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Timing and type of hemispherectomy for Rasmussen's encephalitis: Analysis of 45 patients

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ABSTRACT

Objective: To describe the surgery outcomes of RE patients in one centerto identify the indication for surgical treatment that results in the most favorable outcome.
Method: Forty-five RE patients from a single center were retrospectively reviewed. Preoperative evaluations included assessments of clinical manifestations, cognitive status, a physical examination, MRI, positron emission tomography (PET), electroencephalography (EEG), and magnetoencephalography (MEG). The surgical outcomes included seizure outcome, neurological function, EEG, a cognitive evaluation, and antiepileptic drug withdrawal.
Results: A total of 45 children (29 male) with RE were included in this study. The mean follow-up period from the first operation was 31.7months (range 6–96). The patients who underwent anatomical hemispherectomy or hemisphere disconnection had better seizure outcomes without greater perioperative complications compared with the patients who underwent functional hemispherectomy. Reoperative hemispherectomy was a safe and effective treatment for patients with postoperative epilepsy recurrence. After the last surgery, 34 patients (74.4%) were evaluated as Engel class I. Most of the patients had favorable neurological outcomes. Analysis revealed that the patientswith IQs greater 70 who underwent operations were more likely to suffer from IQ declines but were also more likely to have higher IQs in the future.
Significance: Compared with functional hemispherectomy and hemisphere disconnection, anatomical hemispherectomy elicited better seizure outcomes with an acceptable level of complications. Early stage operations might lead to better cognitive status, but they are associated with a high risk of IQ decline.

1. Introduction

Rasmussen's encephalitis (RE) is a rare neurological syndromethat leadsto intractable focal seizure, cognitive deterioration and hemiparesis (Varadkar et al., 2014) and has an incidence of approximately 2 casesper 10 million people aged 18 years and younger per year (Bien et al., 2013). Naturally, occasional seizures are noted in the prodromal stage (Bien et al., 2002a). In the acute stage, patients usually suffer from increasingly frequent focal epilepsy and neurological dysfunction with progressive unilateral hemisphere cortical atrophy. In the residual stage, seizures can be relieved, but cognitive disorder and hemiparesis remain and have severely adverse effects on the patients' daily lives (Oguni et al., 1992).

The pathogenesisof RE remains unclear, but a series of studies have revealed a correlation with T-cell-related autoimmune processes (Bauer et al., 2002; Bien et al., 2002b). The diagnosiscan be challenging, particularly for early stage patients (Bien et al., 2005; Olson et al., 2013). Focal epilepsy is observed in different diseases, and only approximately half of patients who present with epilepsia partialis continua (EPC) were ultimately proven to have RE (Kravljanac et al., 2013). EEG has value in assisting lateral judgments of RE (Longaretti et al., 2012). Neuroimaging usually reveals progressivehemisphere cortical atrophy with grey or whitematter T2/fluid-attenuated inversion recovery (FLAIR) hyperintense

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signals (Bien et al., 2002a; Pradeep et al., 2014), whereas normal MRI findings can be observed in the early stage (Guan et al., 2014; Varadkar et al., 2014). The typical pathological changes of RE patientsusually consist of reactive astrocytosis, neuronal loss, abundant foci of perivascular mononuclear cells, thickened meninges with lymphocytic infiltration and microglial nodules (Rasmussen et al., 1958; Deb et al., 2005; Varadkar et al., 2014). Pathology features similar to those of focal cortical dysplasia are found in partial RE patients (Wang et al., 2013; O'Rourke et al., 2014).

Conservative treatment, including steroid pulses, immunosuppressive agents, antiviral drugs and plasma exchangehave proven to be effective for partial RE patients in short-term (Bien et al., 2013; Bittner et al., 2013; Takahashi et al., 2013). In most cases, hemispherectomy is eventually performed to control the intractable seizures, which left untreated will inevitably cause hemiparesis, hemianopia and occasionally aphasia (Bien et al., 2013; Takahashi et al., 2013; Hartman and Cross, 2014). However, with the administration of new types of antiepileptic drugs (AEDs) and other medical treatments, the progression of this disease can be substantially inhibited reduced (Bien et al., 2013; Takahashi et al., 2013; Varadkar et al., 2014). As stated by Adam L.etal.,the decision of when to perform hemispherectomy in RE is one of the most difficult decisionsthat patients,families, and physicians will ever have to make (Hartman and Cross, 2014). The present study reports the surgical treatment strategies and outcomes of 45 RE patients from a single center.

