CONGENITAL DESTRUCTIVE HEMISPHERIC LESIONS AND EPILEPSY

CLINICAL FEATURES AND RELEVANCE OF ASSOCIATED HIPPOCAMPAL ATROPHY

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ABSTRACT - We studied the clinical, EEG and MRI findings in 19 patients with epilepsy secondary to congenital destructive hemispheric insults. Patients were divided in two groups: 10 with cystic lesions (group 1), and 9 with atrophic lesions (group 2). Seizure and EEG features, as well as developmental sequelae were similar between the two groups, except for the finding that patients of group 2 more commonly presented seizures with more than one semiological type. MRI showed hyperintense T2 signal extending beyond the lesion in almost all patients of both groups, and it was more diffuse in group 2. Associated hippocampal atrophy (HA) was observed in 70% of group 1 patients and 77.7% of group 2, and it was not correlated with duration of epilepsy or seizure frequency. There was a good concordance between HA and electroclinical localization. The high prevalence of associated HA in both groups suggests a common pathogenesis with the more obvious lesion. Our findings indicate that in some of these patients with extensive destructive lesions, there may be a more circumscribed epileptogenic area, particularly in those with cystic lesions and HA, leading to a potential rationale for effective surgical treatment.

KEY WORDS: epilepsy, magnetic resonance image, hippocampal atrophy.

Epilepsia secundária a lesões destrutivas hemisféricas congênitas: achados clínicos e relevância de atrofia hipocampal associada

RESUMO - Analisamos os achados clínicos, de EEG e RM de 19 pacientes com epilepsia secundária a insultos destrutivos hemisféricos congênitos. Os pacientes foram divididos em dois grupos: 10 com lesões císticas (grupo 1), e 9 com lesões atróficas (grupo 2). As características das crises e achados de EEG foram similares entre os dois grupos exceto pelo fato dos pacientes do grupo 2 terem apresentado mais comumente crises com mais de um padrão semiológico. A RM mostrou sinal T2 hiperintenso estendendo-se ao redor da lesão e à distância em quase todos os pacientes de ambos os grupos, de modo mais extenso no grupo 2. Observou-se atrofia hipocampal (AH) associada em 70% dos pacientes do grupo 1 e 77,7% do grupo 2 e não houve correlação com a duração da epilepsia ou freqüência das crises. Houve boa correlação entre a AH e localização eletroclínica. A alta prevalência de AH associada em ambos os grupos sugere uma patogenia comum com a lesão mais óbvia. Estes achados indicam que alguns destes pacientes com extensas lesões destrutivas, particularmente aqueles com lesões císticas e AH, a zona epileptogênica pode ser mais circunscrita possibilitando a indicação de uma ressecção restrita para o controle das crises.

PALAVRAS-CHAVE: epilepsia, ressonância magnética, atrofia hipocampal.

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Epilepsy as long-term sequelae is an important factor of morbidity in patients with destructive hemispheric insults early in life, many of them presenting with intractable seizures[1,2]. These insults result either in cystic or atrophic lesions commonly within a particular vascular distribution. The advances in neuroimaging techniques, particularly magnetic resonance imaging (MRI), turned itpossible to re-evaluate the spectrum of structural brain abnormalities associated with the more obvious lesion (cystic or atroph)[3-7]. A striking association has been found between these lesions and atrophy of medial temporal structures, suggesting that they share a common pathogenic mechanism in these cases[5-7].

The aim of this study was to compare the clinical, eletrencephalographic and MRI data of patients with epilepsy secondary to congenital destructive insults during early development associated to hemispheric atrophic and cystic lesions.

METHOD

Patient population

The study population consisted of 28 patients recruited from the Epilepsy Service at UNICAMP. The inclusion criteria were the presence of partial epilepsy secondary to a structural lesion defined by high resolution MRI, compatible with a destructive hemispheric insult during early development. These lesions were divided in two groups, cystic and atrophic. We then compared all clinical and EEG variables between these two groups. Detailed histories of pre- and perinatal events, developmental milestones, childhood febrile convulsions, status epilepticus, head injury, encephalitis and family history of epilepsy were systematically reviewed through the medical records and through direct interview with the mothers. Patients with lesions of known causes such as infection, trauma, developmental malformations (e.g., schizencephaly, arachnoid cyst) or with evidence of any kind of post-natal event that could be related to a central nervous system insult were excluded. Early neurologic exam and mental status were obtained from the patients' medical records.

Informed consent was obtained from all subjects. This study was approved by the Ethics Committee of the Faculty of Medical Sciences of UNICAMP.

