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FULL-LENGTH ORIGINAL RESEARCH

Bilateral perisylvian ulegyria: An under-recognized, surgically remediable epileptic syndrome

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Summary

Purpose: Interest in the association of epilepsy and pseudobulbar palsy was rekindled since the identification through magnetic resonance imaging (MRI) of bilateral perisylvian polymicrogyria (PMG). Seizures are often intractable, but resective epilepsy surgery has not been recommended. However, a similar clinical picture can be encountered in patients with bilateral perisylvian destructive lesions, which fit the description of ulegyria (ULG). We report a series of patients with epilepsy and pseudobulbar palsy due to bilateral perisylvian ULG (BP-ULG), show that hippocampal sclerosis (HS) is often associated and highlight the fact that in this entity, unlike in malformative bilateral perisylvian PMG, seizures may be surgically treated.

Methods: The motor, cognitive, epileptologic, and imaging features of 12 patients with perisylvian ULG followed at three institutions are described. For patients with refractory seizures, we detail extracranial and intracranial electrographic recordings, surgical strategies, histopathologic analyses of the resected tissue, and outcome of surgical treatment. Descriptive statistics were used for quantitative and categorical variables. Student's *t*-test was used to compare means, and a $p < 0.05$ was considered significant.

Key Findings: Pseudobulbar palsy and mental retardation were present in all patients with symmetrical BP-ULG. Five had refractory seizures. There was no relationship between the severity of the pseudobulbar palsy or of the mental retardation and the degree of seizure control with medication. The five patients in whom seizures were refractory to medication had significantly earlier age of onset and longer duration of epilepsy ($p < 0.05$). Dual pathology with associated unilateral HS was present in four. One patient with dual pathology had a temporolimbic electroclinical picture and had an anterior temporal lobectomy (ATL) based upon noninvasive evaluation. The other four had ictal semiology suggesting involvement of both temporolimbic and perisylvian cortex. Intracranial electroencephalography (EEG) showed concomitant seizure onset in the anterior temporal region and in the ipsilateral ULG in three of the four with dual pathology and in the ulegyric cortex in the one without HS. Resection guided by a combination of semiology, MRI, and extra and intracranial EEG led to complete seizure control in two and almost complete seizure control (Engel class II) in two other patients. The only surgical failure was an isolated ATL in a patient with dual pathology, and concomitant seizure onset in both lesions according to semiology and intracranial EEG.

Significance: Our findings suggest that BP-ULG mimics the clinical features of bilateral perisylvian PMG. In patients with refractory seizures, recognition of this entity should lead to consideration of resective surgery despite the bilateral ULG.

KEY WORDS: Bilateral perisylvian ulegyria, Epilepsy, Pseudobulbar palsy, Polymicrogyria, Surgical treatment.

Magnetic resonance imaging (MRI) has rekindled interest in disorders presenting with pseudobulbar palsy and dysarthria in children. The description of bilateral perisylvian polymicrogyria (PMG) in patients with oral apraxia, dysarthria, dysphagia, and excessive drooling (Graff-Radford et al., 1986) led to reports detailing the so-called congenital bilateral perisylvian syndrome (CBPS; Kuzniecky et al., 1989, 1993). Epilepsy also figures prominently, accompanied by variable degrees of mental retardation, pyramidal signs, and arthrogryposis (Brodtkorb et al., 1994; Kuzniecky et al., 1994).

The heightened awareness about CBPS prompts a suspicion of bilateral perisylvian PMG in children with pseudobulbar palsy. However, the same clinical picture can be

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produced by bilateral, roughly symmetrical, perisylvian atrophic gyri and subcortical gliosis, fitting the classical pathologic description of ulegyria (ULG) resulting from perinatal or postnatal hypoxic-ischemic injuries (Friede, 1989; Villani et al., 2003). Although clusters of atrophied gyri may occasionally resemble PMG, the cortical architecture is better delineated, suggesting an insult sustained after completion of the perisylvian gyration (Friede, 1989).