2. Patients and methods

2.1. Patients

We retrospectively reviewed the medical records of 45 consecutive patients with biopsy-confirmed RE who underwent surgery at the Beijing Sanbo Brain Hospital, Capital Medical University between October 2004 and October 2015. Approval from the Sanbo Brain Hospital Capital Medical University Internal Review Board was obtained before this retrospectiveanalysis was conducted.

2.2. Preoperative evaluation

2.2.1. Clinical manifestations

All clinical records of the RE patients were reviewed, and the preoperative data including the following variables were extracted: perinatal period events, history of head injury, fever, vaccination, diarrhea within 6 months before seizure onset, age of seizure onset, pattern of epilepsy (focal, general or uncertain), duration from seizure onset to the beginning of the acute stage (defined by seizures more than 10 times/day orEPC), duration from seizure onset to the beginning of noticeable limb weakness, duration from seizure onset to the beginning of cognitive impairment, any other symptoms, and preoperative muscle strength.

2.3. Neuroimaging

All patients underwent MRItwo or more times. Positron emission tomography (PET) and magnetoencephalography (MEG) were recommended for patients with bilateral interictal/ictal discharges before operation or with epilepsy recurrence after hemispherectomy.

2.4. Electrophysiology

Interictal/ictal scalp EEG signals were recorded using a video-EEG monitoring system (Nicolet vEEG; Viasys Healthcare, Madison, WI, USA) with the electrodes placed according to the international 10–20 system for all patients. Slow wave movements andthe sides of the interictal discharges and the ictal origin were recorded.

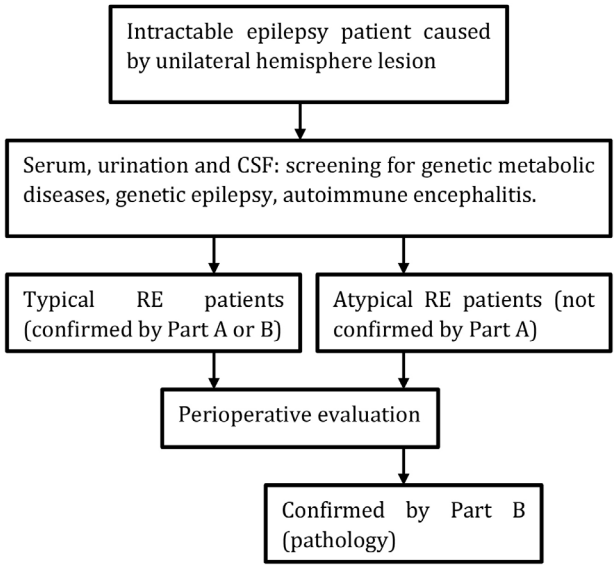

Fig. 1. The algorithm for the diagnosis of RE.

2.5. Neuropsychological testing

Pre- and postoperative neuropsychological tests were conducted for all patients and assessed by a single psychologist. Patients over the age of 14 completed the Wechsler Adult Intelligence Scale (WAIS), 6–13-year-old patients completed the Wechsler Intelligence Scale for children-revised (WISC-R), and 4–6-year-old patients completed the Wechsler Preschool and Primary Scales of Intelligence (WPPSI) test. Children younger than 4 were not administered any preoperative neuropsychological test. The assessments were performed within 1 month prior to surgery, one-half yearafter surgery andannually thereafter.

