Focal Cortical Dysplasia in Pediatric Epilepsy

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Received: October 29, 2019

Accepted: November 12, 2019

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Focal cortical dysplasia (FCD) is the most common cause of intractable focal epilepsy in children undergoing epilepsy surgery. In these patients, seizures usually develop in early childhood and are often explosive from their onset. This review summarizes the classification of FCD and provides recent updates, clinical features, and illustrative electrophysiological and neuroimaging findings, which are expected to help physicians better understand FCD. Children with intractable focal epilepsy should receive timely evaluations for epilepsy surgery. Complete resection of the epileptogenic zone and an early surgical intervention lead to favorable surgical outcomes.

Keywords: Malformations of cortical development; Pediatrics; Epilepsy

Introduction

Focal cortical dysplasia (FCD) is a subgroup of malformations of cortical development characterized by abnormal cortical lamination, neuronal migration, and differentiation. The neuropathological features were first described by Taylor et al. [1] in 1971 in the pathological specimens of ten patients with drug-resistant epilepsy. FCD is the most common etiology in children with intractable focal epilepsies requiring resective epilepsy surgery, whereas hippocampal sclerosis is the most common cause in adults [2].

Magnetic resonance imaging (MRI) technology has evolved markedly in the last few decades and enhanced the diagnostic yield for FCD. However, delineating the extent of dysplastic lesion in patients with subtle MRI findings, and identifying the extent of the epileptogenic zone (EZ) remains a challenging task. Electrophysiology and functional imaging techniques are helpful in the localization of the EZ.

In this article, we review classification of FCD with recent up-

dates, clinical features, and illustrative electrophysiological and neuroimaging to help the physician understand FCD and provide the best therapeutic options for children with FCD.

FCD Types and Classification

Historically, several classification systems for FCD have been proposed [3,4]. In 2011, the International League Against Epilepsy (ILAE) Task Force suggested a three-tiered FCD classification based on histopathological features (Table 1) [5]. This system differentiates isolated FCDs (FCD type I and II) from variants associated with potentially epileptogenic lesions (FCD type III). FCD type I is characterized by isolated dyslamination without any cytologic abnormality. Radial dyslamination (FCD type Ia) is characterized by radial microcolumns composed of more than eight neurons aligned in a vertical direction. Tangential dyslamination (FCD type Ib) refers to the derangements of the six layered horizontal composition of the neocortex. The FCD type Ic is a combination

Table 1. ILAE classification of focal cortical dysplasia and suggestions for an updates

	Histology [5]	Comments [6]
FCD type I (isolated)		
FCD type Ia	Abnormal radial cortical lamination	Molecular biomarkers needed to classify clinical features, radiologic, and histopathological entities.
FCD type Ib	Abnormal tangential cortical lamination	
FCD type Ic	Abnormal radial and tangential cortical lamination	
FCD type II (isolated)		
FCD type IIa	Dysmorphic neurons	Genetic findings of mTORopathies and new variant of bottom-of-sulcus dysplasia needed to be distinguished.
FCD type IIb	Dysmorphic neurons and balloon cells	
FCD type III (associated)		
FCD type IIIa	Cortical lamination abnormalities in the temporal lobe associated with hippocampal sclerosis	Molecular and clinical biomarkers needed to differentiate between primary or secondary etiology.
FCD type IIIb	Cortical lamination abnormalities adjacent to a glial or glioneuronal tumor	
FCD type IIIc	Cortical lamination abnormalities adjacent to vascular malformation	
FCD type IIId	Cortical lamination abnormalities adjacent to any other lesion acquired during early life (trauma, ischemia, encephalitis)	

ILAE, International League Against Epilepsy; FCD, focal cortical dysplasia; mTOR, mammalian target of rapamycin.