Over the years, we examined a series of patients with pseudobulbar palsy and epilepsy associated with bilateral ULG in the perisylvian regions, a number of whom had medically refractory seizures. Herein we report these patients and draw attention to the relevant fact that, unlike in those with CBPS due to PMG, refractory seizures may be amenable to resective surgery. We propose the term bilateral perisylvian ulegyria (BP-ULG) to describe this underrecognized entity.

Patients and Methods

Subjects

Eleven patients were evaluated at the Chonju and Kwangju Epilepsy Programs, in South Korea, and one in Porto Alegre, Brazil. Five had resective surgery, four of whom were described in a previous manuscript focusing on the pathologic aspects of the entity (Kim et al., 2006). Patients were referred due to seizures associated with pseudobulbar palsy and consecutively included on the basis of an MRI picture dominated by clusters of thin, atrophic gyri, with loss of cortical tissue in the depths of the sulci (Fig. 1) and gliosis of the subcortical white matter. These findings conformed to the appearance of gliotic or "sclerotic" microgyria, as described in classical neuropathology textbooks (Blackwood & Corsellis, 1976). These were the only patients with this entity seen in both centers over the years.

Clinical characteristics

Clinical data were collected from chart review and updated through outpatient visits or telephone interviews. Pregnancy and perinatal histories were reviewed for the presence of hypoxic-ischemic or infectious brain insults, but reports about presumed etiology often lacked details. Difficulties with breastfeeding or swallowing, developmental delay, and evidence of learning difficulties were noted. Pseudobulbar signs were classified as severe, moderate, or mild, according to the degree of dysarthria (inability to speak, severe dysarthria but understandable speech, or mild dysarthria) and of the restriction of tongue movements (severe limitation of all tongue movements, limitation of protrusion or lateral movements, or minor limitation of movements). The presence of developmental delay was based on the rate of acquisition of motor and language milestones. Because dysarthria interfered with speech acquisition, we took into consideration reports on the ability to understand speech and to communicate with signs or finger pointing. Seizure types were confirmed through interviews with patients and relatives, as well as video analysis in those undergoing preoperative evaluation. Data on seizure frequency and status of seizure control with medication were also obtained. Seizure outcome following surgery was classified according to Engel's categories (Engel et al., 1993).

Neuropsychological profile

Neuropsychological evaluation was performed in 10 patients through a Korean battery of cognitive tests reported elsewhere (Kim et al., 1994; with the exception of patient 4, evaluated in Brazil according to a protocol described in Palmini et al., 1995). Because formal neuropsychological testing was difficult in most patients due to speech limitations, full scale IQ (FSIQ) could underestimate the true cognitive abilities and potential of these patients. Therefore, we complemented the assessment of cognitive functioning

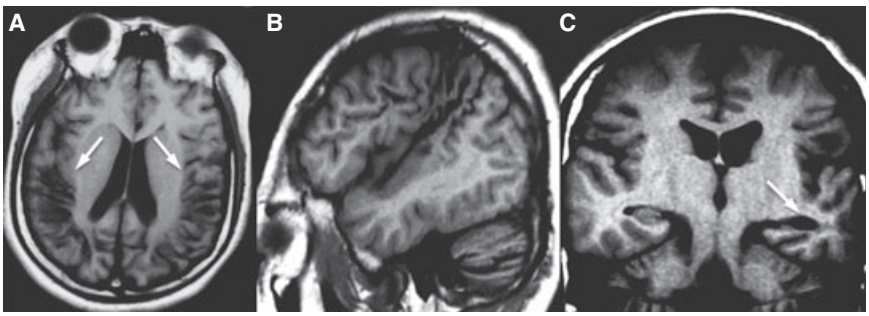

Figure 1.
Composite T_1-weighted MRI sections of patient 1. (**A**) Axial image showing bilateral perisylvian ulegyria with marked cortical atrophy; (**B**) sagittal left side view shows in detail the ulegyric lesion; (**C**) severe left hippocampal atrophy on coronal images. The patient had a purely left temporal electroclinical picture and underwent left anterior temporal lobectomy. He is seizure-free since surgery, 9 years ago.

taking into account the presence and severity of learning difficulties and also the degree of independence for activities of daily living. According to this composite data based on FSIQ and social functioning, overall cognitive dysfunction was rated as absent, mild, moderate, or severe. Patients who were able to attend regular school and finish elementary education, but who could not advance into high school were considered as mildly dysfunctional. Those who were not able to attend a regular school but were independent in activities of daily living were considered as moderately, and those who could not function independently were regarded as severely dysfunctional. Cognitive function of the two patients who did not have FSIQ scores was judged according to schooling and independence on activities of daily living.