2.6. Treatment strategy

All of the patients' diagnoses were made at a multidisciplinary epilepsy conference according to Bien's criteria (supplemental data 1). Some patients with atypical RE clinical course was finally diagnosed via the algorithm (Fig. 1). For patients with seizures frequency lower than 10 per day and with comparatively stable neurological statuses, 3–6 months of observation (including several course of pulse therapy by immunoglobulin and steroid) were considered first. Patient with progressive focal seizure and neurological impairment but atypical hemisphere EEG changing or MR changing were candidate for brain biopsy. The surgical methods included: 1) anatomical hemispherectomy (AH), which was define as a removal of all cerebral hemisphere spare the basal ganglia, including frontal, temporal, perianal, occipital and insular lobe, and hippocampus; 2) functional hemispherectomy (FH), which was define as a removal of central area and pre-temporal lobe, and disconnect other white matters from ipsilateral cortex to thalamus, hippocampus, frontal base, and a whole corpus callosotomy; 3) hemisphere disconnection (hemispherotomy), which was defined as a disconnection of all white matter and grey matter communication of ipsilateral hemisphere. FH or hemispherotomy was the first choice for confirmed RE patients. Wada test was administered for teenager or adult patient with left side affected. For teenager or adult patient with dominant hemisphere involved, conservative therapy was firstly considered before disabling EPC was developed.

2.7. Patient follow-up and strategy for recurrence

The patients were asked to return for follow-ups at 3 months, 6 months, 12 months, and annually thereafter. The assessment included seizure outcome (Engel class (Engel et al., 1993), supplemental data 2), a physical examination, 16 h VEEG, MRI, and a psychological examination. Recurrence was defined the continuation or initiation of intractable seizures 3 months after the operation. For these patients, reoperative hemispherectomy was considered and discussed at least once in a management conference with a multidisciplinary epilepsy team. The follow-up standard for reoperative surgery was the same as the standard for the primary hemispherectomy.

2.8. Data analysis

The data analyses were performed using the SPSS computer software package (version 21, IBM Corp., Armonk, NY). Fisher's exact testswere used to compare the categorical variables. For all results, a value of $P < 0.05$ was considered statistically significant.

3. Results

3.1. General characteristics

A total of 45 children (29 males) with RE wereidentified between January 2004 and December 2014 at the Sanbo Brain Hospital Capital Medical University.No significant family histories of febrile seizures or epilepsy were noted. Three patients (6.6%) had histories of head injuries prior to the epilepsy onsets, and 11 patients (24.4%) had histories of infection prior to epilepsy onset. Left side involvement was noted in 22 patients (48.9%), and bilateral involvement was found in one (2.2%) patient.

3.2. Semiology

The mean age at seizure onset of was 5.7 years (range: 1.1–11.3 years). Twenty-eight patients (62.2%) had focal motor seizures at the beginning of the course. At the time of diagnosis, 32 patients (71.1%) had developed EPC, and 12 patients (26.7%) had two or more seizure patterns. Seven patients (15.6%) did not experience focal seizures from the time of seizure onset to the time of the operation. Twenty-four patients (53.3%) had mild to moderate hemiplegia (can walk with help), 10 patients (22.2%) developed moderate to severe hemiplegia (cannot walk), and 11 patients (24.4%) had obvious unilateral clumsy hands or feet without notable changes in muscle strength (can walk without help but change in gate). The mean duration from seizure onset to limb symptom was 6.4 months (from 2 months to 16 months). Obvious preoperative cognitive decline was noted in 33 patients (73.3%), and declines in speaking and understanding functions were noted in 22 patients (48.9%).

3.3. MRI

An average of 2.6 series of MRIs per patient were performed preoperatively. At the time of the operation, unilateral corticalatrophy was noted in 30 patients (a1,a2, Fig. 2). The MRIs of 5 patients revealed bilateral asymmetric hemisphere atrophy (a5, Fig. 2), and 10 patients developed generally symmetric brain volumes (a4, a6, Fig. 2). Abnormal cortical and/or subcortical hyperintense signals compared with the signals of the contralateral hemisphere on T2 and FLAIRimages (a3, a4, Fig. 2) were observed in 39 patients (86.7%).

3.4. PET

Prior to surgery, 15 out the 45 patientsunderwent PET. Among these patients, 4patients (26.7%) presented with central area focal hypermetabolism due to EPC, 2 patients (13.3%) presented with unilateral focal hypometabolism limited to the temporallobe, and 13 patients presented with multifocal (a1, a2, Fig. 3) or diffuse hypometabolism at involved-side (a3, a4, Fig. 3).

3.5. MEG

Nineteen patients with bilateral interictal spikes or without obvious hemispherectomy atrophy underwent preoperative MEG. Unilateral interictal spikes were detected by MEG in 11 patients, and theother 8 patients exhibited bilateral interictal spikes (b1, Fig. 2). Two patients underwent two or more consecutive MEG assessments, and in both patients, we detected obvious increases in the densities and ranges of the unilateral spikes (b2, b3, Fig. 2).