of both radial and tangential variants. FCD type II refers to disruptions of cortical lamination with dysmorphic neurons. Dysmorphic neurons are the histopathological hallmark of FCD type II lesions. They have enlarged cell body and nucleus with aggregates of Nissl substance and accumulation of neurofilament proteins. Balloon cells, observed exclusively in FCD type IIb, present enlarged cell body and opalescent glassy eosinophilic cytoplasm in hematoxylin-eosin stain. FCD type III refers to cortical lamination abnormalities (FCD type I) associated with or adjacent to other principal lesions. Principal lesions comprise any anatomical lesion with etiologically defined pathogenesis, including epilepsy-associated tumors, vascular malformations, encephalitis, traumatic scars, malformations of cortical development, or mitochondrial/metabolic dysfunction. Dual pathology refers only to patients with hippocampal sclerosis, who have a second epileptogenic principal lesion. Of note, cortical dyslamination in the temporal lobe associated with hippocampal sclerosis is considered as FCD type IIIa, rather than dual pathology. Double pathology refers to two independent epileptogenic lesions, which evolve from independent pathogenesis, not including hippocampal sclerosis. The current ILAE classification presents several challenges. Najm et al. [6] have published a proposal to revise and update the 2011 ILAE classification (Table 1). First, there are concerns about the limited clinical and radiological significance in FCD Ib and Ic. Molecular biomarkers to differentiate FCD Ib and Ic need to be introduced. Second, there is increasing evidence for the role of somatic mammalian target of rapamycin (mTOR) pathway activation in the pathophysiology of FCD type II [7-9]. This would differentiate type II patients with mTORopathies, who could be potential candidates for

mTOR inhibitors. Although mTORopathies are associated with 10% to 20% of FCD type II lesions, Najm et al. [6] suggested that molecular genetic findings of mTOR activation using pathogenic tissue need to be classified as a separate entity in FCD type II. Moreover, new variants of the bottom-of-sulcus type II need to be distinguished. Bottom-of-sulcus dysplasias (BOSDs) are highly epileptogenic clinico-radiologic-histopathologic entities with continuous, localized, rhythmic interictal epileptiform discharges [10]. The characteristic MRI features of BOSDs include cortical thickening, gray-white blurring, increased subcortical T2, fluid attenuation inversion recovery (FLAIR), and a transmantle sign [11]. MRI lesions of BOSDs are highly co-registered with hypometabolism on 2-deoxy-2 (¹⁸F) fluoro-d-glucose positron emission tomography (FDG-PET) [12]. BOSDs are characterized by neuronal dyslamination and dysmorphology at the sulcal depth and a relatively normal gyral crown [13]. The surgical outcome of seizure freedom is as high as 90% if BOSDs are completely resected [10]. Najm et al. [6] have suggested that molecular and genetic mechanisms are needed for a comprehensive classification based on clinical features, imaging characteristics, histopathological findings, and treatment options to classify patients in clinical setting.

Clinical Features

Epilepsy is the most common clinical presentation for FCD. Seizures may start at any age, but usually, develop in early childhood. FCD with cytoarchitectural abnormalities (FCD type IIa and IIb) is associated with earlier age of seizure onset than FCD with architectural abnormalities alone (FCD type Ia) [14,15]. The seizure

frequency is usually high, and seizure onset is often explosive, needing occasional hospitalization. In a cohort of 32 patients with FCD type IIb who ultimately underwent resective surgery, 23 patients (72%) had multiple daily seizures [10].

Most children with FCD present with focal seizures depending on the location of the lesion. However, in very young children, seizure can be generalized, generalized electroencephalography (EEG) abnormalities, and epileptic encephalopathy. Fauser et al. [14] described generalized tonic-clonic seizures in 20.6% of patients, tonic seizures in 15.9% of patients, and atonic seizure in 6.5% of patients. Epileptic spasms, often asymmetric or asynchronous, can be the first seizure type in infants [16].

Seizures are usually pharmacoresistant and may require epilepsy surgery. In contemporary surgical series, cortical dysplasia is the most common pathological substrate in children undergoing epilepsy surgery [17]. However, a minority of patients have shown transient response to medication and remained seizure-free for several years [14].

