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Parasagittal hemispherotomy in hemispheric polymicrogyria with electrical status epilepticus during slow sleep: Indications, results and follow-up

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ABSTRACT

Purpose: Polymicrogyria (PMG), although the most common brain malformation, represents a low percentage among patients operated on for epilepsy. In cases of hemispheric PMG, electrical status epilepticus during slow sleep (ESESS) may occur leading to an aggravation of the neurological condition and a risk of drug resistance. In such cases, surgical treatment can be offered.

Methods: From a population of 230 children who underwent hemispherotomy for epilepsy, we retrospectively reviewed the patients with unilateral PMG and drug-resistant ESESS focusing on clinical charts, electrophysiological data and post-surgical outcome.

Results: Eighteen patients were operated on at a mean age of 7.2 years. The average age was 2 years at seizure onset and 4.4 years at diagnosis of ESESS. All the patients preoperatively had some degree of developmental delay associated with a hemiparesis. During ESESS all of them evidenced a cognitive decline and eight experienced a worsening of the hemiparesis; ESESS was resistant to at least three antiepileptic drugs.

The outcome of epilepsy, with a mean follow-up of 12.8 years showed that ESESS disappeared in all patients while 16 of 18 became seizure-free. An improvement of behavior and cognitive condition was observed in all.

Conclusion: Hemispherotomy can be helpful in patients with drug-resistant ESESS and hemispheric PMG while keeping in mind that more often an accurate medical treatment can be sufficient. The main benefit of surgery is to definitively stop the seizures and to withdraw the medical treatment while keeping in mind the risk of motor aggravation.

1. Introduction

Polymicrogyria is one of the most frequently occurring brain malformation and is characterized by an excessive number of small gyri associated with lamination abnormalities (either a four layer lamination or a dyslamination). PMG is a heterogeneous malformation with variable localizations within the brain. An overview of all the topographic types of PMG shows that unilateral hemispheric PMGs are rare (2/328) [1].

PMG is presumed to result from two different disorders: either genetic pathologies including several gene abnormalities or prenatal insults such as CMV foetopathy and antenatal ischemia [1,2].

The pathogenesis of PMG is attributed to an intrauterine event (brain hypoperfusion) associated with a cortical laminar necrosis predominating in layer 5 occurring between the 13th and 24th weeks of gestation.

Regarding clinical presentation and sex ratio all the series report a male predominance. Variable neurological deficits can occur in PMG patients depending on the anatomical location of the malformation. A mental deficit is present in about 70% of the patients [3,4], and epilepsy occurs in 80%–90% of the patients. In extended PMG, an electrical status epilepticus during slow sleep (ESESS) can occur during childhood complicating pre-existing focal epilepsy [5,6].

The epileptic seizures associated with ESESS are atypical absences (atonic and myoclonic). Interictal EEGs show focal and generalized abnormalities during wakefulness, and during slow sleep there are continuous spikes and waves [7,8].

In cases of drug-resistant epilepsies associated with PMG, surgical treatment can be offered to the patients. Some series report surgical options in select patients, mostly focal resections [8] and a few hemispherotomies [3,4,9–11].

Our personal series of 18 consecutive patients who underwent a hemispherotomy for drug-resistant epilepsy and ESESS due to hemispheric PMG focuses on patient selection criteria and postoperative

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results pertaining to epilepsy and cognition.

2. Patients and methods

From our database, we retrospectively reviewed all of the patients with hemispheric PMG who underwent a parasagittal hemispherotomy (PSH) in our institution between 2000 and 2017. Over the same period, a total number of 230 patients underwent a PSH for drug-resistant epilepsy of various etiologies.

All patients were referred by several neuropediatric departments in France and abroad but evaluated in a single center (Rothschild Foundation) and operated on by three senior neurosurgeons (OD GD SFS) using the PSH surgical technique [12].

A comprehensive medical history of epilepsy and family background was obtained for each patient. They had pre- and post-clinical examinations done by a pediatric neurologist: a neuropsychological evaluation was performed pre- and post-operatively using various developmental scale tests according to the patient's age (Brunet Lezine, Vineland, WPPSI III, NEPSY, PEP, K-ABC).

Every patient underwent a presurgical prolonged scalp video-EEG (at least 24 h) with scalp electrodes set using 10/20 montage. In our team, recorded seizures are usually a requirement for surgery to be offered. However, this was not the case in five patients operated on at the beginning of the 2000s, either because they came from abroad or because of their behavioral disturbances. More recent patients all had recorded seizures. The previous EEGs were all carefully reviewed as well.

PMG was diagnosed with MRI (T1, T2, FLAIR- weighted sequences in three planes without contrast), and only patients with isolated PMG were selected. PMG cases associated with the following malformations - hemimegalencephaly/dysplasias, Sturge Weber syndrome, and ischemic disorders with porencephaly cysts - were excluded as well as cases of bilateral and lobar PMG.

The decision to operate was made by a multidisciplinary team.

The outcome of the epileptic seizures was assessed using Engel's classification [13]. All of the patients received outpatient follow-up in our institution three months after surgery including routine EEGs and MRIs, followed by yearly visits to our outpatient clinic.

3. Results

3.1. Presurgical clinical data (Tables 1–3)

Between 2000 and 2017, eighteen consecutive patients with isolated hemispheric PMG (six females and twelve males) underwent a PSH. The mean age at surgery was 7.2 years (4.9–11.1). In the same period, eight patients with hemispheric PMG were denied surgery for the following reasons: the absence of ESESS or well-controlled ESESS with antiepileptic drugs in patients who had minimal or no cognitive regression and who were subsequently at risk for post-operative deterioration. Other reasons were infrequent focal seizures or a mild motor deficit with the preservation of hand use.