3.6. Surgical treatment

Before the confirmed diagnoses, four patients underwent brain biopsy with or without local resection or lobectomy. One underwent central area multiple subpial transection (MST), and one underwent corpus callosotomy. After diagnosis, 5patients underwent anatomical hemispherectomy, 22 patients underwent functional hemispherectomy, 17 patients underwent disconnective hemispherotomy, and one patient underwent multilobular resection. The mean age atthe time of operation was 8.0 years (range: 3.1–17), and the mean duration from seizure onset to the operation was 24 months (range: 4–120). Reoperative hemispherectomy was performed in 10patients, and the mean duration between the two surgeries was 44.2 months (range: 6–71).

No major intraoperative complications or mortalities were encountered regardless of the type of operation. Postoperative intracranial infection was noted in two patients after FH and one patient after hemispherotomy. Intracranial hemorrhage was noted in one patient after FH. Intracranial drainage was administered. Additional neurological deficits were not observed in these four cases. Postoperative fever was noted in allpatients during the postoperative period and had a mean duration of 18.6 days (range: 7–37). Following anatomical hemispherectomy, five patients exhibited hydrocephalus on MRI as indicated by a midline shift after years withoutnotable clinical signs (b1, b2, Fig. 1). Incomplete disconnection of the frontal base and corpus callosum was observed in 4 patients who patients underwent functional hemispherectomy (c1, c2, Fig. 1).

3.7. Seizure outcome

The mean duration of the follow-up from the diagnosis was 31.7 months (range: 6–96). Twenty-nine patients (64.4%) became seizure-free after the first hemisphere operation. Ten patients with recurrent epilepsy underwent reoperative hemispherectomy. Five of the 10 patients who underwent reoperative hemispherectomy became seizure-free, and 4 of these patients exhibited 90% reductions. At the last follow-up, according to Engel's criteria, 34 patients (74.4%) were Engel class I, 7 patients (16.7%) were Engel class II, and 4 patients (8.9%) were Engel class III, including one patient who presented with a seizure origin in the contralateral hemisphere after AH and was considered to have bilateral RE (Guan et al., 2011). The analysis revealed thatthe patients who underwent functional hemispherectomy were more likely to suffer from epilepsy recurrence compared with the patients who underwent anatomical hemispherectomy and hemisphere disconnection ($p = 0.041$, Table 1). Other factors, such as seizure pattern, EEG pattern, and

