.5% of patients with FCD Type II but not in those with FCD Type I.[14] In the present study, the distribution of heterotopic neurons in the subcortical and deep white matter of the resected specimen was qualitatively comparable between cases with and without the transmantle sign on preoperative MRI. Thus, we can consider that sensitivity of the transmantle sign in the present study was 37.5%. This rate illustrates the difficulty in detecting epileptogenic lesions in deep brain structures.

During the embryonal stage of development, neurons are generated in the ventricular zone and migrate radially along the glial cell guides to the cortex. Interneurons generated in the proliferative zone of the striatum migrate tangentially into the cortex.[13] Abnormality in neurogenesis must relate to the transmantle malformation of brain tissues, including the striatum and periventricular white matter. Genetic abnormalities, such as *TSC1* and *TSC2* (tuberous sclerosis genes), were detected in some types of FCDs.[20] A genetic mechanism could be one of the factors contributing to brain malformations.

Several articles have documented striatal lesions associated with epilepsy. Gastaut et al.[7] reported a case of West syndrome with a calcified tumor of the basal ganglia, which was detected by CT. Sasaki et al.[19] described the case of an 8-year-old girl with intractable epilepsy resulting from cortical dysplasia. She had suffered bilateral striatal necrosis after pneumonia and was transiently seizure free for 6 months. These authors believe that the striatum may be involved in the propagation pathway for epileptic seizure activity. RamachandranNair[18] reported the case of a female infant with a low-grade glioma in the right basal ganglia spreading to the cortical area. In this case, the relationship between striatal lesions and epileptogenesis or propagation of seizure was suggested but unproven.

The association between seizure control and the resection of deep structures was suggested in an article about hemispherotomy, a procedure performed for seizure control in a patient with hemispheric lesions. Cook et al.[6] reported that removing most of the thalamus, basal ganglia, caudate nucleus, and associated deep hemispherical structures seems important, because these areas were often implicated in recurrent seizures in functional hemispherectomy cases in which these areas had not been removed. This report may support our findings from a surgical viewpoint.

Conclusions

In summary, in cases of intractable focal epilepsy, the epileptogenic lesions may exist in the cortex as well as the deep brain structures, such as the periventricular white matter and the striatum. All cases in the present study showed favorable surgical outcomes without any morbidity, which offers the possibility for safe resection to attain freedom from seizures. Pathological abnormalities such as dysmorphic neurons and astrocytosis in deep brain structures would play a key role in the epileptogenesis.

Disclosure

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Author contributions to the study and manuscript preparation include the following. Conception and design: Kaido, Otsuki. Acquisition of data: Kaido, Otsuki, Kakita, A Takahashi, Kaneko, H Takahashi, Honda, Nakagawa, Sasaki. Analysis and interpretation of data: Kaido, Kakita, Sakakibara, A Takahashi, Kaneko, Yuko Saito, Ito. Drafting the article: Kaido, Kakita, Yoshiaki Saito. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Kaido. Administrative/technical/material support: Otsuki, Sugai. Study supervision: Otsuki.

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Original article

Surgical management of cortical dysplasia in infancy and early childhood ☆

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Abstract

Purpose: To describe operative procedures, seizure control and complications of surgery for cortical dysplasia (CD) causing intractable epilepsy in infancy and early childhood. *Methods:* Fifty-six consecutive children (less than 6 years old) underwent resective epilepsy surgery for CD from December 2000 to August 2011. Age at surgery ranged from 2 to 69 months (mean 23 months) and the follow-up was from 1 to 11 years (mean 4 years 4 months). *Results:* Half of the children underwent surgery during infancy at an age less than 10 months, and the majority (80%) of these infants needed extensive surgical procedures, such as hemispherotomy and multi-lobar disconnection. Seizure free (ILAE class 1) outcome was obtained in 66% of the cases (class 1a; 55%): 85% with focal resection ($n = 13$), 50% with lobar resection ($n = 18$), 71% with multilobar disconnection ($n = 7$) and 67% with hemispherotomy ($n = 18$). Peri-ventricular and insular structures were resected in 23% of focal and 61% of lobar resections. Repeated surgery was performed in 9 children and 5 (56%) became seizure free. Histological subtypes included hemimegalencephaly (16 patients), polymicrogyria (5 patients), and FCD type I (6 patients), type IIA (19 patients), type IIB (10 patients). Polymicrogyria had the worst seizure outcome compared to other pathologies. Surgical complications included 1 post-operative hydrocephalus, 1 chronic subdural hematoma, 2 intracranial cysts, and 1 case of meningitis. No mortality or severe morbidities occurred. *Conclusions:* Early surgical intervention in children with CD and intractable seizures in infancy and early childhood can yield favorable seizure outcome without mortality or severe morbidities although younger children often need extensive surgical procedures.