Regarding anamnesis, three patients had a prenatal risk factor of ischemia: a twin pregnancy with early death of the twin, maternal peritonitis, and an intrauterine growth retardation of unknown origin. For the others, there was no anamnesis or family history of brain malformation and/or epilepsy, and pregnancy and delivery were uneventful.

All of the patients had drug-resistant epilepsy with a first-time seizure occurring at a mean age of 2 years (0.1–4.2). The first seizure consisted of focal motor in seven patients, generalized in another seven, and atypical absences in four. In five of them, the first seizure was a complex febrile seizure (focal or generalized). All eighteen patients presented an ESESS encephalopathy that occurred at a mean age of 4.4 years (2–7.6). The average length of time between the first seizure and ESESS was 2.2 years. ESESS encephalopathy was associated with atypical absences in all patients. The other seizures presented by the patients were: focal motor, seizures with sudden fall, and generalized seizures. Seizure frequency was daily in fourteen patients (6 with more than 100 per day) and monthly in the other four. The mean duration between the ESESS and PSH was 3.1 years, and the mean duration between the first seizure and PSH was 5.2 years.

Neurological exams displayed a congenital hemiparesis or hemiplegia in all of the patients. Only five patients were able to grip with the palm. Every patient but one was able to walk unassisted with a limp. At the time of ESESS or during frequent motor seizures, eight patients presented with an increased motor deficit and two were in a wheelchair mainly because of repeated seizures creating a high risk of falling.

During ESESS, 14 patients presented with a cognitive regression associated with behavioral issues such as hyperactivity and attention deficit disorder.

On the basis of the international classification of diseases for intellectual disabilities (ICD 10), neuropsychological tests showed a severe mental deficit (defined as IQ < 35) in five patients, a moderate mental delay (defined as IQ between 35–55) in twelve, and borderline intellectual functioning (IQ between 70 and 84) in one.

3.2. Electrophysiology (Table 4)

Interictal EEGs recorded normal bilateral background activity in four patients and slow background activity in the others that was unilateral in six, bilateral in three, and bilateral but asymmetrical in five. Nine patients presented with diffuse spikes during wakefulness. All of the patients had focal or hemispherical spikes homolateral to the malformation during wakefulness (Fig. 1) with a contralateral spreading in five. All patients presented with continuous spikes and waves during sleep (Fig. 2), the epileptiform discharges being bilateral and symmetrical. Among the thirteen patients with recorded seizures, the scalp video-EEG recorded atypical absences with hypotonic falls (eleven) (Fig. 3), motor seizures (two), and epilepsia partialis continua (one). One patient had two types of seizures. In the same thirteen patients, ictal EEGs showed generalized discharges in four, diffuse but asymmetrical in another four, and a focal onset in five. To summarize, differences in physiological activity between both hemispheres were not always present (only half of our patients), and the seizures were not lateralizing better. Only three patients (23%) had clinically lateralizing ictal features whereas nine (69%) had a lateralized ictal discharge. Combining clinical and electrical data, two patients (15%) had no lateralized ictal features at all.

3.3. Images

Fourteen patients had unilateral hemispheric PMG (Fig. 4a and b) and four had unilateral multilobar PMG (Fig. 5) that was located in the right hemisphere in ten patients and in the left in eight. The contralateral hemisphere was normal in all.

3.4. Medical treatment before surgery

Following the onset of the epilepsy, antiepileptic drugs consistent with focal seizures were administered to the patients. After the occurrence and diagnosis of ESESS, all of the patients were prescribed a suitable treatment consisting of the following: ethosuximid, sultiame, steroids, various combinations of benzodiazepines, and a ketogenic diet, but they all presented a drug resistance or intolerance to steroids or had a relapse. At the time of the surgery, all of the patients were taking between two and five different types of AEDs.

3.5. Surgical treatment and follow-up (Tables 1,2)

Surgical treatment consisted of a PSH (left in eight and right in ten) for all of the patients (Fig. 6a and b). One patient (patient 14)

Table 1
Demographic data.

Patient number	Sex	Prenatal anamnesis	Presurgical neurological exam	MRI: PMG extension	Side of PMG	Age at first surgery (years)	Second surgery	Post surgical motor aggravation	Follow up duration (years)	Engel	AEDs
1	F	no	R hemiplegia	hemispheric	L	6.7	no	no	15.5	2	yes
2	M	NA	R hemiplegia	hemispheric	L	7.5	VPS (1 mo post PSH)	no	17.3	1	no
3	M	NA	R hemiparesis	fronto-parieto-temporal	L	7.9	no	yes	15.5	1	no
4	M	no	L hemiplegia, no hand use, wheelchair, behavioral disorder hyperkinesia	hemispheric	R	7.2	no	no	14.2	1	no
5	F	no	R hemiparesis	hemispheric	L	9.1	VPS (6 mo post PSH)	no	14.9	1	no
6	M	NA	R hemiparesis	fronto-temporo-parieto-occipital	L	5.6	no	no	20.6	1	no
7	M	no	R hemiplegia	hemispheric	L	6.9	no	no	16.2	1	no
8	M	no	L hemiparesis	hemispheric	R	11.1	no	yes	14.8	1	no
9	M	Foetal anasarca following peritonitis, prematurity 32 weeks	L hemiparesis, preservation of hand use	centro-parieto-temporo-occipital	R	7.1	no	yes	16.9	1	no
10	M	NA	R hemiparesis, preservation of hand use	hemispheric	L	5.3	no	yes	13.7	1	no
11	M	no	L hemiparesis, preservation of hand use, hyperkinesia	hemispheric	R	7	no	yes	13.4	1	no
	M	Intrauterine growth delay birth weight: 1700 g prematurity 35 weeks	L hemiparesis preservation of hand use, able to make sentences, no behavioral disorder	hemispheric	R	6.7	no	12	13.2	1	no
13	M	no	R hemiplegia (no finger use), R hemianopsia	hemispheric	L	10.5	no	no	12.9	1	no
14	F	no	L hemiplegia, no hand use, walking unassisted	hemispheric	R	5.7	completion of callosotomy (3.5 y post PSH)	no	3.6	2	yes
15	F	no	L hemiplegia loss of walking ability	hemispheric	R	4.9	no	no	12.6	1	no
16	F	twin pregnancy with intrauterine death of the twin; birth weight 2100 g	unable to walk, L hemiparesis with hand use, speaks a few words	hemispheric	R	6.3	no	yes	2.9	1	no
17	F	no	L hemiplegia without hand use, no language	hemispheric	R	9.9	no	no	0.55	1	no
18	M	no	left hemiparesis, poor hand use	hemispheric	R	5.8	no	yes	11.3	1	no