Imaging

MRI was obtained with a 1.0 T Siemens Magnetom (Siemens AG, Erlangen, Germany) in the 11 Korean patients and with a 1.5 T in the patient from Porto Alegre. The presence, location, and symmetry of the ULG were analyzed on T_1-weighted coronal and axial images, whereas the extent of increased subcortical signal indicative of gliosis was evaluated on T_2-weighted and on fluid-attenuated inversion recovery (FLAIR) images, when available. Furthermore, the presence of hippocampal atrophy and abnormal signal indicative of hippocampal sclerosis was also noted.

EEG

All patients had 16–32 channel electroencephalography (EEG) (EMSA – BNT 36, Stellate System, Montreal, QC, Canada) studies during sleep and wakefulness. Prolonged video-EEG monitoring with scalp/sphenoidal electrodes was performed in five patients with refractory seizures who underwent comprehensive preoperative evaluation. Four of these were further studied with subdural grids and strips (Ad-Tech, Inc, Racine, WI, U.S.A.). Lateralizing clinical and scalp/sphenoidal findings allowed unilateral implantation in two patients, covering the anterior and basal temporal structures and the exposed surface of the perisylvian ULG. The other two patients had bilateral implantation: one in neocortical and anterobasal temporal and perisylvian regions, and the other in the neocortical perisylvian and parietal regions.

Surgery

Five patients had resective surgery, four following intracranial EEG evaluation. One with dual pathology (i.e., the association between BP-ULG and unilateral hippocampal sclerosis [HS]), but a purely unilateral anterior temporal electroclinical presentation, had an isolated anterior temporal lobectomy (ATL) following noninvasive evaluation. Of the other three with dual pathology, two had resection of both lesions and one had an ATL complemented by unilateral subpial transections of the ULG. The other patient, without associated HS, had a unilateral resection of the perisylvian ULG. Intraoperative acute electrocorticography (ECoG) and electrical stimulation to localize the motor area of the hand were performed in all (Palmini et al., 1995). Excision of the ulegyric lesions were as extensive as possible in front and (most commonly) behind the motor strip. In the motor cortex, the lesion was resected up to the inferior limits of the motor representation of the hand, as defined by cortical stimulation.

Histopathology

Histopathology was performed after fixation and formalin inclusion of resected perisylvian and/or temporal lobe tissue. Routine hematoxylin and eosin (H&E), Luxol fast blue-periodic acid of Schiff (LBPAS), and immunohistochemical stains for glial fibrillary acidic protein (GFAP; Dako, Glostrup, Denmark), neurofilament protein (NF-M/H; Sternberger, Mannheim, Lutherville, MD, U.S.A.), and neuron-specific enolase (NSE; Dako) were performed.

Statistical analysis

Descriptive statistics were used for quantitative and categorical variables. Student's *t*-test was used to compare means, and a $p < 0.05$ was considered significant.

Results

Clinical and demographic features

Eight patients are male. Seizure onset ranged from 1 month to 29 years (mean 8.9 years) and all were evaluated between ages of 14 and 42 years. Five had medically refractory seizures and were operated at a mean age of 26.9 years (range 21–42), after 10–30 years of recurrent seizures (mean 18.2). A history of significant perinatal hypoxia, associated with traumatic delivery or other causes of perinatal distress was present in seven patients (58%).