Previous electroencephalographic data were reviewed and all patients had serial routine EEG studies using the 10-20 system with additional anterior temporal and zygomatic electrodes. Seven patients had long-term video-EEG monitoring with scalp electrodes for recording of their habitual seizures. The seizures were classified according to the International League Against Epilepsy[8]. Estimated IQ was measured using the sum of vocabulary and block design scaled scores of the Wechsler Adult Intelligence Scale – Revised (WAIS – R)[9-11].

MRI acquisition and analysis

All patients had MRI studies (Elscint 2T Prestige) including: *a)* spin-echo T1-weighted sagital images (slice thickness of 6 mm; tip angle of 180; TR= 430; TE= 12; matrix of 200x350; FOV=25x25 cm); *b)* fast spin-echo T2-weighted coronal oblique images perpendicular to the long axis of the hippocampus (slice thickness of 4 mm; tip angle of 120; TR=5800; TE= 129; matrix of 252x320; FOV=18x18 cm); *c)* inversion recovery T1-weighted coronal oblique images perpendicular to the long axis of the hippocampus (slice thickness of 3 mm; tip angle of 200; TR IR=2800; TE= 14; matrix of 130x256; FOV=16x18 cm); *d)* fast spin-echo T2-weighted axial images (slice thickness of 4 mm; tip angle of 120; TR= 6800; TE= 129; matrix of 252x328; FOV=21x23 cm). Additional MRI acquisitions were performed for some patients, such as proton density coronal images (TR= 4600; TE= 16-18) and FLAIR (TR= 2800, TE= 14). The characteristics of the cystic and atrophic lesions were visually analyzed with specific attention to their extension and topography as well as to the presence of adjacent cortical signal abnormalities and coexistence of distant structural lesions. Temporal lobe (TL) structures were evaluated for the following criteria: *a)* atrophy of the anterior portion of the TL; *b)* asymmetry of temporal horns of lateral ventricles; *c)* hyperintense T2 signal of the medial temporal structures ; *d)* abnormality of the internal structure of the hippocampus and e) hippocampal atrophy. Hippocampal atrophy was classified into *mild* (discreet but definite atrophy evident in 3 or more coronal cross-sections with little or no hyperintense signal / loss of internal structure), *moderate* (significant atrophy of the hippocampus in most of the cross-sections with pronounced hyperintense T2 signal and loss of internal structure) and *severe* (size of the abnormal hippocampus being less than half of the contralateral hippocampus on all cross-sections, with a flat shape in at least 3 cross-sections, associated with pronounced hyperintense T2 signal and loss of internal structures on IR images).

Statistical analysis

We tabulated clinical and MRI data of each group and used the chi-square or Fisher exact test to determine statistical differences. We used t-test to analyze age differences between the two groups of patients. We used Spearman rank correlation to correlate duration of epilepsy and frequency of seizures with the degree of HA.

RESULTS

Nine patients were excluded from the study: one had an arachnoid cyst, one had a neurosurgical sequelae, one had a thrombophilic disorder presenting with a stroke in childhood, four had a possible history of encephalitis in infancy, one had the antecedent of status epilepticus and one have developed a motor deficit by the age of four. Nineteen patients were included and analyzed separately in two groups: *Group 1* consisted of 10 patients presenting a cystic lesion on MRI and *Group 2* with 9 patients presenting an atrophic lesion.

Clinical features

Their identifying clinical characteristics are summarized in Table 1.

Thirteen patients had history of hemiparesis from infancy. They did not present any antecedents of a post-natal event prior to the identification of the motor deficit that could be responsible for it. From the remaining six patients, five of them (Patients 1, 4, 10, 18 and 19) had very subtle motor deficits or visual field defects that were only identified later on life by a neurologist. They had seizures starting very early on life and also did not have significant post-natal antecedents (table 1). The last case (Patient 9) had a normal neurological exam and had no post-natal antecedents prior to the first seizure by the age of nine.

We found no significant differences between the two groups in gender and age at examination. All patients were born at term. Mean ages of first seizure and onset of recurring seizures were higher in group 1 (5.1 and 10.3 years) than in group 2 (2.07 and 7.22 years), but there was no statistical difference ($p>0.3$). Gestational and perinatal complications were identified in 8/10 (80%) patients of group 1 and in 4/9 (44.4%) patients of group 2 ($p=0.07$). These complications were commonly related to prolonged delivery, fetal distress and bleeding during gestation. Prenatal antecedents in the first two trimesters of gestation were only found in patients of group 1. Except for one patient from group 1, all had an abnormal neurological exam including hemiparesis-hemiatrophy and visual field defects. Mental retardation was present in one patient from group 1 and in two patients from group 2. IQ was measured in all but one case (Patient19) who had a severe visual deficit.