F: female; M: male; L: left; R: right; PMG: polymicrogyria; AEDs: antiepileptic drugs; mo: months; y: years; PSH: parasagittal hemispherotomy; NA: not available; VPS: ventriculo-peritoneal shunt.

Table 2
Seizure description.

Patient number	Age at Sz onset (months)	First seizure type	All types of seizures (age at onset)	Age at ESESS onset (months)	Duration of ESESS before surgery (months)	seizure frequency before hemispherotomy
1	12	complex febrile	R. focal motor, atypical absences	54	38	daily
2	51	GTCS	R focal motor, atonic, atypical absences	70	21	daily
3	28	atonic	Atonic, GTCS, atypical absences	54	40	daily
4	8	GTCS	R > l focal motor, secondary generalized, atypical absences	49	26	daily
5	32	complex febrile	L > R focal motor, atonic seizures, atypical absences	47	62	daily
6	30	R focal motor	R focal motor seizure, atypical absences	56	11	daily
7	20	R focal motor	R focal motor, secondary generalized, atypical absences	49	37	monthly
8	7	complex febrile	GTCS, L focal motor, atypical absences	72	13	monthly
9	24	GTCS	L focal motor, atonic seizures, atypical absences	79	55	daily
10	33	absence	Atonic, focal motor, atypical absences	51	12	daily
11	30	absences with drop attacks	Atypical absences, atonic, GTCS	48	36	monthly
12	16	atypical absences	atypical absences with drop attacks	34	46	daily
13	48	R focal motor	absences and GTCS	72	54	monthly
14	1,5	L focal motor	focal, atypical absences	92	35	daily
15	24	febrile GTCS	atonic, absences	26	32	daily
16	12	complex febrile	myoclonic absences	24	51	daily
17	18	L focal motor	Focal, atypical absences, drop attacks, myoclonic	24	94	daily
18	50	drop attacks	atypical absences	54	15	daily

GTCS : generalized tonic-clonic seizures; L: left; R: right; mo: months; min: minutes; y: years.

Table 3
Neuropsychological data.

Patient number	motor/cognitive regression during ESESS	Age at preoperative test (years)	preoperative neuropsychology	Postoperative neuropsychology	Age at postoperative test (Years)
1	cognitive regression		NA	VIQ: 57 PIQ: 50	17 .5
2	cognitive regression	7.5	VIQ: 42 PIQ: 46 TIQ: 48	VIQ: 48 PIQ: 42 TIQ: 51	11 .5
3	cognitive and motor regression	4.5	VIQ: 50 PIQ: 54 TIQ: 53	VCI: 59 PRI: 62	19
4	cognitive regression	7	moderate delay	NA	NA
5	cognitive and motor regression	9	severe mental delay	VIQ: 45 PIQ: 45 TIQ: 46	20
6	cognitive regression	5.5	TIQ: 42; VIQ: 51; PIQ: 41	VIQ: 75 PIQ: 52 TIQ: 58	13 .5
7	cognitive and motor regression	6.8	IQ < 40	VIQ: 45 PIQ: 46	20
8	cognitive and motor regression	11.1	IQ < 40	NA	NA
9	cognitive and motor regression	7	TIQ: 40 VIQ: 45 PIQ: 41	VCI: 79 PRI: 58 WMI: 75	18
10	cognitive and motor regression	1.2	DQ 51	VCI 76 PRI: 50	14
11	NA	7	DQ between 2 and 4 y	VCI: 53 PRI: 45	15
12	cognitive and motor regression	6.7	TIQ: 41 VIQ: 47 PIQ: 43	VCI: 45 PRI: 56	15
13	NA	9.6	TIQ: 40 VIQ: 46 PIQ: 46	VIQ: 46 PIQ: 53 TIQ: 47	12 .5
14	no	4	Estimated : 2 y	VCI: 44 PRI: 45	7
15	cognitive and motor regression	4.5	TIQ: 73 PIQ: 64 VIQ: 89	VIQ: 99 VIQ: 90 TIQ: 94	7
16	loss of walking ability	6.3	QIV: 44 QIP: 45	DQ between 3 and 4 .5 y	8
17	NA	9.8	DQ : 1 y	NA	NA
18	stagnation	5.6	DQ: 24 - 30 mo	VIQ: 45 PIQ: 50 TIQ: 40	11

Y: years; mo: months; DQ: developmental quotient; TIQ: total intellectual quotient; VIQ: verbal intellectual quotient; PIQ: performance intellectual quotient; NA: Not available; VCI: verbal comprehension index; PRI: perceptual reasoning index; WMI: working memory index;

underwent a second surgery for completion of an incomplete callosotomy and persistence of the seizures. Two patients (patients 2 and 5) needed a definitive shunt due to hydrocephalus and subdural hygroma respectively. Histological results were consistent with polymicrogyria in all of the cases.