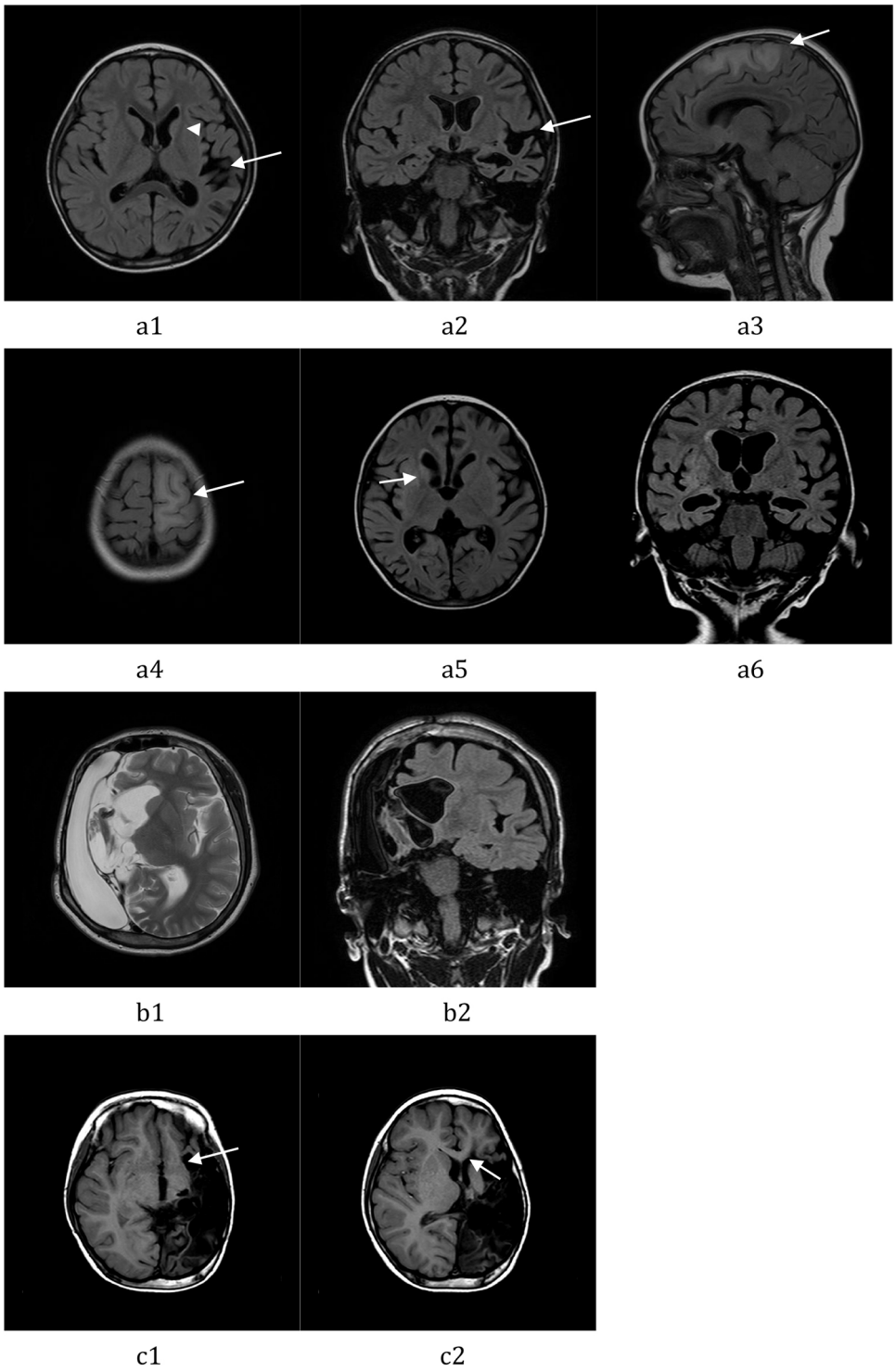

Fig. 2. MRI before and after operation.
Cortical atrophy around sylvian fissure and caudate nucleus and mild dilation of left ventricle (a1, a2); Hyper intensity of FLAIR signal at left frontal and perinatal subcortical area (a3, a4); asymmetrical ventricle dilation (a5); symmetrical hemisphere atrophy (a6); three years after anatomical hemispherectomy, severe midline shift and brain stem shift (b1, b2); six years after primary hemispherectomy, incomplete disconnection at frontal base (c1), corpus callosum (c2).

the timing of the operation, were not statistically related to seizure outcome (Table 2).

3.8. Functional outcomes

After the surgical treatments, the majority of cases exhibited increased hemiparesis and impairment of fine finger movements. Two patients who were initially unable towalk independently were able to walk without assistance after surgery and rehabilitation. The hemiparesis remained stable in 3 patients after surgery. Seventeen patients experienced mild declines in muscle strength, and 25 patients experienced moderate to severe declines. The analysis revealed that patients with moderate to severe weakness (average muscle strength less than 4) exhibited less muscle strength