Seizure patterns were similar between the two groups: the most common were sensorimotor partial seizures and complex partial seizures (CPS), with or without secondary generalization. Three patients from group 2 and none from group 1 presented with drop attacks. There was no difference in estimated seizure frequency between the two groups. All patients had medically intractable epilepsy at the time of investigation, except one from group 1 who was seizure-free on medication for more than one year.

The interictal surface EEG showed epileptiform abnormality lateralized to the same side of the lesion in 7/10 (70%) patients from group 1 and in 7/9 (77%) patients from group 2. Lateralization to the opposite side of the lesion was observed in one patient of group 2. Ictal surface EEG was recorded in 7 patients, 4 from group 1 and 3 from group 2. The EEG seizure onsets were concordant with the interictal data and lateralized to the same side of the lesion in 5 patients (three from group 1 and two from group 2), and were nonlocalizing in two patients (one in each group). One of these two patients (Patient 3) had bitemporal seizure onset with electrical activity of higher voltage over the right hemisphere, contralateral to the lesion and the interictal EEG data (Fig 1).

MRI feature

MRI features are summarized in Table 2.

Visual analysis of MRI: *Group 1*: 7/10 (70%) of patients had hippocampal atrophy (HA); 5 were unilateral and concordant with the side of the cystic lesion (Fig 2); two were bilateral, more severe ipsilateral to the cystic lesion. Four of these had additional amygdalar atrophy. All 7 patients with HA had the cyst extending to three lobes, all with some involvement of the temporal lobe. The remaining three patients without HA from group 1 had extratemporal lesions confined to one lobe. Hyperintense T2 signal was observed around the cyst and at distance in 8/10 (80%) patients. *Group*

Table 1. Clinical and EEG features.

Patient #/age at evaluation/sex	Age at first seizure	Age at begining of recurring seizures	Etiologic factors	Febrile convulsions	Neurological exam/ IQ	Seizure type/ frequency	Interictal surface EEG	Ictal surface EEG
Group 1								
1/23y/F	neonatal	11y	first trimester bleeding	n	L homonimous hemianopsy, L hemiparesis/ borderline	CPS, sec Gen/weekly	bitemporal (L>R)	NA
2/25y/M	6 m	12y	first and second trimester bleeding	y	L hemiparesis-hemiatrophy/retarded	SPS (L hemibody), daily	R temporal	R temporal
3/24y/F	1y	9y	multiple abdominal trauma in pregnancy	n	R hemiparesis-hemiatrophy/borderline	CPS, sec Gen /weekly	L temporal	bitemporal (R>L)
4/33y/F	6 m	1y	prolonged delivery / fetal distress	n	R hemiparesis, R homonimous hemianopsia/ low average	CPS, sec Gen /weekly	L temporal	L temporal
5/34y/M	3y	3y	none	n	R hemiparesis-hemiatrophy /low average	CPS, sec Gen /monthly	nonlocalizing	NA
6/38y/F	1y	10y	coiling of cord/fetal distress	n	L hemiparesis-hemiatrophy /high average	CPS/monthly	bitemporal (R>L)	NA
7/48y/F	25y	27y	NA	NA	R hemiparesis-hemiatrophy /borderline	SPS (R hemibody), sec Gen/controled	L temporal	NA
8/31y/M	11y	16y	fetal distress	n	L hemiparesis-hemiatrophy /low average	SPS (L leg)/daily	normal	NA
9/16y/M	9y	9y	third trimester trauma	n	normal/low average	VPS, sec Gen /monthly	L temporo-occipital	NA
10/21y/F	neonatal	5y	prolonged delivery and fetal distress	n	R inferior quadrantic defect /borderline	CPS, sec Gen /weekly	L temporal	L temporal
Group 2								
11/17y/M	neonatal	7y	prolonged delivery/ fetal distress	n	R hemiparesis/ low average	CPS, sec Gen /weekly	bitemporal (L>R)	NA
12/18y/F	6y	10y	none	n	L hemiparesis/average	CPS; SPS (L hemibody); drop attacks/daily	R fronto-temporal	R frontal
13/18y/M	8 m	5y	fetal distress	n	R hemiparesis/retarded	SPS (R arm)/weekly	L temporal	nonlocalizing
14/37y/F	2y	2y	none	n	L hemiparesis-hemiatrophy /retarded	CPS, sec Gen /monthy	bitemporal (R>L)	NA
15/32y/F	1y	22y	none	y	L hemiparesis-hemiatrophy /borderline	SPS (L hemibody), sec Gen/weekly	bitemporal (R>L)	NA
16/32y/ M	6y	6y	none	n	L hemiparesis-hemiatrophy/low average	SPS (R arm); drop attack; CPS, sec Gen/daily	L fronto-temporal	NA
17/ 20y/F	2y	10y	none	y	R hemiparesis-hemiatrophy, R inf. quadrantic defect /borderline	SPS (R arm), sec Gen; CPS; drop attacks /daily	L temporal	L temporal
18/36y/F	1y	1y	none	n	R hemiparesis/low average	SPS (R hemibody); CPS/monthly	L temporal	NA
19/19y/M	neonatal	2y	maternal infection/ prolonged delivery/fetal distress	n	R amaurosis, severe L visual deficit/NA	CPS/monthly	nonlocalizing	NA

IQ, intelligence quotient; L, left, R; right; NA, not available; CPS, complex partial seizure; SPS, sensorimotor partial seziures; VPS, visual partial seizure; sec Gen, secondary generalization; y, year; m, month.