The mean duration of time between surgery and the last follow-up was 12.8 years (range 0.5–20.6 years). All of the patients regained their ability to walk within three months postoperatively. Eight patients who

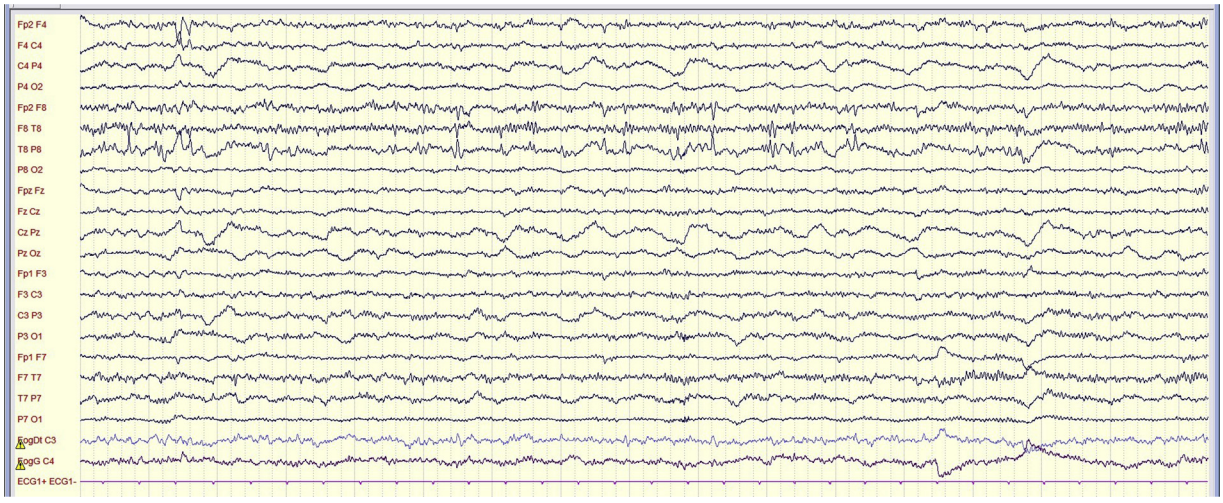

Fig. 1. Wakefulness. Right temporal and frontal asynchronous spikes and waves (longitudinal montage).

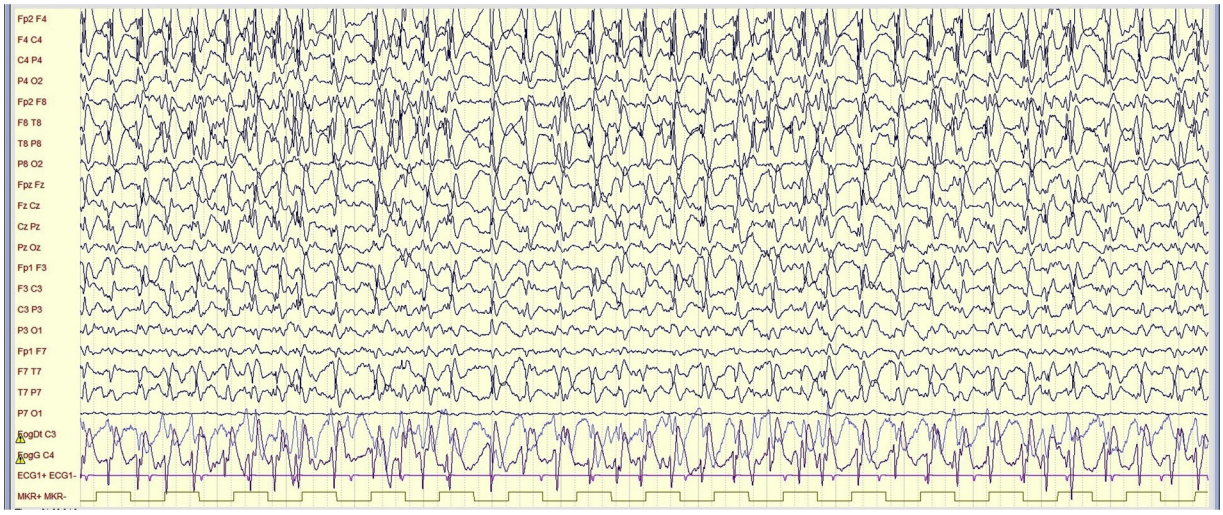

Fig. 2. Sleep: Continuous spikes and waves with a maximum over the right frontal region. Lack of any physiological activity (longitudinal montage).

had an incomplete motor deficit presented with a permanent aggravation of or the loss of hand and finger use. All patients presented with an anticipated hemianopia.

Regarding epilepsy outcome and according to Engel's classification, sixteen of the eighteen patients are currently seizure-free (Engel 1A) and fifteen are drug-free. Two patients (patiens 1 and 14) have shown significant improvement of their epilepsy and are classified as Engel 2.

Cognitive outcome data are available for 16 patients (Table 3) the patient with borderline IQ regained a normal IQ two years following surgery and has not been heard from since; three patients currently have heterogeneous results and are classified as having borderline and mild deficits; ten patients have a moderate deficit and one presents with a severe intellectual deficit. Altogether, ten patients presented an improvement in neuropsychological testing of at least 10 points. The other patients remained stable. There were no cases of cognitive degradation or acquired language deficits after surgery.

Post-surgical EEGs confirmed the disappearance of ESESS in all patients (even in those who are not Engel 1) allowing a clear asymmetry to be observed. The pathological hemisphere showed a lack of background activity and multifocal spikes and waves (Fig. 7). On the normal hemisphere, physiological activities were present. Some spikes and waves coming from the disconnected hemisphere were visible, mostly in the frontal and occipital electrodes. During sleep, one third of the patients still had continuous spikes and waves (Fig. 8) on the pathological hemisphere whereas two thirds had multifocal spikes which were not permanent.