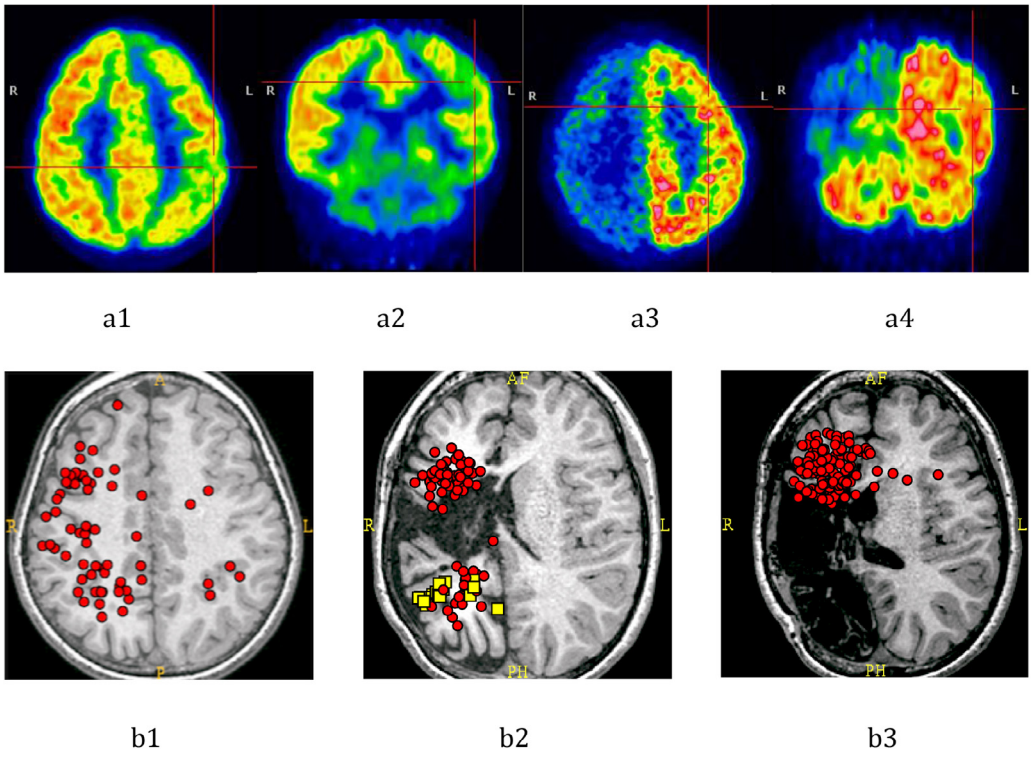

Fig. 3. PET and MEG finding of RE patients.
Multifocal hypometabolism at left frontal and parietal lobe (a1, a2); severe diffuse hemisphere hypometabolism (a3-a4); diffuse interictle spikes were recorded before operation mostly located at frontal, parietal, and occipital lobe mainly at right hemisphere (red spots on b1); more interictle spikes were found mainly at right frontal and parietal lobe 11 months after primary hemispherotomy (red spots on b2); the regions responsible for left upper limb movement were found mainly at right parietal lobe (yellow spots on b2), which was likely to be related to a incomplete disconnection of white matter of left central thalamic radiations; huge quantities of interictle spikes (red spots) were located at right frontal lobe, and active region responsible for left upper limb was not detected 6 months after reoperative hemispherectomy (b3).

Table 1
Baseline comparison of patients underwent different type of hemispherectomy.

	AH (n = 6)	FH (n = 21)	Disc (n = 18)	P value
Gender (male%)	5 (83.3%)	12 (57.1%)	12 (66.7%)	0.503
Age at seizure onset (y)	4.7	5.1	6.4	0.255
First seizure pattern				
Focal seizure	4	11	11	
General seizure	1	6	3	
Other seizure[a]	1	4	4	
Time to limb symptom (m)	5	6.6	7.4	0.532
Side (left%)	4 (66.7%)	7 (42.8%)	11 (61%)	0.183
Hemiplegia				
Clumsy limbs	2	6	3	
Mild to moderate	3	11	10	
Severe	1	4	5	
Age at surgery (y)	5.9	7.2	8.9	0.130
Seizure outcome (Engel I%)	6 (100%)	10 (42.9%)	13 (72.2%)	0.041

Table 2
Factors related to seizure outcome.

	Total	Seizure-free (n, %)	P value
Semiology			0.209
Focal epilepsy only	28	20 (71.4%)	
Additional epilepsy pattern	17	9 (52.9)	
Interictal EEG			0.271
Ipsilateral discharge	30	21 (70.0%)	
Bilateral discharge	15	8 (53.3%)	
Ictal EEG			0.130
Ipsilateral origin	34	24 (70.6)	
Bilateral origin	11	5 (45.6)	
Hemisphere atrophy			0.826
Moderate to severe	30	19 (63.3%)	
Mild or no atrophy	15	10 (66.7)	
Duration from seizure onset to operation			0.944
Less than 18 months	20	13 (65.0%)	
More than 18 months	25	16 (64.0%)	

decline after hemispherectomy compared with the patients with mild paralysis before surgery (p = 0.017). Neither the degree of hemispheric atrophynor the timing of the operation was statistically related to muscle strength decline. At the last follow-up, all of the patients were able to walk independently. Complete aphasia was not observed in this series. Obvious postoperative declines in language function were noted in 15 of the 23 patients who underwent left hemispherectomy. After six months, all 15 of these patients were able to understand language and express themselves correctly, but they wereslow to speak and react. Obvious improvementsin languagefunction were noted in 4children at follow-up.