Table 2. MRI features.

Patient#	Localization of the lesion	Mesial temporal structures					
		Hippocampus				Amygdala	Temporal horn dilatation
		Atrophy	Axis	Internal structure	Hyperintense T2 signal		
Group 1							
1	R temporo-parieto-occipital / ↑ T2 signal in R temporal pole	R (moderate)	abnormal	normal	absent	normal	present
2	R fronto-temporo-parietal / contiguous with R lateral ventricle	R (severe)	abnormal	abnormal	present	atrophy	present
3	L fronto-temporo-parietal/contiguous with L lateral ventricle/ atrophy of remanescent L hemisphere/ ↑ T2 signal in L temporal	L (severe)	abnormal	abnormal	present	atrophy	present
4	L temporo-parieto-occipital/contiguous with L lateral ventricle/ ↑ T2, ↓T1 signals arround the cyst (mainly in temporal lobe) / ↑T2 signal arround L occipital horn	L (severe) R (mild)	L-abnormal R-normal	L-abnormal R-normal	L-present R-absent	normal	L-present R-absent
5	L parietal	absent	normal	normal	absent	normal	absent
6	R temporo-parieto-occipital / contiguous with R lateral ventricle / ↑ T2 signal arround the cyst / R temporo-parietal atrophy with ↑ T2 signal	R (moderate)	abnormal	abnormal	present	normal	present
7	L fronto-temporo-parietal / contiguous with L lateral ventricle / very discrete ↑ T2 signal arround the cyst / contra-lateral hemispheric atrophy / global ventricular dilatation	L (severe) R (moderate)	L- abnormal R-abnormal	L- normal R- normal	L- present R-absent	Bilateral atrophy (L>R)	global ventricular dilatation
8	R parietal / contiguous with R lateral ventricle / extense ↑ T2 signal arround the cyst	absent	normal	normal	absent	normal	absent
9	L occipital / mild ↑ T2 signal arround the cyst	absent	normal	normal	absent	normal	absent
10	L parieto-occipital and posterior temporal contiguous with L lateral ventricle / L anterior temporal atrophy / ↑T2 signal arround the cyst and R occipital horn	L (moderate)	abnormal	normal	L-present R-present	normal	L- present R-absent

cont.

Table 2. Cont.

Group 2							
11	L parieto-occipital with ↑ T2 signal / mild ↑ T2 signal in contral-lateral homologous area / moderate dilatation of L occipital horn	L (mild)	normal	normal	present	normal	absent
12	R fronto-central, parietal (superior and medial convexity) / subcortical ↑ T2 signal extending until the R lateral ventricle associated to an encephaloclastic lesion with ↑ T2 signal arround it	absent	normal	normal	present (head)	normal	absent
13	R hemispheric with perisylvian accentuation / subcortical ↑ T2 signal	R (mild to moderate)	abnormal	abnormal	present	atrophy	present
14	R hemispheric	R (severe)	abnormal	abnormal	present	normal	present
15	R hemispheric with diffuse subcortical ↑ T2 and FLAIR signals / R brainstem atrophy / global R lateral ventricle dilatation	R (severe)	abnormal	abnormal	present	atrophy	present
16	L hemispheric accentuated in perisylvian region (fronto-opercular, insular and temporo-parietal) with subcortical ↑ T2 signal / mild dilatation of L frontal and occipital horns	absent	normal	normal	absent	normal	absent
17	L hemispheric (> in perisylvian region) / subcortical ↑ T2 signal in L perisilvian and temp.-occipital/ perisylvian clastic lesion contiguous with the L lat. ventricle / L insular, basal ganglia clastic lesions / global L ventricular dilatation	L (moderate)	abnormal	NA	present	atrophy	present
18	L perisylvian, temporal / clastic lesion in pariteo-occipital region with L occipital horn dilatation / ↑ T2 signal in L perisylvian region and arround the clastic lesion	L (moderate)	abnormal	abnormal	present	normal	present
19	occipital bilateral with ↑ T2 signal	R (moderate) L (mild)	R- abnormal L- normal	R-abnormal L- normal	R-present L-absent	R-normal L-normal	R-present L-absent

+ T2 signal, hyperintense T2 signal.