4. Discussion

Our report focuses on a single center experience of a group of 18 patients with hemispheric or unilateral multilobar PMG who underwent a PSH to treat drug-resistant epilepsy. This is, to date, the largest series of hemispheric surgeries for PMG patients published in English medical literature. We have shown that 88% of the patients became seizure-free following surgery, and 83% were able to discontinue antiepileptic drug treatment. Cognitive improvement was observed in 66% of the patients. Post-operative morbidity was low and included two patients who needed a ventriculo-peritoneal shunt for hydrocephalus. Nevertheless, eight patients experienced a worsening of hemiparesis, and all of them presented a hemianopia. None of the patients presented a cognitive

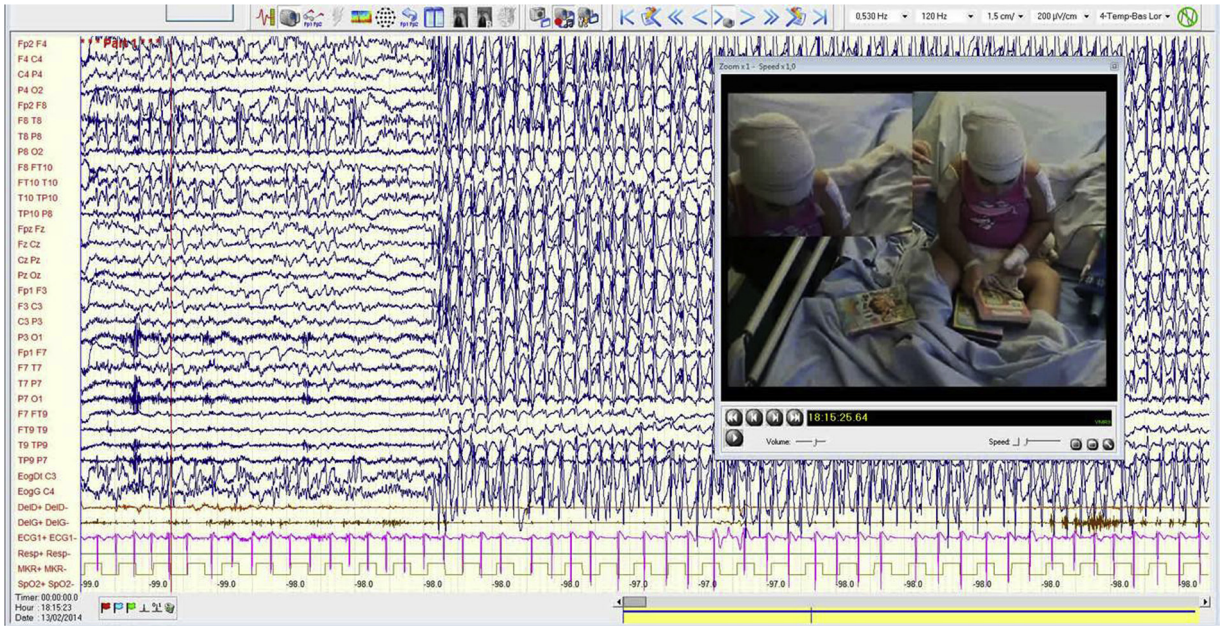

Fig. 3. Atypical absence with fall (longitudinal montage).

Table 4
Neurophysiological data.

Patient number	Age presurgical EEG (years)	Awake EEG: background activity	Awake EEG: Diffuse SW burst	Awake EEG: focal spikes	Sleep EEG continuous bilateral SW activity	video-EEG seizures recording	Ictal EEG
1	6.6	slow L > R	no	L C-P,T	yes	Atypical absences 1 / 10minutes	generalized, bilateral SW discharges
2	7.4	slow L > R	no	L C-T-O	yes	Atypical absences (subcontinous). Some of them are followed with clonic movements of the R arm	posterior L SW followed by generalized, bilateral SW discharges
3	7.8	normal on the R	yes	L F-C-T-P	yes	Atypical absences 20 / h	generalized, bilateral SW discharges
4	6.1	normal	no	R C-T-O and bifrontal	yes	clonic right and left limbs and face (subcontinuous)	generalized, bilateral SW discharges
5	8.8	slow L > R	no	L hemisphere	yes	Atypical absences several/h	rhythmic activity L temporal followed by generalized SW discharges
6	5.5	normal	yes	F-P-O-C-T L > R	yes	Atypical absences, 12 in 4 days	generalized, bilateral L > R SW discharges
7	6.1	normal on the R	no	L-C-T-O and bifrontal	yes	0	
8	10.3	slow R > L	no	L F-C > right F	yes	0	
9	6.9	normal on the L	no	R F-T-O	yes	0	
10	5	normal on the R	no	F-T L > R	yes	2 partial motor seizures/24h	generalized, bilateral SW discharges
11	6	slow bilateral (7 Hz)	yes	R F	yes	0	
12	5.7	normal on the L	yes	R hemisphere	yes	atypical absences 1/2h	generalized, bilateral R > l SW discharges
13	10.4	normal	bilat max L F	L F-T	yes	0	
14	5.6	normal on the L	yes	R hemisphere	yes	atypical absences 10 in 48h	generalized, bilateral R > l SW discharges
15	4.1	normal	yes max R	multifocal F-T R with rare LF diffusion	yes	atypical absences 6 in 24h	generalized, bilateral R > l SW discharges
16	5.9	slow bilateral	yes with R maximum	R C-T-P	yes	atypical absences several/h	R temporal SW with generalized diffusion
17	9.6	slow bilateral	yes	R F-C with L diffusion	yes	atypical absences several/h	focal R F spikes (1); usually bifrontal SW with R maximum
18	5.6	7 Hz L, no R	yes	R C-F, and T asynchronous	yes	atypical absences every 5 minutes	R F-T SW followed by generalized, bilateral SW discharges

R: right; L: left: F: frontal; C: central ; T: temporal ; P: parietal ; O: occipital ; S: spikes ; SW: spikes and waves; H: hour.