In this series, preoperative intellectual assessmentswere conducted in 30 patients, and 25 of these patients underwent postoperative intellectual assessments (5 childrenwho underwent surgery declined to participate in the postoperative neuropsychological test). In these 25 patients, the mean IQ prior to surgery was 72.7, and the mean IQ after surgery was71.0 at the postoperative assessment. At the last follow up, the IQs of 14 patients had declined, andthe IQs of 6 patientshad increased. It seems that the patientswith IQs less than 70were more likely to exhibit improvements in IQ. There were no obvious correlationsof postoperative IQ with EEG pattern, the degree of hemisphere atrophy, or the timing ofthe operation (Table 3).

Table 3
Correlations between IQ and preoperative clinical features.

	Total	Stable or better[a] (n, %)	P value	Favorable[b] (n, %)	P value
Interictal EEG			1.000		0.691
Ipsilateral discharge	10	5 (50.0%)		3 (30.0%)	
Bilateral discharge	15	7 (46.7%)		6 (40.0%)	
Hemispheric atrophy			1.000		1.000
Moderate to severe	18	9 (50%)		7 (38.9%)	
Mild or no atrophy	7	3 (429%)		2 (28.6%)	
Duration from seizure onset to operation			0.429		0.401
Less than 12 months	9	3 (33.3%)		2 (22.2)	
More than 12 months	16	9 (56.3%)		7 (43.8%)	
Preoperative IQ			0.004		0.401
More than 70	16	4 (25%)		7 (43.8%)	
Less than 70	9	8 (88.9%)		2 (22.2%)	

[a] Stable or better: The IQ after the hemispheric operation was equal to or greater than that before the operation.
[b] Favorable: The IQ after the hemispheric operation was equal to or greater than 80.

3.9. Changes in AED treatment

At the last follow-up, an average of 1.4 types of AEDs were being administered. Successful AEDs withdrawal was achieved in only 2 patients after an average of 61 months after surgery, and these patients were completely seizure-free over the 2 years after AED withdrawal. Failed AEDs withdraw attempts were reported in 6 patients, and they continued to take AEDs after experiencing seizure recurrence.

4. Discussion

Due to the rarity and variation in the clinical manifestation of RE, clinicians have little experience in the diagnosis and treatment of this catastrophicepilepsy syndrome. Antiepileptic drugs, immunoglobulins and high doses of steroids, and immune modulators, such as tacrolimus, have been proved to have little effect in terms of the control of seizuresand the slowing of the progression of RE (Varadkar et al., 2014). Because inflammation usually involves one hemisphere, focal excision, multiple subpial transection and callosotomy are unsatisfactory in most cases (Rasmussen, 1978; Piatt et al., 1988). Hemispherectomy remains the most effective treatment to control the seizures of RE patients. However, with the clinical application of multiple non-invasive treatments (Bien et al., 2013; Takahashi et al., 2013), the timing and necessity of this operation should be considered again.

In our series, the rate of left-brain involvement was 48.9%, and bilateral involvement was observed in only one patient. Fourteen patients (31.1%) had preceding eventsprior to seizure onset. The mean age at seizure onset was 5.7 years. The majority of the patients had frequent focal epilepsy, and more than half of the patients developed EPC before surgery. These findings were generally similar to the natural history described by Bien et al. (2002a).

