Original article

Epileptic Disord 2013; 15 (4): 417-27

Congenital hemiparesis, unilateral polymicrogyria and epilepsy with or without status epilepticus during sleep: a study of 66 patients with long-term follow-up

Roberto Horacio Caraballo, Ricardo Oscar Cersósimo, Pablo Sebastián Fortini, Lorena Ornella, María Celeste Buompadre, Carolina Vilte, Juan Pablo Princich, Natalio Fejerman

Department of Neurology, Hospital Nacional de Pediatría Juan P Garrahan, Buenos Aires, Argentina

Received April 08, 2013; Accepted August 28, 2013

ABSTRACT – *Aim*. We retrospectively analysed the electroclinical features, treatment, and outcome in patients with unilateral polymicrogyria (PMG), focussing on epileptic syndrome with or without encephalopathy, with status epilepticus during sleep (ESES) or continuous spikes and waves during slow sleep (CSWS) syndrome. *Methods*. From June 1990 to December 2012, 39 males and 27 females, aged 5-26 years, were studied. We did not include patients with bilateral PMG or cases with unilateral PMG associated with other cerebral lesions. The mean follow-up period was 12 years (range: 3-22 years). *Results*. Mean age at epilepsy onset was 6.5 years. Focal motor seizures occurred in all cases and 25 had secondary generalised seizures. Six patients also had complex focal seizures. Interictal EEG recordings showed focal spikes in all cases. For 43 of 53 patients with epilepsy, aged 2-9.5 years, the electroclinical features changed. An increase in frequency of focal motor seizures was reported in 20 patients, negative myoclonus occurred in 32 patients, atypical absences in 25 patients, and positive myoclonus in 19 patients. All patients had a continuous symmetric or asymmetric pattern of spike-wave activity during slow-wave sleep. *Conclusion*. For patients presenting with congenital hemiparesis, negative or positive myoclonus, and absences and focal motor seizures with ESES/CSWS, unilateral PMG should be considered. Brain MRI is mandatory to confirm this cortical malformation. The most commonly used treatments were clobazam, ethosuximide, and sulthiame, alone or in combination. For refractory cases, high-dose steroids were administered and surgery was performed in two patients. Outcome was relatively benign.

Key words: congenital hemiparesis, epilepsy, negative myoclonus, continuous spikes and waves, sleep, unilateral polymicrogyria

Correspondence:
Roberto Caraballo,
Department of Neurology,
Hospital de niños "Prof Juan P Garrahan",
Combate de los Pozos 1881,
Buenos Aires, CP 1245, Argentina
<rhcaraballo@arnet.com.ar>

doi:10.1684/epd.2013.0612

Polymicrogyria (PMG) is secondary to abnormal cortical organisation. In PMG, the neurons reach the cortex but do not form normal cortical or intracortical connections and result in multiple small gyri. The classic form is represented by four-layered polymicrogyric cortex with a molecular layer, an organised intercellular layer, a cell-sparse layer, and a slightly unorganised inner cellular layer. However, a broad range of histological abnormalities has been found including cases with an unlayered and completely unorganised cortex (Barkovich *et al*., 1996; Palmini, 2000; Kuzniecky and Barkovich, 2001; Barkovich *et al*., 2001). PMG may be generalised, focal, or multifocal (Barkovich *et al*., 1996). Unilateral PMG may affect the whole hemisphere or only part of it. Large malformations are associated with hypoplasia of the affected hemisphere (Guerrini *et al*., 1993).

Recently, in a new classification proposal of malformations of cortical development, PMG was divided into four groups: A) with schizencephalic clefts or calcifications, presumably due to infection or vascular causes; B) without clefts or calcifications, which may be genetic or disruptive; C) as part of genetically-defined multiple congenital anomaly syndromes (some of which have an atypical histology); and D) in conjunction with inborn errors of metabolism (also with atypical histology) (Barkovich *et al*., 2012).