Neurocognitive dysfunction is also problematic in children with FCD. Intellectual disabilities have been demonstrated in approximately 26% to 79% of children with FCD [18,19]. Krsek et al. [20] observed higher rates of cognitive impairment in FCD type I patients (96%) than in FCD type II patients (27%). Their study showed that 31% to 57% of children exhibited motor or language development delays. Conversely, another study showed that children with FCD type II were more likely to have lower intelligence quotient than those with FCD type Ia [15]. Such inconsistencies may be related to clinical factors such as the age of epilepsy onset, the extent of FCD lesion, and the duration of epilepsy. The pathophysiology of neurocognitive dysfunction in FCD remains unclear. However, the detrimental influences of frequent early seizures on the cognitive potential of children are well-documented [21-23]. Therefore, early surgical intervention in intractable epilepsy should be considered to stabilize cognitive function.

Diagnostic Evaluations

1. Electroencephalography

1) Scalp EEG

Studies have shown that the most characteristic interictal pattern consisted of continuous rhythmic or pseudo-rhythmic spikes or sharp waves, observed in 40% to 64% of cases [12,24]. The interictal EEG could display focal or regional spikes or polyspikes, focal background slowing, spike trains or continuous epileptiform discharges. Interictal EEG findings did not distinguish between patients with mild and severe cortical dysplasia. Moreover, there were no differences in the incidence of localized interictal epileptiform

discharges between mild and severe dysplasia [24,25]. Scalp EEG is limited in its spatial resolution and ability to detect activity generated deep in the brain. However, a recent study showed a correlation between scalp and intracranial EEG (iEEG) seizure-onset pattern (SOP). In a comparison of SOP in 61 patients with focal epilepsy, ≥ 13 Hz paroxysmal fast activity on scalp EEG corresponded to low-voltage fast activity (LVFA) at iEEG onset in patients with malformations of cortical development [26].

2) Intracranial EEG

iEEG provides information about the ictal onset zone with a seizure propagation pattern. It can also identify functional areas or eloquent cortex. The main indications for iEEG monitoring are: the FCD is invisible or ill-defined on MRI, a discordance between electro-clinical data and presurgical evaluation, or in case of proximity or involvement of eloquent cortex [27].

Typical interictal iEEG features are rhythmic spike discharges (RSDs) or pseudorhythmic spikes (Fig. 1). A study showed that the intralesional interictal activity was characterized by continuous rhythmic, or pseudorhythmic spikes or polyspikes with a frequency between 1 to 3 Hz [19]. The frequency of RSDs was usually maximized within the location of FCD. However, RSDs can be seen in multiple pathologies with epileptogenicity, not specific for FCD. Interictal RSDs are as important as ictal discharges. The typical interictal pattern has the highest sensitivity for the EZ [28]. The intracranial interictal discharges were modulated by sleep stages, with an increased prevalence of rhythmic discharges in drowsiness and non-rapid eye movement (NREM) sleep and decreased discharges during REM sleep [29].

Ictal discharges frequently arise from the same areas as the RSDs, and their area is often larger than the interictal activity. Five ictal onset patterns have been described in FCD: (1) LVFA; (2) spike-and-wave activity; (3) sharp activity at ≤ 13 Hz; (4) alpha-theta sharp waves; and rarely (5) delta brush [30,31]. Overall, the most common pattern was LVFA [32,33]. LVFA is defined as clearly visible rhythmic activity > 13 Hz, usually with low initial amplitude < 10 to 30 μ V (Fig. 2). Spike-and-wave activity indicates medium to high voltage spike-and-wave complexes typically occurring at a frequency of 2 to 4 Hz. Sharp activity at ≤ 13 Hz is identified as low to medium voltage sharply-contoured rhythmic activity, most commonly in the alpha-theta range. Delta brush characterized by rhythmic delta waves at 1 to 2 Hz with superimposed 20 to 30 Hz brief bursts of activity overriding each delta wave are rarely seen. These delta brush pattern has been observed in premature infants and patients with anti-N-methyl-D-aspartate receptor encephalitis [34,35]. Lagarde et al. [36] demonstrated the SOP prevalence, according to the types of FCD. LVFA was the

Fig. 1. Continuous rhythmic spike discharges with the frequency of 1.5 to 2 Hz. In this interictal intracranial electroencephalography recording from a patient with right postcentral focal cortical dysplasia type IIb, continuous rhythmic high voltage spike discharges were recorded at contacts Ch 4, 5, 6, 11, and 12. Electrode contacts of Ch 4, 5, 6, 11, and 12 were located in lesional/perilesional tissue.