Keywords: Epilepsy surgery; Infant; Focal cortical dysplasia; Hemimegalencephaly; Polymicrogyria; Hemispherotomy; Multilobar disconnection; Seizure outcome

1. Introduction

Frequent epileptic seizures in infants cause severe epileptic encephalopathy associated with progressive developmental delay. Cortical dysplasia (CD), or malformations in cortical development, is increasingly recognized as a cause of intractable epilepsy in infancy [1,2].

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The CD spectrum covers distinct focal cortical lesions to extensive hemispheric pathology and is classified histologically as focal cortical dysplasia (FCD), heterotopia, polymicrogyria (PMG), schizencephaly, lissencephaly, and hemimegalencephaly (HMC) [3,4]. Among these, FCD and HMC are the 2 most frequent types in reported surgical series thus far.

Histologically, FCD is subclassified as FCD type I, type IIA, and type IIB [4]. FCD type I presents as neocortical dyslamination, ectopic white matter neurons, and/or giant neurons. FCD type II is characterized by the additional presence of dysmorphic neurons (type IIA) and balloon cells (type IIB). Magnetic resonance imaging (MRI) of FCD type I is frequently negative, but may show slight signal changes in subcortical white matter [5]. FCD type II MRI typically shows thickened cortical ribbon, blurred gray-white junctions, cortical and subcortical signal changes, and transmantle sign. HMC demonstrates an enlarged unilateral hemisphere with gross anatomical malformations in cortical and subcortical structures associated with variety of histopathological abnormalities identified in other forms of CD [6].

A contemporary series of resective surgery for CD reports that more than 60% of patients are seizure free, with higher rates for complete removal of the lesion [7–10]. Morbidity (<3%) and mortality (0.2%) are low for patients with CD undergoing epilepsy neurosurgery. Moreover, patients operated on at younger ages reportedly show larger increases in developmental quotient (DQ) after surgery [1,11–12]. Attention, therefore, is now focused on early surgery to avoid the negative influence of frequent intractable seizures on the immature brain causing epileptic encephalopathy in early life.

However, early epilepsy surgery in infancy was reported to have high intraoperative complications and mortality rate [13,14]. Duchowny et al. [13] reported that the surgical mortality was 6% in their series of 31 infants who were under 3 years of age. Basheer et al. [14] also reported that age (<2 years old), weight (<11 kg), and hemidecortication were risk factors for transfusion and post-operative hydrocephalus developed in 13% of the 24 children in their series.

Recently, introduction of less-invasive disconnective surgical procedures such as hemispherotomy [15–16] and posterior multilobar disconnection [18,19], which totally disconnect epileptic cortices from the rest of the brain but spare major vasculature, have been facilitating safe and reliable epilepsy surgery in children. Although the patient number is still small, recent literature reported favorable outcomes in radical epilepsy surgery for CD in early infancy [8,20,21]. However, more data are needed to clarify the indication of surgical procedures, timing, outcome, and risk of epilepsy surgery for CD presenting in infancy and early childhood.

2. Patients and methods

2.1. Subjects

We retrospectively studied 56 consecutive children (33 male patients, 23 female patients) who had medically refractory epilepsy with CD and underwent resective surgery at less than 6 years of age at the National Center of Neurology and Psychiatry from December 2000 to August 2011. Patients with tuberous sclerosis, dysplastic tumors, and encephalomalacia were excluded from the study.

Age at seizure onset ranged from birth to 27 months (median: 1 months, mean: 4 months) and age at surgery ranged from 2 to 69 months (median: 10 months, mean: 23 months) (Fig. 1). Twenty patients were operated within 6 months of birth. The follow-up period from the last surgery ranged from 12 months to 11 years (median: 4 years, mean: 4 years 4 months). All patients had drug-resistant multiple daily seizures, such as epileptic spasms, tonic seizures, or epilepsia partialis continua. No patient had a history of perinatal or postnatal systemic complications suggesting brain injury. In 4 cases, resective surgery was indicated at 1 month to 2 years (mean: 16 months) after callosotomy, which had revealed lateralized epileptogenicity.

2.2. Pre-surgical evaluation

All patients underwent comprehensive pre-surgical evaluations including electroencephalography (EEG), 1.5- or 3.0- Tesla MRI, ictal video-EEG monitoring, fluorodeoxyglucose-positron emission tomography (FDG-PET), magnetoencephalography (MEG), and developmental assessments. All, but 5, patients demonstrated MRI abnormalities, which varied from a subtle focal cortical or subcortical change to hemispheric structural abnormality. Subtraction ictal 99mTc-ethyl cysteinate dimer single-photon emission tomography (SPECT) coregistered to MRI (SISCOM) was indicated in 27 cases. Intracranial EEG monitoring with subdural and depth electrodes was performed under sedation and intensive care over 3 days in 7 patients (3 frontal, 2 temporal, 1 central, and 1 parietal lobe) over 35 months of age.

2.3. Peri-operative management

Central venous catheterization for blood transfusion was mandatory for infants less than 6 months. Blood transfusion, packed red blood cells, and fresh frozen plasma (FFP) was used during surgery as required. FFP of 10 ml/kg was routinely transfused for small infants who were less than 7 kg perioperatively for hemispheric surgeries, for which total blood loss was 150–250 ml and total time was 5–6 h.

