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Clinical Study

Clinical characteristics and post-surgical outcomes of focal cortical dysplasia subtypes

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ABSTRACT

We retrospectively studied 105 patients with a focal cortical dysplasia (FCD) diagnosed on pathological examination, and investigated the long term postoperative seizure outcomes, different clinical characteristics of the three FCD subtypes, particularly type I and II, and surgical outcomes for each group. FCD is a common cause of drug-resistant epilepsy, which is divided into three different subtypes according to its involvement at different stages of brain development. Each of these groups may have different characteristics and may even have different surgical outcomes. After treatment, 55% of patients were completely seizure-free, with two significant predictive variables for poorer outcomes: focal MRI findings and electrode implantation. FCD type I had relatively poor surgical outcomes compared to FCD type II and type IIIa. Compared with FCD type I, type II, particularly IIb, had a higher frequency of seizure attacks, predominantly located in the extratemporal lobes, and was more readily detected and diagnosed via focal lesions on MRI and localized electroencephalogram abnormalities. FCD type II patients seem to show better surgical outcomes than FCD type I, but the difference was not significant. Larger cohort studies are needed for further evaluation of the seizure outcomes of different FCD subtypes.

1. Introduction

Focal cortical dysplasias (FCD) were first described in detail by Taylor et al. in the 1970s [1]. Today, FCD is considered an important cause of drug-resistant epilepsy in children and adults, occurring in approximately 30–40% of children with epilepsy, with a higher prevalence in boys than girls, and 20% of adults with epilepsy [2,3].

There are several different classifications of FCD. Among them, in 2004 Palmini et al. [4] divided FCD into type I (Ia and Ib) and type II (IIa and IIb), a classification which was widely adopted. In 2011, the International League Against Epilepsy revised the FCD classifications [5]. In addition to slight changes in the definition of FCD type I subtypes, FCD type III was established. This subtype is a special FCD subtype that includes type IIIa (FCD type I with hippocampal sclerosis), type IIIb (FCD type I with glial or glioneuronal tumor), type IIIc (FCD type I with cerebral vascular malformations) and type IIId (FCD type I with any other lesion acquired during early life, for example, trauma, ischemic injury, encephalitis).

Previous studies have reported that 50–70% of patients with cortical dysplasia are seizure-free after surgery [6–8]. The best predictor of a postoperative seizure-free status is whether the entire lesion was removed [9]. However, data on the long term postoperative seizure outcomes in patients with FCD are lacking.

We retrospectively studied 105 patients with a postoperative pathological diagnosis of FCD at our center. These patients were all operated on by one experienced neurosurgeon (L.C.) and followed for at least 24 months. The goal of our study was to investigate the long term seizure outcomes for FCD patients who were evaluated and operated upon with modern techniques. We also aimed to analyze the predictive factors for postoperative seizure-free status in our cohort. Finally, we analyzed the different clinical characteristics and seizure outcomes of FCD type I and II.

2. Methods

2.1. Patients

From May 2007 to May 2012, there were 146 patients with proven FCD who were operated on by Lixin Cai. First, we excluded 19 patients with a diagnosis of FCD IIIb, IIIc and IIId, as the underlying lesions (tumor, cerebral vascular malformation *et cetera*) may have the main epileptogenic role rather than the FCD. Second, 22 patients were excluded because of incomplete follow-up data. Further patients were excluded due to the following reasons:

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15 were lost to follow-up, one had a stereotactic ablation, three had corpus callosotomy, and three underwent epilepsy surgeries before the evaluation at our center. Finally, 105 patients were included in the analyses.

2.2. Presurgical evaluation and resective surgery

Every patient underwent an individualized presurgical evaluation including history, assessment of semiology, 1.5 T or 3.0 T MRI and video electroencephalography (EEG), which captured at least three spontaneous seizure attacks. Visual and neuropsychological examinations were conducted if necessary. An invasive intracranial electrode or stereotactic deep electrode (hippocampus) implantation was performed if there were inconsistent findings or the epileptogenic zone was closely related to the eloquent cortex. These procedures were accompanied by electrical cortical stimulation (ECS) after the first surgery, if necessary. Microsurgical resections were conducted with the aim of removing the epileptogenic zone (EZ). For patients with the EZ located in the temporal lobe, we performed a standard anterior temporal lobectomy with an amygdalohippocampectomy to enhance the probability of good seizure outcome. For EZ that were not in the temporal lobe, the patients underwent a lesionectomy based on the results of their presurgical evaluation.

2.3. Pathological diagnoses

A histologic diagnosis was obtained by processing the surgical specimens, as previously described [10]. Solitary FCD type I or type II were chosen, according to the pathological reports, and hippocampal sclerosis-related FCD type I was defined as FCD type IIIa. We did not subdivide FCD type I into further subtypes because of the changes in the diagnostic criteria in 2011.