Colamaria and co-workers (1989) reported a boy with congenital hemiparesis, unilateral PMG, and epilepsy. The authors described an ictal asterixis, an electroclinical phenomenon that, according to the polygraphic EEG recording, corresponded to a negative myoclonus (Colamaria *et al*., 1989). Subsequently, patients with congenital hemiparesis, unilateral PMG, and a particular type of epilepsy have been published (Colamaria *et al*., 1991; Caraballo *et al*., 1992, 1997, 1999; Guerrini *et al*., 1993, 1996, 1998a). These patients started with focal motor seizures evolving into particular electroclinical features, characterised by myoclonias, pseudoataxia, atonic seizures, and absences. The interictal EEG showed bilateral, symmetric and asymmetric, continuous or subcontinuous spikes and spike-waves during slow sleep, with a more benign course than that in patients with epilepsy associated with cortical dysplasias (Caraballo *et al*., 1992, 1997, 1999; Guerrini *et al*., 1993, 1996, 1998a; Aicardi, 1994; Dalla Bernardina *et al*., 1996). Subsequently, more detailed electroclinical descriptions have been reported, confirming favourable evolution (Caraballo *et al*., 2007). Bilateral perisylvian polymicrogyria or congenital bilateral perisylvian syndrome has been described (Barkovich, 2010, Barkovich *et al*., 2012; Guerrini and Barba, 2011).

PMG may occur as an isolated lesion or associate with different entities (Guerrini and Barba, 2011). PMG has been associated with different chromosomal abnormalities (Leventer *et al*., 2008; Dobyns *et al*., 2008 Jaglin *et al*., 2009; Barkovich, 2010). PMG has also been related to mutations of several genes, such as *SRPX2, PAX6, TBR2, KIAA1279, RAB3GAP1,* and *COLI8A1* (Glaser *et al*., 1994; Sertié *et al*., 2000; Brooks *et al*., 2005; Aligianis *et al*., 2005; Roll *et al*., 2006; Baala *et al*., 2007). In addition, copy number variations have been described (Guerrini and Parrini, 2010).

Here, we retrospectively analysed the electroclinical features, treatment, and outcome in 66 patients with unilateral PMG, focussing on epileptic syndrome with or without encephalopathy, with status epilepticus during sleep (ESES) or continuous spikes and waves during slow sleep (CSWSS) syndrome, with long-term follow-up.

Material and methods

From June 1990 to December 2012, 66 patients with congenital hemiparesis associated with unilateral PMG, with or without epilepsy, were included for investigation. We did not include patients with bilateral PMG or cases with unilateral PMG associated with schizencephaly, porencephaly, heterotopias, or ulegyria. The mean period of follow-up was 12 years (range: 3-22 years) with repeat clinical examinations and EEGs. Video-EEG recordings were carried out in 15 patients. Polygraphic EEG recordings were not performed. The lack of polygraphic EEG recordings is a limitation of this study. However, all the myoclonic seizures were observed by the first author, and in some patients, the seizures were also registered by video-EEG recording. Based on clinical phenomenon rather than EEG abnormalities, we were able to distinguish whether the myoclonus was negative or positive. Computed tomography (CT) and MRI was obtained in all cases. All patients were psychometrically evaluated with the Wechsler Intelligence or Terman Merrill Scales. Antiepileptic drugs (AEDs) were given in all cases with epilepsy, and modified according to clinical and EEG evolution. Therapeutic alternatives, such as the ketogenic diet and surgery, were also considered. Karyotypes and metabolic investigations were performed in 61 and 6 patients, respectively.

EEG recordings were performed with the 10-20 international system using 22 electrodes. Serial EEG recordings during wakefulness and sleep were obtained for all patients. We analysed seizure onset, semiology, distribution, and frequency, as well as interictal and ictal EEG findings.

MRI was performed on a 0.5-T and 1.5-T scanner for 35 and 36 patients, respectively. Intermediate- and T2-weighted axial and coronal images and T1-weighted sagittal images were obtained for all patients.

Results

General features

Thirty-nine males and 27 females, aged 5-26 years (mean: 15 years), were studied. Congenital hemiparesis was present in 64 patients, affecting limbs on the left side in 36 and on the right side in 28 cases. Sixty patients with hemiparesis had a mild degree of spasticity and four a moderate degree. Mental impairment was mild in 35 cases (IQ: 60-69) and moderate in 25 (IQ: 50-59). Six patients had a normal IQ. Brain CT and MRI showed unilateral PMG, localised in the fronto-temporal region in 39 cases, in the fronto-temporal and parietal regions in 5 cases, and in the parieto-occipital regions in 22 (*figures 1 and 2*). The CT showed periventricular calcifications associated with PMG in 5 patients.

A personal history of febrile seizures was found in 10 cases (19%) and a family history of febrile seizures and epilepsy was found in 3 and 2 cases, respectively.

Fifty-nine cases were sporadic, 5 patients had congenital cytomegalovirus, 1 patient had Stickler syndrome, and another was a familial case.