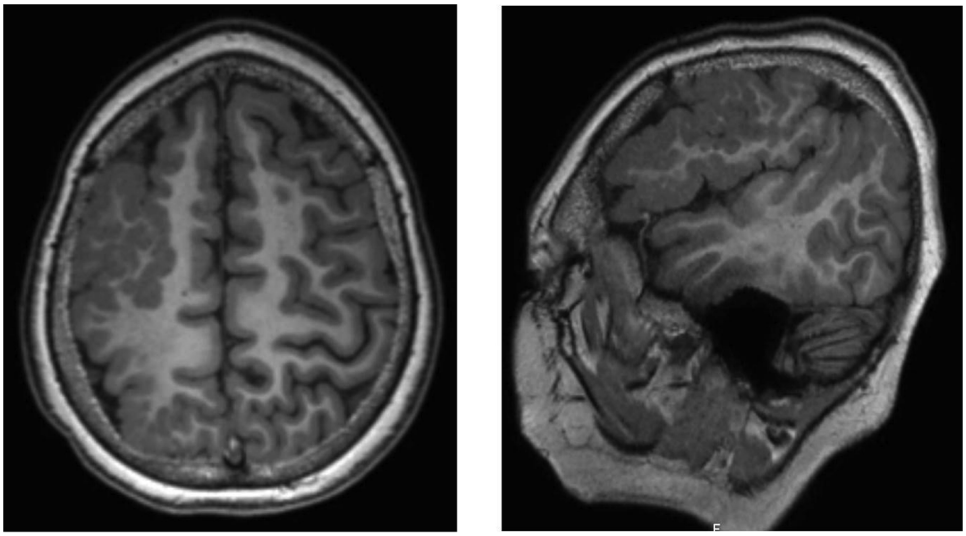

Fig. 4. MRI scan, T1 weighted sequence in axial (4a) and sagittal view (4b) showing right hemispheric polimycrogyria (patient 16).

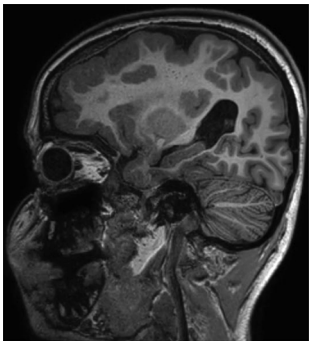

Fig. 5. MRI scan, T1 weighted sequence in sagittal view showing multilobar polimycrogyria (sparing occipital lobe) (patient 17).

aggravation.

4.1. Hemispherotomy: a rare indication in PMG

PMG, although being the most common brain malformation, represents only a low percentage of the patients operated on for epilepsy (in pediatric as well as in adult series). Of the 230 patients who underwent a PSH between 2000 and 2017 in our institution, fewer than 10% were PMG patients (7.8% to be exact).

In a much larger series involving histopathological studies that spanned 25 years and included 2623 children operated on for all types of epilepsy, PMG was found in only 2.1% of the patients [14]. In a review of English medical literature (Table 5) we found a total of 19 patients who underwent a hemispherotomy (three of these patients having associated hemimegalencephaly) from five papers reporting a total of 191 patients having hemispheric PMG [3,4,9–11]. So the surgical rate is very low in PMG compared with other hemispheric malformations and acquired hemispheric pathologies [15].

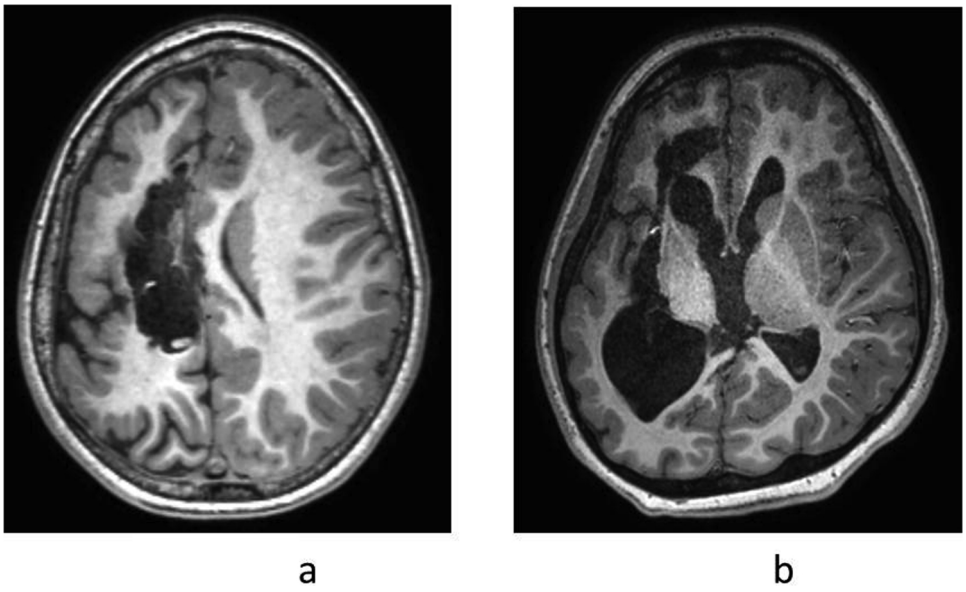

Fig. 6. postoperative MRI scan control, T1 weighted sequence in axial view showing peri-thalamic disconnection scar in patient 16 (a) and patient 17 (b).