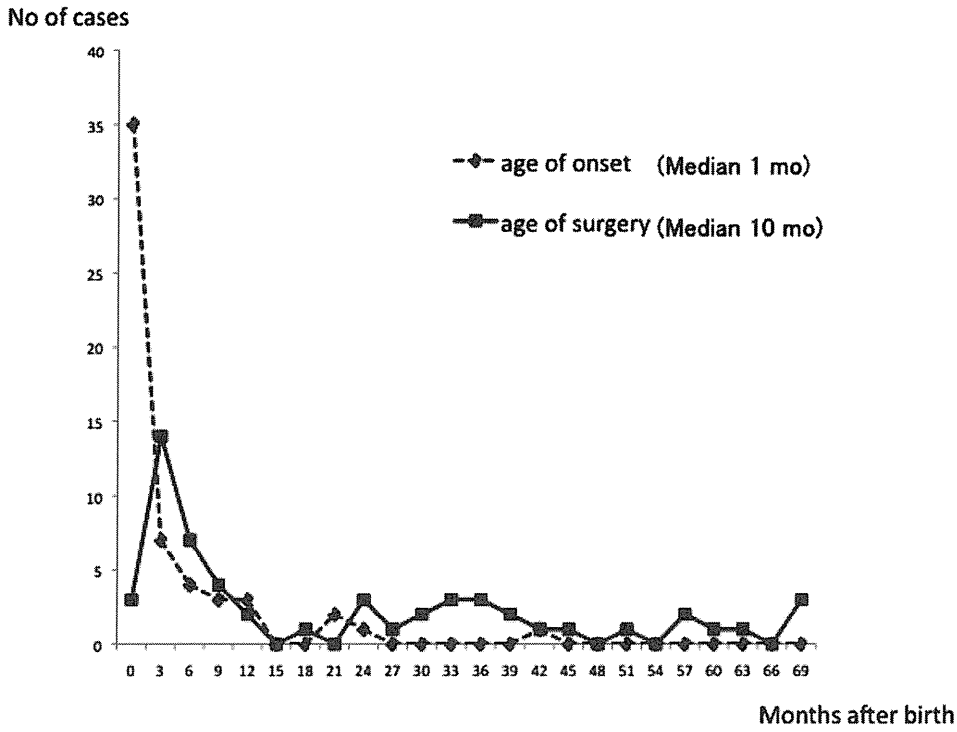

Fig. 1. Age of onset and age of surgery (months) in 56 children.

2.4. Method for assessing outcomes

Seizure outcomes were assessed using the International League Against Epilepsy (ILAE) classification [22].

2.5. Statistical analyses

Fisher's exact test was used to compare surgical outcome (seizure free vs. not free) to surgical procedures (focal resection vs. others) and histological subtypes (PMG vs. others). We considered $P < 0.05$ as statistically significant.

3. Results

3.1. Surgical procedures

The surgical procedure used and age at surgery for the 56 children is shown in Fig. 2. Twenty-eight patients (50%) were operated on during infancy (<12 months). Extensive surgical procedures, including hemispherotomy and multilobar disconnection, were more often indicated in infants than in older children.

Focal resection (Fig. 3), less than 4 cm at the largest diameter, was indicated in 13 patients. The resection area included all MRI-visible lesions, together with MRI non-visible areas, demonstrating the congruency of ictal hyper-perfusion, MEG dipole clustering, and FDG-PET hypometabolism. In 3 of these patients (23%), periventricular and insular regions, which were continuous to the cortical lesion, were also resected. Lobar resection (Fig. 4) was indicated in 18 patients. Periventricular and insular structures were also resected in 11 cases (61%), all of which were added in extensive frontal lobectomy. Multilobar disconnection (Fig. 5) was indicated in 7 patients; 2 to the anterior and 5 to the posterior half of the hemisphere. Hemispherotomy (Fig. 6) was indicated in 18 patients, 17 by vertical and 1 by horizontal approach.

3.2. Seizure outcome

Seizure outcome at the last follow-up was ILAE class 1 in 37 cases (66%); there were no class 2 cases, two class 3 cases (4%), five class 4 cases (9%), and twelve class 5 cases (21%) (Fig. 7). Thirty-one children (55%) were completely seizure free after surgery (class 1a). Upon comparison of the type of surgical procedures, class 1 outcome was obtained in 85% of patients with focal resection, 50% of patients with lobar resection, 71% of patients with multilobar disconnection, and 67% of patients with hemispherotomy. Although the differences were not statistically significant, better seizure outcome was obtained after focal resection compared to the other procedures ($0.05 < P < 0.1$).

3.3. Histopathological diagnoses

Histological subtypes included HMC (16 patients), PMG (5 patients), and FCD type I (6 patients), IIA (19 patients), and IIB (10 patients). The histopathology,