Seizure manifestations and EEG findings

Fifty-three of 66 patients (80%) had epilepsy. The mean and median age at onset of epilepsy was 6.5 and 4 years, respectively (range: 0.5-13 years). Focal motor seizures occurred in all cases and 25 had secondary generalised seizures. Six patients also had complex focal seizures. Seizures occurred only during wakefulness in 30 patients, during sleep in 8, and both during wakefulness and sleep in 15 cases. The duration of the seizures was brief (less than 5 minutes) in 19 patients, moderate (between 5 and 10 minutes) in 28, and prolonged (more than 15 minutes) in 6. During this initial period, no other types of seizure were documented.

Interictal EEG recordings showed unilateral fronto-temporal spikes in 25 cases, unilateral fronto-central spikes in 7, and parieto-occipital spikes in 10. Bilateral spikes, predominantly in the dysplastic hemisphere, were observed in 11. In 10 patients, the EEG abnormalities occurred only during sleep. In all but 19 cases with spikes during wakefulness, the EEG abnormalities increased during sleep. In addition to the spikes, 45 patients also had focal fast polyspikes and slow waves, especially during sleep, consistent with a structural cause. Hyperventilation did not increase seizure frequency. Intermittent photic stimulation was negative in all cases (*table 1*).

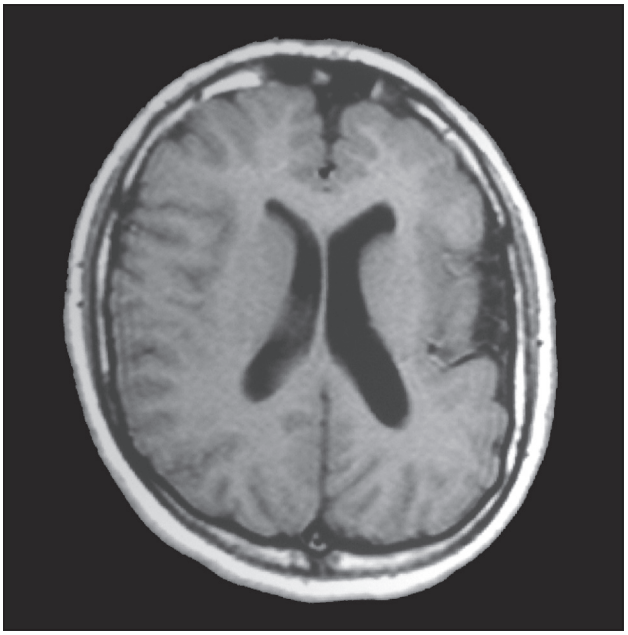

Figure 1. Axial T1-weighted MRI sequence showing left fronto-parietal PMG with ipsilateral hemisphere atrophy in a 10-year-old boy.

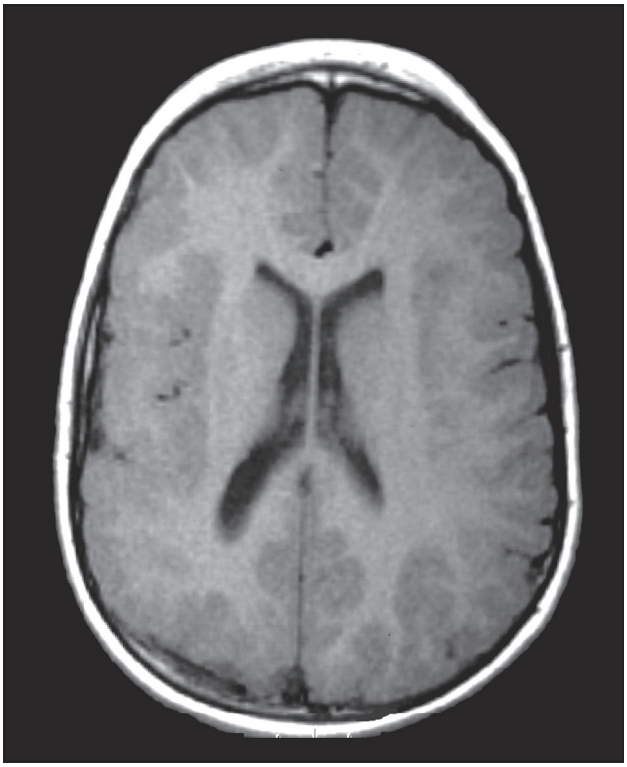

Figure 2. T1-weighted MRI sequence showing right hemisphere atrophy with PMG in the left parieto-occipital cortex in a 9-year-old boy.