Nine patients had delayed acquisition of motor and language milestones, having walked and produced the first speech sounds between 18 and 36 months of age. All these had symmetrical BP-ULG. One of the three without developmental delay did not have symmetrical perisylvian lesions (Tables 1 and 2), and all met our criteria for cognitive dysfunction: four had mild, six moderate, and two severe cognitive dysfunction, the latter being totally dependent for activities of daily living. The FSIQ of the testable patients is shown in Table 1.

Ten patients had pseudobulbar palsy and four were either unable to speak or severely dysarthric and had limitations of voluntary tongue movements. Pseudobulbar signs manifested from early infancy as difficulty sucking and swallowing, often leading to evaluation for esophageal atresias or gastroesophageal reflux. Later, there were difficulties or inability to speak, whistle, or blow. Pseudobulbar signs were absent in only one patient with BP-ULG, and were also

Table 1. Demographic and clinical data on 13 patients with perisylvian ulegyria

Pt no./Sex	Age onset	Age operation[a]	Duration epilepsy[a]	Perinatal insult	Dev delay[b]	Pseudobulbar signs[c]	Other abn neuroexam	FSIQ	Mental retardation
1/M	3 m	21	20	Hypoxia	+	++	Spastic hemiparesis, right	45	+++
2/F	4 y	29	25	Negative hx	–	+	Slight hemiparesis, left	Unavailable	+
3/M	12 y	42	30	Negative hx	–	++	–	Unavailable	++
4/M	8 y	38	30	Traumatic delivery	+	+	Clubbed fingers, toes	69	+
5/M	11 y	21	10	Hypoxia	–	–	–	45	+
6/M	3 y	30	30	Negative hx	–	+	–	47	++
7/F	12 y	24	12	Traumatic delivery	+	++	Severe amblopia and strabismus	45	++
8/F	19 y	29	10	Traumatic delivery	+	+	–	61	++
9/F	2 y	19	17	Traumatic delivery	+	+	–	34	++
10/F	1 m	14	14	Hypoxia	+	+++	Spastic diparesis	30	+++
11/F	6 y	17	11	No	+	+	–	42	++
12/F	29 y	39	10	No	–	–	–	72	+

abn, abnormalities; dev, developmental; F, female; FSIQ, full scale IQ; hx, history; M, male; mo, month(s); Pt, patient; y, years.
[a]Age at presentation.
[b]–/+ designate presence or absence of delay in development.
[c]Severity of the pseudobulbar palsy: absent (–), mild (+), moderate (++), severe (+++). See text for definition.

Table 2. Imaging, epileptological, and surgical data

Pt no.	MRI findings	Seizure types	Scalp EEG, interictal[a]	Subdural recording, ictal	Operation	Pathology	Seizure control[b]	Post-op complications	Follow-up (y)
1	BP-ULG, symmetric + Lt HS	CPS; sec G	Lt T	–	Lt ant T lobectomy[c]	HS	I	None	9
2	BP-ULG, symmetric + Rt HS	CPS; sec G	Rt C-T-Par	Rt T and C	Rt ant T lobectomy[c] + Rt C resection	Ulegyria + HS	II	Transient worsening of dysarthria	8
3	BP-ULG, symmetric + Rt HS	CPS; sec G	Rt C-T-Par	Rt F, C, T	Rt ant T lobectomy[c] + Rt C resection	Ulegyria + HS	II	None	6
4	BP-ULG, symmetric + Lt HS	CPS; sec G	Bilat C-T	Lt C, T	Lt ant T lobectomy[c] + Rt C MST	HS	IV	None	6
5	BU, Par-Occ, symmetric,	Par Mot; sec G	Bilat C- T-Par	Rt Par	Rt Par resection	Ulegyria	II	None	3
6	BP-ULG, symmetric	Par Mot; sec G	Bilat T-Par	–	–	–	–	–	–
7	BP-ULG, asymmetric	GTC	Bilat T	–	–	–	–	–	–
8	BP-ULG, symmetric	GTC	Bilat C-T	–	–	–	–	–	–
9	BP-ULG, symmetric	GTC	Bilat C-T	–	–	–	–	–	–
10	BP-ULG, symmetric	GTC	Bilat C-T	–	–	–	–	–	–
11	BP-ULG, symmetric	GTC	Bilat C	–	–	–	–	–	–
12	BP-ULG, asymmetric	GTC	Bilat F-C	–	–	–	–	–	–