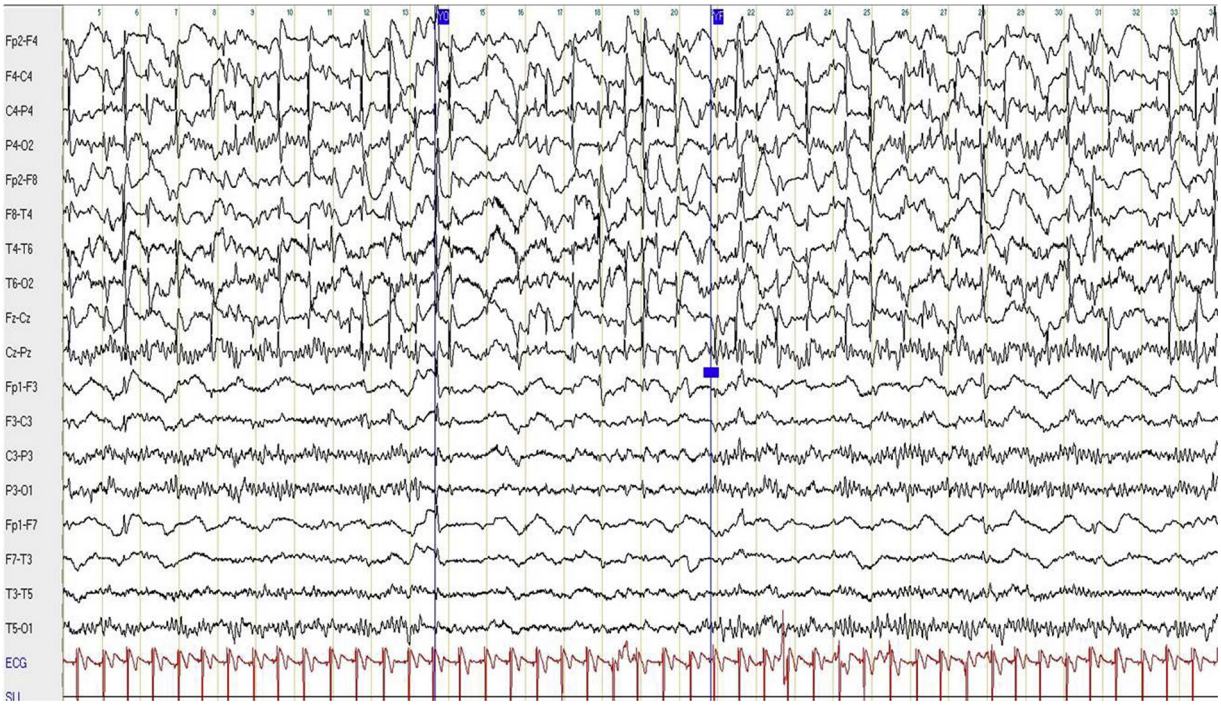

Fig. 7. Postoperative EEG: wakefulness showing normal posterior rhythm on the left hemisphere (patient 16).

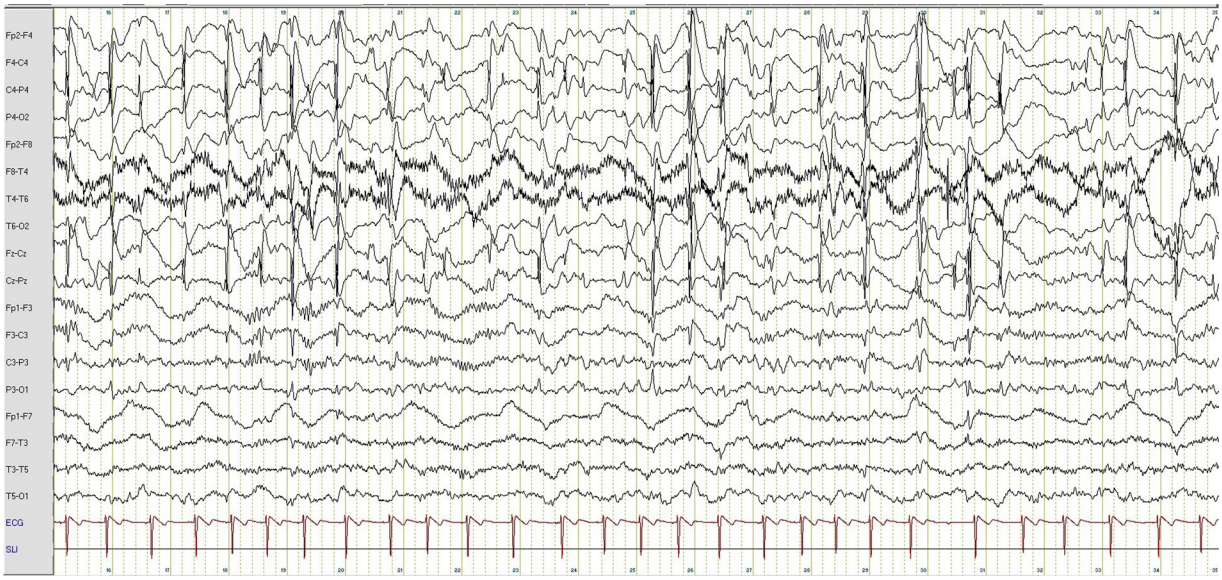

Fig. 8. Postoperative EEG: sleep stage 2 showing continuous spikes and waves over the right hemisphere which could be seen on the left. Presence of spindles on the left hemisphere (patient 16).

Table 5
Published pediatric series of hemispherotomy in PMG.