Fig. 2. Low-voltage fast activity at seizure-onset. In this ictal intracranial electroencephalography recording from a patient with right postcentral focal cortical dysplasia type IIb (the same described in Fig. 1), seizure-onset (arrows) was characterized by a visible rhythmic activity at 20 to 30 Hz, initially <10 uV in amplitude, which remained confined for several seconds to Ch 21, 29, 46, 51, and 52. Electrode contacts of Ch 21, 29, 46, 51, and 52 were considered as seizure-onset zone.

most frequently observed, but slow or rhythmic activities were also seen at seizure onset in patients with FCD type I. In FCD type II, preictal spiking or burst of polyspikes followed by LVFA were the most frequent patterns.

High frequency oscillations (HFOs), namely ripples and fast

ripples, are reliable biomarkers of epileptogenicity and good indicators of seizure onset zones (SOZ) [37,38]. HFOs, which reflect pathological hypersynchronous events, are usually recorded from implanted intracranial micro-electrodes with sampling rates of 1,000 Hz or higher. They can also be detected with macro elec-

Fig. 3. Characteristic features on magnetic resonance imaging. (A) Axial T2-weighted image and (B) T2-weighted fluid attenuation inversion recovery (FLAIR) image demonstrate thickening of the right frontal cortex lobe with increased T2 signal intensity (arrows). (C) Axial T1-weighted image shows blurring of the grey and white matter in the right post-central gyrus (arrow). (D) Coronal T2-weighted image, obtained from the same patient as (C), shows T2 hyperintensity in the right post-central gyrus (arrow). (E) Axial T2-weighted image and (F) coronal T2 FLAIR image show increased T2 high-signal intensity in subcortical white matter and gray matter in the left parietal lobe (arrows).

trodes during short-term electrocorticography in the operating room. HFOs are recorded when the EEG is high-pass filtered at 80 and 250 Hz using a finite impulse response filter to eliminate ringing. A ripple is defined if an event is visible between 80 and 250 Hz, whereas a fast ripple is defined an event visible on the side of the 250 Hz filter. Spikes and HFOs are generated as a result of hypersynchronous events and may co-occur frequently. A study revealed the rates and durations of HFOs were frequent and longer in the SOZ than outside of the SOZ [39]. Although HFOs could occur independently of spikes, spikes with fast ripples determined SOZ with the highest sensitivity [37,40]. As the rates of HFOs are high in FCD, they can be reliable biomarkers to define the extent of the epileptogenic dysplastic tissue in FCD [41]. Additionally, HFO rates differ across lesional, perilesional, and nonlesional tissue in FCD, being higher within the borders of the MRI-visible dysplastic lesion and rare in the remote cortex [42]. Although it is difficult to differentiate between pathologic and physiologic HFOs,

resection of brain tissue generating high rates of HFOs in addition to the SOZ would lead to better seizure outcomes [40,43]. Seizure propagation from SOZ can also display typical SOPs, such as sharp activity at 13 Hz and LVFA [31]. A study showed the rapid propagation from SOZ in patients with FCD than in those with nondysplastic lesions [44].

2. Magnetic resonance imaging

There are several characteristic features on MRI that identify the dysplastic cortex. MRI findings include: (1) increased cortical thickness, often associated with abnormal gyral patterns; (2) blurring of gray-white matter junction on T1-weighted images and T2-weighted images; and (3) increased T2 and FLAIR signal intensity in subcortical white matter and cortical gray matter (Fig. 3). Abnormal cortical gyrations and sulcations are better evaluated by three-dimensional (3D)-volume sequences and surface rendering reconstructions. The transmantle sign is a T2-weighted white mat-

ter signal hyperintensity tapering toward the ventricle [13]. It is reported to be specific to FCD type II but is found in only 34% of the FCD type II patients.