BP-ULG, bilateral perisylvian ulegyria; BU, bilateral ulegyria; HS, hippocampal sclerosis; CPS, complex partial seizures; sec G, secondarily generalized seizures; Rt, right; Lt, left; ant T, anterior temporal; C, central; T, temporal; F, frontal; Par, parietal; Occ, occipital; GTC, generalized tonic–clonic seizures; MST, multiple subpial transections; Par Mot, partial motor seizures.
[a]Predominant epileptiform abnormalities.
[b]According to Engel's classification (25).
[c]Including resection of mesial temporal structures.

not seen in the patient with a bilateral parietal lesion (Table 1). Finally, two had spastic hemiparesis, one spastic diparesis, one severe amblyopia and strabismus, and one clubbed fingers and toes.

MRI features

MRI features compatible with ULG were seen in all patients, consisting of shrunken gyri, much thinner than the adjacent normal cortex (Fig. 1). Increased signal on T_2-weighted images, suggestive of gliosis, was seen in the subcortical white matter. Ulegyric changes were bilateral in all patients, with symmetrical involvement of the perisylvian regions in 11 and of both parietal lobes in one. Additional areas of atrophy without ULG were seen in the frontal regions of five patients. Four patients (30%) had dual pathology (Fig. 2) and signs suggestive of unilateral HS

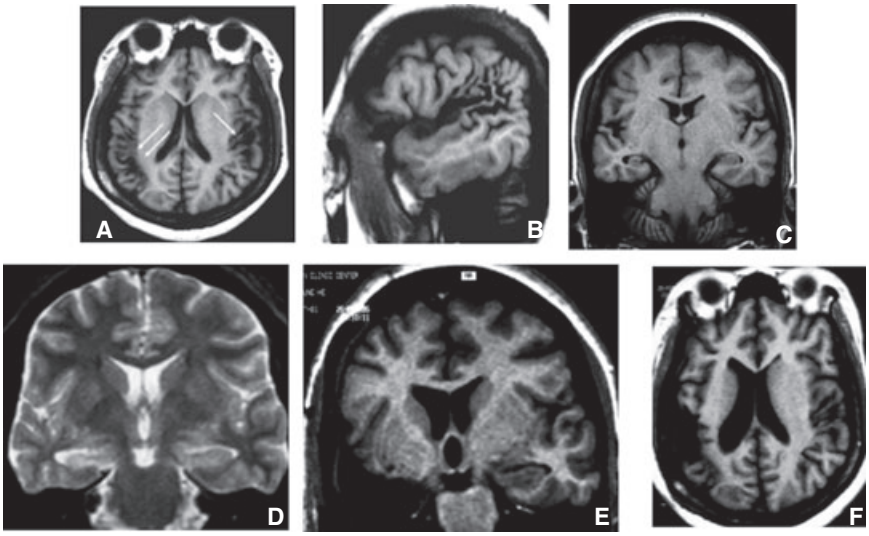

Figure 2.
Composite MRI images of patient 2. (**A**, **B**) are axial and sagittal T_1-weighted images showing the BP-ULG; (**C**, **D**) are coronal T_1 and T_2-weighted MRI sections, respectively, showing that the right hippocampus is atrophic and displays increased signal, leading to a diagnosis of hippocampal sclerosis (confirmed on pathology); (**E**, **F**) are postoperative T_1-weighted sections of the temporal and perisylvian resections.

lateralized to the side of predominant interictal and ictal epileptiform abnormalities.