Authors	Total Nb of epileptic patients	Nb of ESESS	Overall operated patients	Patients with hemispherotomy	FU following hemispherotomy
Carabello et al. [3]	53	43	2	1	NA
Cossu et al. [4]	64	4	24	5	Engel 1 for 5 pts
Wang et al. [9]	12	1	12	5 (3 with hemimegalencephaly)	Engel 1 for 2 pts
Maillard et al. [10]	58	NA	58	4	Engel 1 for 3 pts
Jeong et al. [11]	4	4	4	4	Engel 1 for 4 pts

NA : not available; pts : patients.

4.2. Some arguments can explain the difficulties in making a surgical decision in cases of PMG

1) **Epileptic particularities**: patients with PMG and only focal seizures generally have a low seizure rate. Thanks to the knowledge that ESESS usually remits before a mean age of 13 years [7,3], medical treatment is considered sufficient in cases of ESESS encephalopathy. However, when ESESS is associated with a cortical malformation there is a low remission trend compared to non lesional ESESS [5]. Moreover, in the cases where ESESS remits with time, focal seizures still persist in most of the patients and a lifelong treatment is then often necessary [3]. The bilateralization of the epileptic abnormalities of ESESS encephalopathy contributes to complicating the surgical decision as well.
2) **The role of eloquent cortex:** In PMG patients, eloquent cortex can be functional. Various studies including language functional MRIs and cortical stimulations of eloquent areas during SEEG studies [16,17] clearly demonstrated that PMG cortex carries some function. In our personal series, at least five patients had the use of their hands and fingers before surgery that then disappeared postoperatively. A positive point is that none of the patients in the series who had the left hemisphere operated on experienced any language aggravation.

4.3. Criteria for proposing hemispherotomy in our patients

1) The major criterion should be drug-resistant epilepsy and mainly drug-resistant ESESS associated with a high number of disabling seizures. A majority of our patients were at risk for multiple falls, some of them were confined to a wheelchair, and almost all were unable to attend school.

Defining drug resistance in the cases of epileptic encephalopathy is a challenge for two reasons: a) the definition of drug-resistant epilepsy by ILAE [18] which allows the consideration of a surgical option after the failure of adequate trials of two appropriate AEDs doesn't mention epileptic encephalopathy and thus doesn't apply to ESESS and b) regarding medical treatment of ESESS and duration, if several options are proposed with a certain degree of agreement on the use of some AEDs such as steroids [19] and benzodiazepines and the prohibition of others (carbamazepine, phenobarbital, phenytoine) due to the risk of aggravation [19–23], there are no clear points of reference on the duration of steroid treatment beyond one year [19]. Finally, there is a current lack of general agreement on treatment guidelines of ESESS. Our patients were all drug-resistant to the association of steroids, BZD, and other additional antiepileptic drugs (or with side effects to steroids) and were all treated more than one year as the mean duration of treatment time for ESESS was 2.8 years.

1) Neurological criteria

Patients should have a pre-existing hemiparesis. In case of incomplete hemiparesis, parents and if possible patients, should be aware of and accept the risk of worsening motor deficits. The lack of presurgical hemianopia should not be considered a contraindication due to the adaptive abilities of young children following surgery.

1) EEG criteria

In our team we take EEG testing into account in the decision to perform hemispherotomies using well-defined criteria [24]. In patients with PMG however, it is more challenging. The most constant and relevant lateralized feature to consider should probably be the recording during wakefulness of continuous multifocal spikes over the pathological hemisphere, the contralateral diffusion being not as important. More generally, those patients belong to the category of focal epilepsies with generalized abnormalities. Successful hemispherotomies have been reported in patients of several etiologies with generalized EEG findings. The rate of seizure freedom was similar with or without SSWC (slow spike-waves complex) [25], including patients with ESESS [26]. The ESESS pattern can be found in patients with hemispheric epilepsies related to other etiologies, more frequently vascular sequelae [11], [27]. In those cases, clinical data and MRI abnormality are critical to the decision to proceed with surgery.

4.4. Outcome

In the cases reported in the current literature, as well as for our patients, the follow-up is satisfactory regarding epilepsy, and they all show either a cognitive improvement or an arrest in cognitive decline. No patients who underwent a left side hemispherotomy exhibited any verbal deterioration following surgery which is consistent with the finding that, in case of early unilateral injury, some authors found evidence of equipotentiality of the left and right hemispheres in the development of verbal and nonverbal abilities [28]. Furthermore, the lack of deterioration or even improvement of speech, regardless of the side on which the hemispherotomy was performed, has been described for years independent of pathology [29]. Nevertheless, severity and persistence of neuropsychological deficits are thought to correlate with the duration of ESESS [20].

ESESS disappearing postoperatively has already been mentioned [4,11]. It is not clear why some patients still have synchronous spikes and waves over the whole pathological hemisphere following surgery and others do not. The fact that the spikes and waves coming from the pathological hemisphere are seen on the healthy one is frequently observed in our experience after hemispherotomies of all etiologies and could be explained, in our opinion, by a field effect and not by an anatomic diffusion.

To conclude, we have demonstrated that PSH can be helpful in patients with drug-resistant ESESS and hemispheric PMG while keeping in mind that more often an accurate medical treatment can be sufficient. The main benefit of PSH is to definitively stop the seizures and to withdraw the AEDs while taking into account the risk of motor aggravation. On the contrary, with medical treatment only, patients are at risk of continually having seizures and remaining on AEDS for life. Consequently, we recommend performing a hemispherotomy after the failure of at least two appropriate AEDs as it is already recommended for focal drug-resistant epilepsies [18] in patients having a pre-existing motor deficit and a cognitive or behavioral aggravation.

Declaration of Competing Interest

The authors declare that they have no conflicts of interest concerning this article.

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