Studies have reported normal MRI findings in 20% to 50% of patients with FCD [24,45]. MRI features are often subtle and difficult to detect, especially in FCD type I. Even with experienced neuroradiologists, 40% of patients with FCD type I and 10% to 20% of patients with FCD type II are reported to be MRI-negative [46,47]. In infants with an incompletely myelinated brain, abnormalities in signal intensity of white matter with blurred gray-white matter can be seen as a normal finding. Thus, FCD lesions in infants could become less distinct or disappear with the maturation of myelination. Conversely, the lesions could become evident over time as myelination progress from 41% to 88% [48]. Therefore, interpreting the brain MRI of infants requires caution in differentiating between true dysplasia and the process of myelination.

Advances in MRI techniques and additional sequences can be helpful in the detection and delineation of the dysplastic lesion [49,50]. Morphometric MRI analysis is a voxel-based imaging processing methods that identifies differences in brain anatomy with groups and compares them with a standard database [51]. Diagnostic yield of dysplastic lesion is improved by morphometric MRI combined with conventional visual analysis [52]. Higher magnetic field MRI has immense potential to identify and characterize oth-

erwise inconspicuous lesions accurately [53,54]. Over the last several years, ultra-high-field (UHF) 7T MRI has been available in research settings and has shown exceptional diagnostic benefits [55,56]. Owing to a higher signal-to-noise ratio and smaller voxel size for a given acquisition time, UHF MRI allows for better depiction and visualization of FCD [57,58]. Several high-resolution structural sequences have been introduced and considered a promising approach for the improvement of FCD diagnosis. Magnetization prepared 2 rapid acquisition gradient echoes (MP2RAGE) is a 3D T1-weighted sequence with a sharp contrast between gray and white matter and minimal effect of B1 inhomogeneity [59]. This MP2RAGE can be a suitable sequence to delineate the lesion with high gray-white matter contrast, such as FCD [60]. A new sequence called fluid and white matter suppression (FLAWS) has been reported to be useful for the detection of FCD EZs [61]. FLAWS sequence acquires two images of 3D high spatial resolution images with white-matter signal suppression and cerebrospinal fluid (CSF) signal suppression. Following FLAWS-contrast images are calculated by suppressing both the white matter and CSF signals, which results is high gray-matter specific contrast.

Ultra-high resolution and new sequences would provide opportunities for a successful surgical option to patients with MRI-negative intractable focal epilepsy. Although detection rates have been increased, delineating the extent of the epileptogenic lesion on the

Fig. 4. Features of neuroimaging in a 6-year-old girl with left parieto-temporal focal cortical dysplasia type IIb. (A) Interictal 2-deoxy-2 (^{18}F) fluoro-d-glucose positron emission tomography shows hypometabolism in the left parieto-temporo-occipital area. (B) Ictal single-photon emission computed tomography demonstrates hyperperfusion in the left parieto-temporal area.

structural MRI still needs to be solved. For surgical resection planning, multimodality presurgical evaluation and MRI analysis play an essential role in determining the localization and extent of EZ.

3. Positron emission tomography

PET is a nuclear medicine imaging modality based on the metabolism of FDG. FDG is a glucose analog that can be transported into the cell by the glucose transporter 1 (GLUT1) receptor. FDG does not undergo glycolysis process and becomes metabolically trapped within the cell, serving as a marker for tissues with higher metabolism. As the half-life of FDG is extremely short, it is often difficult to obtain reliable ictal PET. Therefore, the majority of patients are scanned in the interictal phase with hypometabolism in EZ (Fig. 4A). Interictal hypometabolism of FDG-PET can localize FCD in approximately 75% to 83% of patients [24,62]. FDG-PET is highly informative in patients with MRI-negative epilepsy [12,63]. In a series of 23 patients with negative MRI with histologically proven Taylor-type FCD, FDG-PET showed high sensitivity (78%) for detecting FCD [63]. In their study, identification of Taylor-type FCD was increased up to 95% with MRI coregistration. FDG-PET/MRI coregistration improved the detection of FCD and proved useful for planning iEEG studies in patients with normal MRI [64].