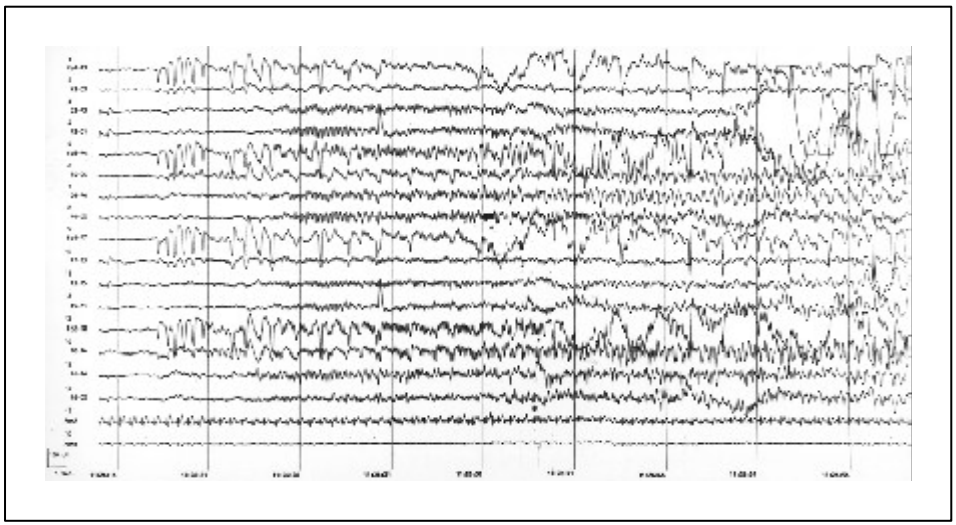

Fig 1. Patient 3. Scalp ictal EEG showing a bitemporal seizure onset, with electrical activity of higher voltage over the right temporal region, contra-lateral to the lesion on MRI.

2: HA was present in 7/9 (77.7%) patients, all unilateral except in one patient who had a bilateral occipital lesion; 3 of them had associated amygdalar atrophy and 5 had temporal atrophy. Two patients had normal hippocampi, one of these had atrophy of the anterior temporal lobe.

The atrophic lesion extended to the entire hemisphere in 4/9 (44.4%) patients, involved two lobes in 2/9 (22.2%), and three lobes in 2/9 patients. Hyperintense T2 signal extending beyond the area of atrophy was present in all patients from group 2, except one. In addition, the abnormal T2 signal was in general more diffuse in patients of group 2 (Fig 3).

Relationships between MRI and clinical-EEG findings

Unilateral or bilateral HA corresponded to complex partial seizures (CPS) with limbic type semiology in 71.4% of group 1 patients and 57,1% of group 2 patients, and was concordant with interictal EEG localization over the TL in 85.7% of group 1 patients and in 71.4% of group 2. Among the three patients with bilateral HA, two had interictal EEG temporal epileptiform abnormality ipsilateral to the most atrophic hippocampus and in the remaining patient the EEG was non-localizing.

HA was also associated to ipsilateral atrophy of the anterior TL. In group 1, all patients with HA had concomitant TL atrophy. In group 2, 71.4% of patients with HA had TL atrophy. There were six patients (three in each group) with extratemporal lesions: four without associated HA (one fronto-central, two parietal and one occipital) and two with associated HA (one parieto-occipital and the other occipital bilateral).

Duration of epilepsy and frequency of seizures did not correlate statistically with the presence of HA ($p > 0.2$).

Surgical results

Seven cases (Patients 1, 2, 3, 4,10, 13,17) underwent anterior temporal lobe removal including amygdala and anterior portion of the hippocampus. All had associated HA on MRI and the temporal resection was proposed as a first step of a escalated approach where other interventions could be necessary. Patients 2 ,4,10 and 17 had seizures recorded from the TL ipsilateral to the HA. Ictal recordings were not available and not localizing in patients 1 and 13 respectively but both patients