Epilepsy syndrome

There were four distinct epileptologic pictures. Half of the patients had occasional generalized tonic–clonic seizures and were fully controlled on medication. The other six patients had one of three distinct semiologic presentations: exclusively temporolimbic, temporal-plus, or exclusively perisylvian. The four patients with dual pathology had either exclusively temporolimbic or temporal-plus semiology (see below). The two with bilateral ulegyria without dual pathology (one refractory) had only perisylvian attacks. One patient with BP-ULG and HS had only typical temporal lobe seizures and anterior temporal spikes. He has been seizure-free for many years, following the ATL (Table 2). The other three with dual pathology and subdural recordings showing concomitant seizure onset in temporal and perisylvian regions had either autonomic or somatosensory auras, such as perioral or brachial numbness. In some seizures, the aura was followed by clonic perioral movements and then automatisms, whereas other attacks presented as automatisms followed by perisylvian motor manifestations. Patients in whom seizures were refractory to medication had earlier mean age of onset (7.0 vs. 10.1 years) and significantly longer duration of epilepsy (23.0 vs. 14.8 years, $p < 0.05$) as compared to those in whom seizures were responsive to antiepileptic drugs (Tables 1 and 2).

Scalp/sphenoidal EEG findings are detailed in Table 2. Bilateral independent epileptiform discharges were observed in nine patients, involving centrotemporoparietal regions. The other three had only unilateral discharges. In patients without associated HS, temporal spikes often involved mid to posterior electrode positions (T3/T4 and T5/T6). There was no relationship between the severity of pseudobulbar palsy or of the mental retardation and the degree of seizure control with medication. Indeed, two of the patients with the mildest degrees of pseudobulbar palsy and mental retardation were refractory to medication and underwent surgery.

Invasive EEG recordings were performed in four patients. Implantation was bilateral in two and unilateral in the other two. In the three patients with dual pathology, seizure onset was unilateral and simultaneous from perisylvian and anterior temporal lobe regions. In the other, without associated HS, seizure onset was focal in the parietal cortex (Table 2).

Surgical treatment, outcome, and pathology

Resective surgery was performed in five patients, supplemented by multiple subpial transections in one (Table 2). Resections were based in the electroclinical constellation of findings (Table 2). Of the four patients with dual pathology, one had only an ATL, two had a resection of both lesions, that is, the sclerotic hippocampus and the ipsilateral ulegyric cortex, and the other an ATL complemented by subpial transections. Patient 1 had BP-ULG and MRI evidence of HS, a typical temporolimbic seizure pattern, and isolated basal and lateral temporal unilateral epileptiform abnormalities. He had an ATL based on noninvasive evaluation and

is seizure-free since surgery. Two of the other three patients with dual pathology had a "temporal-plus" seizure pattern (Ryvlin & Kahane, 2005) and simultaneous seizure onset on intracranial electrodes in anterobasal temporal and perisylvian regions. They had resection of both lesions in one hemisphere and have had only rare seizures since operation (Engel class II). The other patient with a similar picture had an ATL complemented by subpial transections over the ipsilateral perisylvian region and continues to seize (Engel outcome class IV). The fifth patient, the only operated without HS, had seizure onset around the ULG area in one hemisphere and resection of the lesion and perilesional tissue. He has only rare seizures since operation. Postoperative follow-up ranged from 3 to 9 years (mean 6.3, Table 2). One patient had transient worsening of the dysarthria. Histopathologic analyses revealed shrunken and sclerotic gyri in the specimens resected from three patients. Discrete calcifications or cystic changes were evident in two. Microscopically, variable degrees of subpial and subcortical gliosis, laminar cortical necrosis, glial nodules, amyloid bodies, and secondary demyelination were seen (Kim et al., 2006). The four patients with MRI picture suggestive of HS had confirmatory pathology.

Discussion

That unilateral ULG may be associated with refractory seizures and amenable to surgical treatment was already known (Usui et al., 2008). Here, we show that the condition we denominate BP-ULG presents a clinical picture often indistinguishable from bilateral perisylvian PMG yet, in sharp contrast with the latter (Kuzniecky et al., 1994), refractory seizures can be treated with resective surgery, despite the bilaterality of the lesions.