4. Single-photon emission computed tomography

Single-photon emission computed tomography (SPECT) is a nuclear medicine imaging modality that allows the quantitative and qualitative assessment of regional cerebral blood flow. SPECT requires an intravenous injection of a radioactive tracer to monitor cerebral blood flow. There is increased ictal regional cerebral blood flow or decreased uptakes in the inter-ictal phase (Fig. 4B). Subtraction ictal SPECT co-registered MRI (SISCOM) utilizes subtraction of interictal SPECT from the ictal SPECT and the resulting image is co-registered with MRI. SISCOM has helped to localize epileptogenic foci in presurgical evaluation, especially in patients with intractable epilepsy [65,66]. Studies indicate that the sensitivity of SPECT for detecting FCD is 87% to 89% [67,68]. The injection time is critical for ictal SPECT. A study showed that an injection time less than 30 seconds corresponded to a well-localized SPECT image [69]. Early radiotracer injection is important for successful seizure localization with ictal SPECT. Performing ictal SPECT in pediatric patients may be complicated as it may be difficult to recognize the clinical onset of seizures and rapid propagation of seizure activity. However, ictal SPECT provides additional relevant data to localize the EZ in children with FCD [70]. Moreover, it has a predictive value for favorable surgical outcomes when the zone of ictal SPECT hyperperfusion is

completely resected [69,71].

Surgical Outcome

Epilepsy surgery is a safe and effective treatment option in children with drug-resistant epilepsy. The surgical approach depends on the extent of the dysplastic cortex based on the preoperative evaluation. Focal or lobar resection is the most common neurosurgery performed in FCD [17]. Corpus callosotomy, hemispherectomy, and vagus nerve stimulation can be considered as palliative surgery, depending on the patient evaluation.

The overall seizure-free outcome after surgery ranges from 50% to 75% at 2 years after surgery (Table 2) [72-74]. Patients with FCD type IIb have better surgical outcomes than those with mild pathology subtypes [33,45,75]. In a pediatric surgical series by Krsek et al. [20], 75% of FCD type II patients had a favorable outcome, whereas only 21% of FCD type I patients achieved seizure freedom ($P < 0.001$). In a similar series, 88% of FCD type IIb patients were seizure-free compared with 21% of FCD type I and 57% of FCD type IIa patients [18]. Most seizure recurrences after epilepsy surgery occur during the first 2 postoperative years [18,76,77]. Therefore, postoperative outcomes at 2 years may reflect the long-term seizure outcome. In patients who are seizure-free after surgery, withdrawal of antiepileptic drugs (AEDs) is generally considered. AED withdrawal rates after surgery vary from 14% to 48% depending on parental preferences and physician practices [18,78,79]. TimeToStop trial demonstrated that early AED withdrawal did not affect long-term seizure outcome [80]. The European pediatric epileptologists who participated in the TimeToStop study generally started tapering off AEDs between the median of 3 and 5 months after successful epilepsy surgery, which is earlier than nonparticipants [81].

The surgical outcomes vary depending on the patient's age at surgery, pathological substrate, the extent of the lesion, and type of surgery. Studies have reported several prognostic factors associated with favorable surgical outcome in FCD patients (Table 2) [15,18,45,73,82-84]. In a meta-analysis of FCD surgical series, focal seizures, temporal location, detection of MRI lesion, severe type of histopathology, and complete resection were found to be significant prognostic factors [85]. The most important predictor for seizure freedom is complete resection of the EZ [18,45,74,77,83,86,87]. Complete resection of the visible lesion or the EZ was associated with a higher rate of seizure freedom (odds ratio, 3.91; 95% confidence interval, 3.03 to 5.32) [85]. The success of epilepsy surgery depends on the accurate localization and complete resection of the EZ. However, the EZ may not co-localize with the pathology or may be larger than the dysplastic lesion [88]. This issue makes

Table 2. Population characteristics and outcomes of epilepsy surgery for focal cortical dysplasia