The type of hemishperectomy was based on the consideration of safety and surgeon's technique preference. The more dilation of lateral ventricle of a patient, the less brain tissue removal was needed. In analysis, anatomical hemispherectomy and hemisphere disconnection elicited better seizure outcomes than did functional hemispherectomy (Table 1), besides, there were fewer perioperative complications in the anatomical hemispherectomy and hemispherotomy group (one intracranial infection) than in the functional hemispherectomy group (two intracranial infections and an intracranial hemorrhage). For the patients with seizure recurrence, MEG was recommended to locate the interictal discharges and to determine whether a stimulated zone was present in the affected hemisphere due to body movement. For the patients with ipsilateral EEG ictal origins and MEG interictal discharges, reoperative hemispherectomy was considered. Because the anatomy becomesless clear after primary hemispherectomy, neuronavigation is highly recommended.

In RE patients, the seizure freedomrates are between 62.5 and 90% (Varadkar et al., 2014). Hemisphere disconnection reduces the numbers of early and delayedsurgical complications and result in seizure outcomesthat are similar to those of anatomical hemispherectomy (Griessenauer et al., 2015). However, as demonstrated in the present study, anatomical hemispherectomy elicited better seizure outcomes without increasing the perioperative risk. This finding may be related to the surgical procedures and the mechanism of RE. We noticed that the recurrence cases who underwent functional hemispherectomy were generally operated on 3–4 years earlier than the seizure cases. This difference may indicate that functional hemispherectomy and hemisphere disconnection have learning curves. In contrast, because one patient in this study underwent selective resection after electrode placement and exhibited a 50% remission of epilepsy after the operation, we still have little knowledge about whether chronic inflammation and epileptogenic zones remain multifocal in the cortical hemisphere or affect the contralateral hemisphere. RE is known to likely result from an autoimmune process mediated by both cellular and humoral immunities. The remaining affected brain tissues have no neurological function and merely provide mechanical support, but we still know little about whether these tissues can directly or indirectly generate autoantibodies that attack the contralateral cortical hemisphere. More information about the long-term seizure and cognitive outcomes of each type of surgery would be of great value for answering this question. Until a deeper understanding the mechanism of RE is achieved, we cannot completely localize the exact affected cerebral area in RE patients.

The timing of the hemispheric operation is a quite challenging issue for epilepsy specialistsand the families of RE patients. In most cases, surgery is ultimately utilized to control focal seizures and achieve an improved cognitive status. However, because the natural course of this condition varies widely across patients (Bien et al., 2002a), we still lack practical tools for prognoses regarding cognitive decline and seizure outcomes. In the present study, we found that the patients with IQs lower than 70 were likely to exhibit increases after surgery; however, only 22.2% of the patients achieved IQs higher than 80 in this group after surgery. In contrast, although the patients with higher IQs (>70) were more likely to exhibit declines, 43.8% of the patients in this group had IQs greater than 80 in the follow-up. Although this pattern did not

reach statistical significance, these resultsindicate an earlier surgical intervention may lead to better cognitive status in RE patients but may also be more likely to lead to an IQ decline.

Bilateral involvement of the brain is a controversial issue. Because we are not aware of the exact etiology of chronic inflammation or the mechanism of epilepsy, we can hardly define bilateral RE. In this study, bilateral interictal discharges were recorded in 15(33.3%) patients, and 6 (13.3%) patients had bilateral ictal origins. However, after hemispherectomy, most of these patients become seizure-free or experienced seizure reduction greater than 90%. However, one of these patients developed a different seizure pattern, and an EEG revealed a contralateral ictal origin after the operation. We suppose that this patient had bilateral epileptogenic zones; however, we were not aware of the pathological shift to the contralateral cortex. Because RE is a rare cause of intractable epilepsy, it is possible that this patient's epilepsy was due to a different cause. Fortunately, only approximately 1–2% of RE patients are ultimately proven to have bilateral epileptogenic origins (Tobias et al., 2003; Guan et al., 2011; Frigeri et al., 2013; Peariso et al., 2013). The treatment for patients with the so-called bilateral RE is much more challenging. Although in the case of our patient, hemispherectomy reduced the original frequency of seizures by approximately half, the change in cognitive function was unclear. A long-term follow-up and, if possible, an autopsy would be of great value torevealing the essence of bilateral RE.

In conclusion, compared with functional hemispherectomy and hemisphere disconnection, it seemed that anatomical hemispherectomy elicited better seizure outcomes with acceptable complications. Early-stage operations might lead to better cognitive status, but the risk of IQ decline is high.

Conflict of interest

All authors report no conflict of interest.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.eplepsyres.2017.03.003.

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