Of interest, ULG is seldom addressed in the epileptologic literature (Cusmai et al., 1993; Wolf et al., 1993; Lopez-Gonzalez et al., 1996; Marin-Padilla et al., 2002; Villani et al., 2003), and several reports are case studies from the pre-MRI era (Janzer & Friede, 1979; Norman, 1981). Underreporting of ULG and epilepsy may result from the frequent association with cerebral palsy (which dominates the clinical picture and is the main focus of attention in these children) but also from the potential confusion with PMG. The clustering of thin gyri resembles PMG and the classical neuropathologic literature often refers to ULG as "sclerotic microgyria" (Blackwood & Corsellis, 1976). However, the differences between the two entities are readily apparent on MRI, which also displays the increased white matter signal associated with the ulegyric lesion. Furthermore, a history of perinatal traumatic events related to hypoxic-ischemic or metabolic encephalopathy is frequent in ulegyria and infrequent in malformative PMG (Palmini et al., 1994). Similar to others (Kuchukhidze et al., 2008), we could confirm the etiology in around 60% of patients, but it is likely that the others did have a similar hypoxic-ischemic etiology, not adequately documented.

Our patients with BP-ULG had pseudobulbar signs from early infancy and developed dysarthria and oral dyspraxia, characterized by limitation of tongue and lip movements. These signs are typical of bilateral perisylvian lesions and have been consistently reported in Worster-Drought syndrome (Clark et al., 2000; Neville et al., 2001) and CBPS with BP-PMG (Kuzniecky et al., 1989, 1993). These clinical similarities and the attention CBPS due to malformative PMG (McBride & Kemper, 1982; Inder et al., 1999) has been attracting since the inception of MRI may have led to a neglect of BP-ULG as a cause of the so-called "bilateral perisylvian syndrome." The severity of pseudobulbar palsy varied with the anatomic distribution of the lesions, being less severe in patients with more posterior or asymmetric lesions. Despite less severe abnormalities in the neurologic examination, these patients also had intractable seizures. Such variability related to lesion location mirrors that in the spectrum of bilateral PMG (Guerrini et al., 1997; Barkovich et al., 1999; Guerreiro et al., 2000).

The 12 patients could be subdivided into six with only generalized tonic–clonic seizures adequately controlled with medication, and six with an association of somatosensory or temporolimbic auras, early perisylvian sensorimotor signs, automatisms, impairment of consciousness and occasional generalization, only one of whom was adequately controlled. This seizure pattern differs from the typical mesial or lateral temporal neocortical seizures in which somatosensory auras are rare (Palmini & Gloor, 1992). Indeed, this seizure pattern is highly suggestive of "temporal-plus" or extratemporal seizure onset with rapid propagation to limbic temporal structures (Andermann, 2003; Ryvlin & Kahane, 2005; Barba et al., 2007). Of interest, of the four patients with dual pathology, the three with concomitant seizure onset in anterobasal-temporal and ulegyric cortex as shown by subdural grid recording (Table 2) had a temporal-plus seizure pattern and the other, evaluated noninvasively, had a typical temporolimbic semiology. The two with bilateral ulegyria without associated HS had sensorimotor seizures with occasional generalization. Therefore, it is possible that the presence of HS is an important determinant of a temporolimbic or temporal-plus seizure pattern. Along these lines, anterobasal temporal discharges recorded from sphenoidal electrodes were seen in the four patients in whom HS was associated with BP-ULG, although independent slow waves and epileptic discharges involving centroparietal regions were also present in three. In contrast, six of the eight patients without HS had, in addition to perisylvian discharges, unilateral or bilateral neocortical, mid to posterior temporal lobe discharges.