Study	No. of patients	Mean age at surgery (yr)	Pathology	MRI-defined lesion (%)	Follow-up duration after surgery (mean)	% with Engel I outcome	Predictors of favorable outcome
Kloss et al. (2002) [72]	68 (P)	5.9	FCD I and II; tumors and dual pathology were excluded.	95	2 yr or more	50	Complete resection
Cossu et al. (2008) [83]	113 (P)	8.8	FCD/mMCD with tumors, other pathologies	96	4.6 yr	68	Unifocal lesion on MRI, older age at seizure, temporal unilobar resection, complete lesionectomy, glial-neuronal tumors
Krsek et al. (2009) [87]	149 (A&P)	NA	FCD/mMCD with hippocampal sclerosis; tumors and other dual pathology were excluded.	66	6.5 yr; 113 with 5-yr, 55 with 10-yr	55 (at 2 yr)	Complete resection
Krsek et al. (2009) [20]	40 (P)	7	FCD I and II; tumors and dual pathology were excluded.	90	4.39 yr (2–6)	35	Complete resection, FCD II
Phi et al. (2010) [82]	41 (P)	9 (1–17)	FCD	54	6.08 yr (2–12.75)	49 (at 1 yr) 44 (at 2 yr)	Visible lesion on MRI, complete resection
Teutonico et al. (2013) [84]	120 (P)	10 (1–15)	FCD/mMCD with tumor and cryptogenic lesion	80	4.75 yr (1–11.83)	77.5	Older age of onset of infantile spasms (> 24 mo), hypomotor seizures, phasic postictal deficit, FCD II
Muhlechner et al. (2014) [74]	60 (P)	8 (0–20)	FCD/mMCD	100	4.4 yr	78 (at 1 yr) 72 (at 4 yr)	Temporal location, hemispherotomies, absence of interictal spikes on postsurgical EEG, complete resection
Fausser et al. (2015) [77]	211 (A&P)	22.6 (1–66)	FCD type I, II, and IIIa	86	4.75 yr (2–12)	65 at 1 yr	Complete resection, younger age at surgery, unilobar localization
Choi et al. (2018) [18]	58 (P)	9.4 (0.4–17.5)	FCD I and II	82.8	5.1 yr (2–12.4)	62 (at 1 yr) 57 (at 2 yr)	Visible lesion on MRI, complete resection

MRI, magnetic resonance imaging; P, pediatrics; FCD, focal cortical dysplasia; mMCD, mild malformations of cortical development; A, adults; NA, not available; EEG, electroencephalography.

complete resection of EZ more complex and requires multimodal integrative presurgical evaluation. Studies have shown that MRI abnormalities suggestive of FCD were associated with a higher rate of seizure freedom as compared with a normal MRI scan [18,73,82,83]. However, even in the absence of MRI lesions, it is worthwhile to consider epilepsy surgery in patients with drug-resistant epilepsy [89].

It is widely accepted that early surgical intervention and cessation of seizure activity are crucial for children with intractable epilepsy [90,91]. However, it is not simple to say “the earlier, the better.” In patients with an unclear extent of EZ, or younger age with high perioperative risk, or low sensitivity of MRI, later resections may offer advantages in terms of precision of surgical-resection planning [92]. Early surgical intervention in drug-resistant epilepsy can support functional plasticity in children. However, a complete and precise resection of EZ is of paramount importance.

Conclusion

FCD is a significant cause of intractable focal epilepsy and leads to epilepsy surgery in childhood. Epilepsy, neurocognitive dysfunction, and behavioral problems can be present in children with FCD. Integrative evaluations, including electrophysiological studies and neuroimaging, would help to localize and delineate the extent of EZ. Epilepsy surgery can be an effective treatment option for children resistant to medication. Complete surgical resection of EZ based on multimodal evaluations would lead to favorable seizure outcome.

Conflicts of interest

No potential conflict of interest relevant to this article was reported.

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Conceptualization: SAC. Data curation: SAC. Visualization: SAC, KJK. Writing-original draft: SAC. Writing-review & editing: KJK.

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