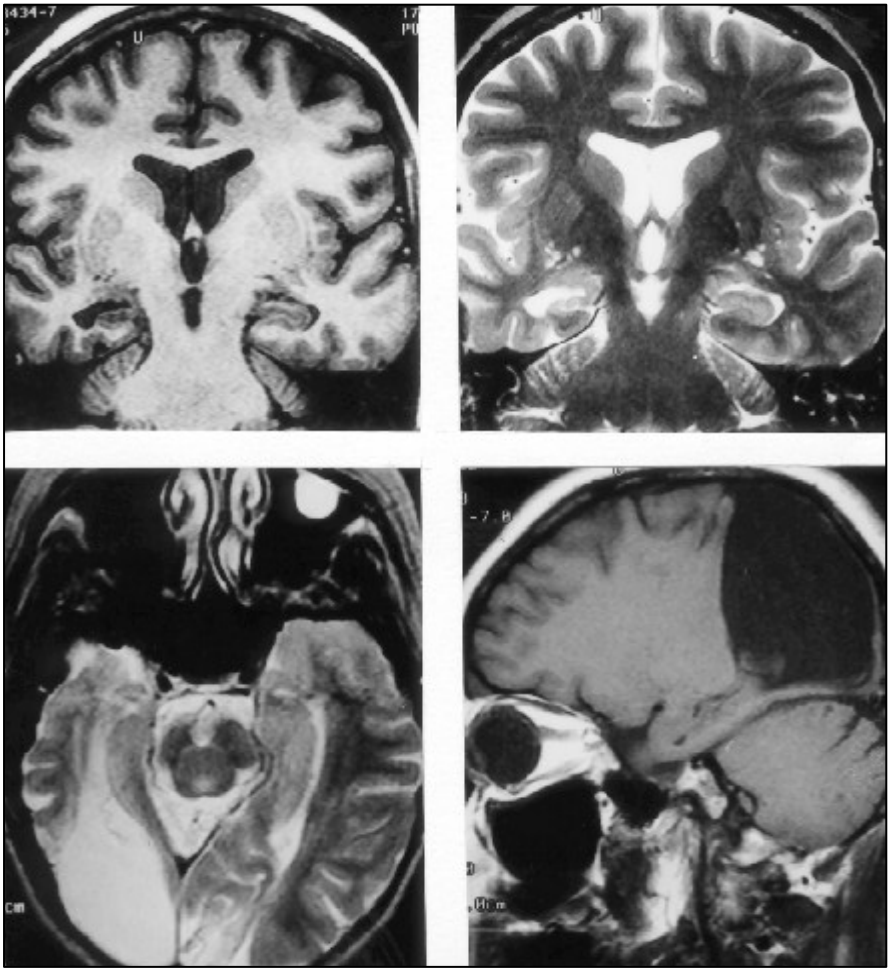

Fig 2. Patient 6. Thirty-eight-year-old woman with intractable seizures since the age of 10. Coronal IR T1-weighted and FSE T2-weighted images (top) showing right temporo-parietal and hippocampal atrophy with hyperintense T2 signal. Axial SE T2-weighted and sagital T1-weighted images (bottom) show the right temporo-parieto-occipital localization of the cysyic lesion, contiguous with the right lateral ventricle.

had consistent interictal activity ipsilateral to the HA. Patient 3 had recorded seizures with bitemporal onsets and voltage dominance contra-lateral to the HA and interictal activity. Surgery was performed ipsilateral to the HA.

Three cases (Patients 1, 3, 4) became seizure free (Engel's class I[12]) and one (Patient10) was almost seizure free (Engel's class II) with a postoperative follow-up ranging from 19 to 25 months (mean, 21.5 months). All these 4 patients had seizures of limbic semiology exclusively.

Patients 2, 13 and 17, who had drop attacks and/or sensorimotor partial seizures associated to complex partial seizures, did not achieved seizure control after an initial temporal lobe resection. All had reoperation with extension of their initial resection guided by eletrocorticography. After this second procedure these patients had their complex partial seizures controled but with persistence of other seizure types. A third intervention was performed in Patient 17 who has been seizure free for