Several recent series converge on a high prevalence of perinatal asphyxia and refractory seizures in patients with ULG (Villani et al., 2003; Gil-Nagel et al., 2005; Kuchukidze et al., 2008). The variability in the degree of

seizure control closely resembles that in patients with CBPS due to PMG, 60% of whom are not responsive to medication (Kuzniecky et al., 1993, 1994). Although the proportion of patients with refractory seizures is apparently similar in both disorders, patients with CBPS due to BP-PMG may have more malignant seizure types and electrographic abnormalities (Kuzniecky et al., 1993, 1994; Guerreiro et al., 2000). In a large series, 73% of patients had atonic or tonic drop attacks, >60% had atypical absences, and most had generalized slow spike and wave complexes, accompanied or not by focal or multifocal EEG discharges (Kuzniecky et al., 1994). This picture, resembling a symptomatic generalized epilepsy syndrome, was not observed in any of our patients, and also was not reported in other series (Villani et al., 2003; Gil-Nagel et al., 2005; Kuchukidze et al., 2008). Nonetheless, within the spectrum of CBPS due to BP-PMG, familial cases may display a less severe picture (Guerreiro et al., 2000). All our patients with bilateral ULG had cognitive dysfunction, mirroring the situation in BP-PMG and suggesting that both entities can interfere with cortical function in a more diffuse fashion.

The association of BP-ULG with HS has been shown previously (Teixeira et al., 2003; Villani et al., 2003). Although this is not a universal finding (Nikas et al., 2008), recent series have found both disorders to co-occur in up to half of patients with ULG (Kuchukidze et al., 2008). In our series, 30% had histopathologically confirmed HS, suggesting that BP-ULG should be included in the group of extratemporal lesions potentially associated with dual pathology (Li et al., 1999; Lawn et al., 2000; Fig. 2). These findings suggest that HS may be either related to the same hypoxic-ischemic episode responsible for the ULG or result from secondary epileptogenesis. In practice, it may be useful to subdivide patients with BP-ULG into those with BP-ULG *only* and those with BP-ULG *plus HS*. This subdivision is likely to have therapeutic relevance, since BP-ULG *plus HS* patients may need resection of both lesions. In fact, we believe the reason that three of our patients with dual pathology and more than one seizure type—a negative prognostic factor for surgical treatment—had favorable results was the resection of both, the hippocampus and the ulegyric cortex (Li et al., 1999). The side of the HS was always concordant with the side of seizure onset, and it is significant that a unilateral epileptogenic zone was identified in all five patients who underwent presurgical evaluation. This suggests that mechanisms of hyperexcitability are not homogeneous in these destructive pathologies, and therefore the presence of bilateral lesions should not preclude surgical consideration.

The best preoperative evaluation approach in patients with BP-ULG is still open to debate. Although we used intracranial electrodes in the majority of operated patients to cover perisylvian and temporal lobe regions, results were compatible with the electroclinical and imaging pictures. Those patients with dual pathology and a pattern of temporal-plus, perisylvian, and temporolimbic semiology had concomitant seizure onset in the two lesions. The one with ULG only had onset around this lesion. Finally, the patient with a very typical electroclinical picture of unilateral mesial temporal lobe epilepsy without perisylvian features was rendered seizure-free with an ATL. Therefore, further understanding of the electroclinical picture of this entity coupled with functional imaging findings may allow consideration of noninvasive approaches complemented by intraoperative ECoG and cortical stimulation.

Refractory seizures are frequent in patients with BP-PMG (Kuzniecky et al., 1993; Barkovich et al., 1999); however, surgical strategies for CBPS due to BP-PMG have been limited to callosotomies to alleviate drop attacks (Kuzniecky et al., 1994), and a resective approach has been ruled out. On the contrary, BP-ULG, its destructive counterpart, often leads to an epileptic picture amenable to resective surgery. The gliotic features of ULG apparently translate into localized unilateral epileptogenesis, and our results suggest that BP-ULG, with or without HS, may identify an underreported surgically remediable epilepsy syndrome. Increased awareness about BP-ULG is likely to generate further reports and lead to the incorporation of the BP-ULG terminology into the epileptologic literature.

Disclosure

Dr. Palmini reported board membership and receiving payment for lectures and travel from Novartis, Abbott, Janssen-Cilag, and Eli Lilly; receiving payment for manuscript preparation from Novartis, Abbott, and Janssen-Cilag; and receiving payment for organization of preceptorships and workshops paid to fund fellowships from Novartis and Biogen. All other authors have no conflicts of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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