2.4. Seizure outcome evaluation and variables

A follow-up was conducted each postoperative year by questionnaire, telephone interview and outpatient consultation. We evaluated the seizure outcomes with dichotomous variables, seizure-free or not seizure-free (including auras). The predictive variables included age at surgery, age at seizure onset, seizure duration, seizure frequency, MRI findings, electrode implantation, side and site of resection (temporal or extratemporal), possible epilepsy-related events and pathological subtypes. The seizure frequency was characterized as daily ($\geqslant$30 times per month), weekly (5–30 times per month) and monthly (1–4 seizures per month). MRI findings were focal or non-focal (multifocal, hemispheric or negative). The following possible epilepsy-related events were also categorized: negative; febrile convulsion, history of meningitis or encephalitis; abnormal delivery history, premature labor or difficult labor, *post partum* apnea or cyanosis; history of head trauma, intracranial hemorrhage or prior brain surgery. Each patient (or parents) gave informed consent for participation in the study and the use of data for scientific purposes.

2.5. Statistical analyses

For the univariate analysis, standard forward stepwise Kaplan–Meier analysis was performed for each categorical variable. We then included independent variables with $p \leqslant 0.1$ in a Cox multivariate regression analysis. For the comparison of FCD type I and II, the Kruskal–Wallis rank sum test and chi-squared analysis were used to analyze numerical variables and categorical variables separately. p values <0.05 were regarded as statistically significant. The data storage and statistical analyses were performed with SPSS software (version 17.0; IBM Corporation, Armonk, NY, USA). The results are presented as the mean ± standard deviation, and range in parentheses.

3. Results

3.1. General characteristics and long term postoperative seizure outcomes

Of the 105 patients, 56 (53%) were male, age at surgery was 23.2 ± 11.3 years (range: 3.0–52.0), age at seizure onset was 10.4 ± 7.9 years (range: 0.5–37.0), and seizure duration was 12.9 ± 8.3 years (range: 1–40). The follow-up period was 52.9 ± 18.0 months (range: 24–90 months). The longitudinal proportions of complete seizure freedom for the overall cohort and different FCD subtypes are shown in Table 1. In the entire postoperative period, 58 (55.2%) patients were seizure-free, and two had only intermittent aura attacks after surgery. Figure 1 shows the Kaplan–Meier curve for the seizure-free patients. For patients who were not seizure-free, 41 (87.2%) had their first postoperative seizure within 6 months, and 95.7% had a seizure within 2 years. Two patients had their first seizure after 36 months, one at 36 and one at 46 months. Both of these patients had tapering or discontinuation of their antiepileptic drugs (AED), and both became seizure-free after resuming their medication. A total of 35 (33.3%) patients completely discontinued their AED and sustained stable seizure control postoperatively.

3.2. Predictive variables for postoperative seizure-freedom

After the Cox multivariable regression analysis, both focal findings on MRI and the absence of electrode implantation increased the likelihood that patients would be seizure-free after surgery.

Table 1
Postoperative seizure-free outcomes for the FCD subtypes

	Postoperative years			
n/N (%)	1	2	4	6
Overall	64/105 (61)	59/105 (56)	30/58 (51)	19/39 (49)
FCD type I	21/47 (45)	20/47 (43)	12/26 (46)	9/19 (47)
FCD type II	18/24 (75)	16/24 (67)	6/11 (55)	3/7 (43)
FCD type IIIa	25/34 (74)	23/34 (68)	12/21 (57)	7/13 (54)

FCD = focal cortical dysplasia.

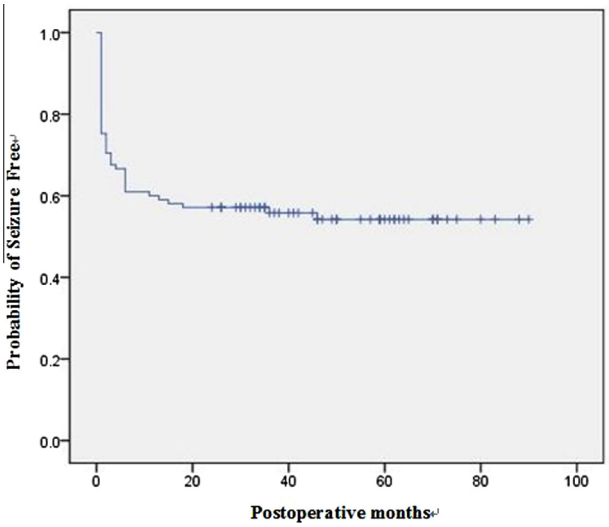

Fig. 1. Kaplan–Meier curve of postoperative seizure outcomes.