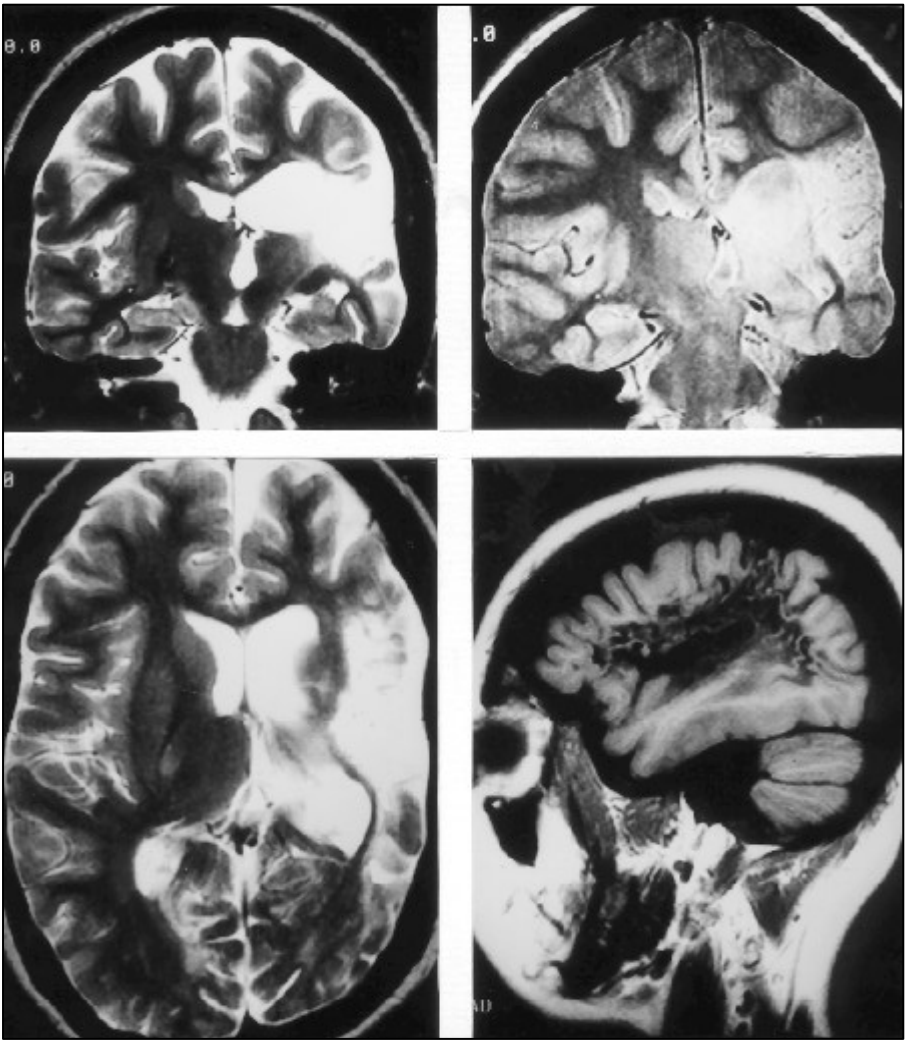

Fig 3. Patient 17. Twenty-year-old girl with intractable partial seizures of left temporal lobe origin. Coronal FSE T2- weighted and proton density images (top) demonstrating left hemispheric atrophy more prominent at the perisylvian region, with diffuse hyperintense signal and left lateral ventricle dilatation. In addition, there is atrophy and hyperintense T2 signal of the left hippocampus. Axial FSE T2-weighted and sagital SE T1-weighted images (bottom) show left hemispheric atrophy more pronounced over the perisylvian region.

13 months after a functional left hemispherectomy. Patients 2 and 13 are under evaluation for redelimitation of their epileptogenic zones.

DISCUSSION

Destructive hemispheric lesions in early periods of development are commonly associated to epilepsy and represent one of the major neuropathologic conditions acquired in the pre- and perinatal periods[1,13-16]. These lesions are the result of extense areas of necrosis of the cerebral tissue predominantly due to hypoxic-ischemic insults but it is well known that other kinds of insults can be involved such as congenital infections, maternal exposure to toxic substances and trauma[14, 17-20].

There are several lines of evidence indicating that the response of the brain to injury changes according to timing of in utero development[1,4,21,22]. Cystic lesions tend to occur in earlier periods of development, usually before the 30th week of gestation, due to the high water content of a brain in myelination process and the deficient response of the astrocytes to the formation of a glial scar[1,4]. After this period, the chances of formation of a glial scar in response to a destructive insult, become increasingly higher. This concept led us to analyze these patients in two distinct subgroups (cystic and atrophic lesions) with a premise that they could present distinct clinical presentations and outcomes. Maximal caution was taken to exclude patients whose lesions could have occurred post-natally.

Gestational and obstetric antecedents were more commonly found in patients of group 1 (cystic lesions), and noteworthy was that antecedents in the first two trimesters of gestation were only seen among patients of this group. One could state that this finding supports the concept that cystic lesions are related to insults at earlier periods of development, but it is well known that a retrospective approach is very limited in search of a causal relationship between gestational/obstetric events and early cerebral insults[23-27]. Intrapartum fetal distress was equally common in the two groups; this may reflect antepartum disturbances secondary to insults in different times of gestation[28].

The more diffuse hyperintense T2 signal observed in patients with atrophic lesions (group 2) indicates that gliosis is more pronounced in this group, as the glial tissue contains more free water than normal brain[1]. Therefore, the extension of the gliosis signal could be regarded as a marker of the time of the insult. This data should however be interpreted with certain reservations. More pronounced T2 signal changes in atrophic lesions may only reflect the presence of more remanescent tissue when compared to cystic lesions. Moreover, most of the patients in this series with cystic lesions also have signs of gliosis around the lesion and at distance, which means that these insults have ocurred in a period when gliosis repair was already well developed. In addition, the nature and magnitude of an insult as well as its capacity to create a communication with the CSF system can be more relevant than the time of its occurence in determining the formation of a cystic or an atrophic lesion[29-33].

Neurodevelopmental status as well as seizure patterns were comparable between the two groups except for the finding that patients in group 2 more commonly presented seizures with more than one semiological type. Drop attacks were present in three patients of group 2 and in none of group 1. Two of these three patients presented a diffuse interictal epileptiform abnormality and all of them had diffuse signs of gliosis on MRI.

We identified CPS in 71% and 57% of the patients with associated HA in the cystic and atrophic groups respectively, similar to previous studies that showed a concordance of 77% between porencephaly associated HA and CPS[6,7].

Most of the correlative studies between HA and EEG reported in the literature show that in more than 90% of the patients with temporal lobe epilepsy (TLE), the MRI and EEG abnormalities are concordant[34]. In a series of porencephaly, that represents a different patient population from the "pure" TLE, HA was concordant with interictal EEG localization to the ipsilateral temporal region in 69.2% of the patients[6]. In the present study we found EEG localization concordant with HA in 85.7% of patients with cystic lesions and in 71.4% of patients with atrophic lesions.

In one patient of our study, the interictal surface EEG showed epileptiform abnormality lateralized to the contralateral side of the lesion, and in another patient, the EEG seizure onset was bilateral but with electrical activity of higher voltage contralateral to the side of the lesion. Sammaritano et al.[35] stressed the importance of a critical interpretation of the EEG in patients with gross focal cerebral lesions. Patients with large hemispheric lesions can present bilateral synchronous or independent interictal epileptic discharges that in some instances "predominate" in the hemisphere contralateral to the lesion. The EEG background activity of the intact hemisphere will be higher in amplitude and can overshadow the low voltage activity of the lesioned hemisphere, leading to a false lateralization.

A previous study in patients with temporal and extratemporal lesional epilepsy of different etiologies, showed that cystic and atrophic lesions had associated HA in 31 and 23.5% of patients respectively, suggesting a vascular pathogenesis to HA in these cases[5]. We have detected HA by visual analysis in 70% of the patients in the group of cystic lesions and in 77,7% in the group of atrophic lesions. Although the frequency of HA in both groups was much higher than in the series of Cendes et al.[5], we found no significant difference between our two groups.

Most of the patients with HA in our series had the more obvious lesion involving the TL. In particular, when we analyzed the six patients without TL involvement, we found that two of them had HA and had the lesion in the territory of the posterior cerebral artery. The posterior cerebral artery supplies the occipital and part of the parietal lobe, the inferomesial and lateral areas of the TL, as well as the hippocampus and part of the parahippocampal gyrus[36]. Remillard et al.[37] described 8 patients with TL epilepsy and visual field defects associated to occlusion of arteries in the posterior territory defined by arteriography. They suggested a perinatal vascular occlusive etiology in these patients. As the hippocampus and TL lie in a watershed area supplied mainly by the anterior choroidal, middle and posterior cerebral arteries, a drop in blood pressure can also be considered a pathogenic mechanism besides arterial occlusion.

Some experimental data support the notion that a systemic perfusion deficit can produce damage to a single hemisphere. The induction of perinatal asphyxia in monkeys with significant hemodynamic repercussion on the fetus commonly produce necrosis in a single hemisphere[38], and only rarely if there is no fetal hypotension associated. One possible explanation for this is a different level of vascular maturation between the hemispheres. Another possibility is that the fetus cephalic position at the moment of the insult can be relevant. Experiments performed by the same center[39] failed to produce assimetric lesions when the acoustic meatus of monkey fetuses were aligned at the same height, with or without associated hypotension.

Although the gliosis sign on MRI did not seem to help in determining the time of the insult in our series, the fact that it is more pronounced in patients with atrophic lesions can be associated with a more widespread epileptogenic zone and a possible worse prognosis to focal resections when compared to the group of patients with cystic lesions. The two patients in our series with an atrophic lesion and diffuse signs of gliosis submitted to surgery did not improve with a limited resection. By contrast, four out of five patients with cystic lesions had good surgical outcome after an anterior temporal lobe resection,. Another factor that seems to have contributed for a worse surgical prognosis in patients of group 2 was the association of other seizure types than those with limbic semiology. The only patient of group 1 with poor surgical result also had more than one seizure type.

In conclusion, our study indicates that both cystic and atrophic lesion groups had a high prevalence of associated HA which may point to common pathogenic mechanisms leading to hippocampal damage concomitant to the more obvious lesion. There was concordance between HA and electroclinical localization to the ipsilateral temporal region in most patients from both groups, which leads to a potential rationale for effective surgical treatment in these patients despite their extensive destructive lesions. Some of these patients can achieve seizure control with a limited resection avoiding the risks and neurological sequelae of a hemispherectomy.

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