Electroclinical changes

Between ages 2 and 9.5 years (mean: 6; median: 5), an evident change in terms of seizures and EEG

Table 1. Neuroradiological findings, initial electroclinical features, and treatment in 66 patients with unilateral PMG.

Gender	39 Male; 27 Female
Congenital hemiparesis **No hemiparesis**	64 2
Localisation of PMG	Fronto-temporal: 39 Fronto-temporo-parietal: 5 Parieto-occipital: 22
Mental impairment	Normal IQ: 6 Mild: 35 Moderate: 25
Epilepsy	53/66 (80%)
Median age at onset of epilepsy	4 years (R: 0.5-7 years)
Type of seizure at onset	Motor focal seizures with or without secondary generalisation Rare complex focal seizures
Interictal EEG	Focal abnormalities: 55 Bilateral abnormalities: 11
AEDs used before worsening of seizures	PHB, PHT, CBZ, OXC, VPA, TPM, LTG, CLB

PHB: phenobarbital; PHT: phenytoin; CBZ: carbamazepine; OXC: oxcarbazepine; VPA: valproic acid; TPM: topiramate; LTG: lamotrigine; CLB: clobazam.

occurred. This electroclinical change was observed in 43 of 53 patients (81%) with epilepsy. An increase in frequency of focal motor seizures with or without secondary generalised tonic-clonic seizures occurred in 20 patients (46.5%), negative myoclonus occurred in 32 patients (74.4%), associated gait instability in 20, drop-attacks in 7, and diminished motor initiative in one hemibody in 5. Atypical absences occurred in 25 patients (58%) and positive myoclonus in 19 cases (44.4%).

In the period of three months before the onset of the electroclinical change, the EEG recordings showed an increase in interictal abnormalities. During sleep, more frequent and bilateral spikes were recorded predominantly in the anterior region and in the dysplastic hemisphere (*figure 3*). Asymmetric and symmetric bilateral spikes and spikes and waves were observed on EEG during wakefulness in all cases during this period of electroclinical change. Some of these bilateral discharges, especially those that were subcontinuous, were associated with negative myoclonus (*figure 4*). The discharges became more frequent during sleep in all patients and featured the continuous symmetric and asymmetric pattern of spike-wave activity during slow-wave sleep in 15 and 28 cases, respectively (*figures 5 and 6*). The bilateral discharges were observed in less than 80% of slow sleep in 14 of these children.

The following cognitive disturbances were observed during the period of electroclinical change: attention deficit hyperactivity disorder in 22 (51%), language deterioration (non-verbal agnosia) in 12 (27.8%), aggressiveness in 12 (27.8%), memory deficit in 10 (23.2%), impaired temporo-spatial orientation in 9 (20.9%), non-verbal communication deficit in 9 (20.9%), and loss of bladder control in 3 patients (6.9%). Intellectual deterioration was observed in 28 patients (65.1%) (*table 2*).

Treatment

From the onset of epilepsy until the appearance of changes in electroclinical features, patients received different AEDs: phenobarbital in 10, carbamazepine in 9, phenytoin in 3, oxcarbazepine in 9, valproic acid in 8, and 3 patients each with valproic acid in combination with carbamazepine, oxcarbazepine, and clobazam, respectively.

During the phase of electroclinical change, no response or worsening of electroclinical features was observed using the following AEDs: valproic acid in 32 patients, lamotrigine in 14, topiramate in 14, carbamazepine in 13, oxcarbazepine in 12, phenobarbital in 12, primidone in 8, clonazepam in 6, levetiracetam in 5, ethosuximide in 3, and sulthiame in 2. Some of these AEDs were prescribed prior to consultation in the centres participating in this study and all of them, except ethosuximide, clobazam, sulthiame, levetiracetam, and clonazepam, exacerbated the electroclinical features of ESES/CSWS in the majority of patients. A switch of these AEDs to ethosuximide, clobazam, or sulthiame may be the first treatment step to significantly improve the electroclinical pattern.

A positive response was observed using the following AEDs, alone or in combination, as well as with other treatment options: ethosuximide in 2 patients; clobazam in 2; sulthiame in 3; clobazam and ethosuximide in 8; clobazam and sulthiame in 8; ethosuximide and valproic acid in 5; ethosuximide and sulthiame in 5; levetiracetam and ethosuximide in 2; ethosuximide, clobazam, and sulthiame in 3; corticosteroids and valproic acid in 2; corticosteroids and sulthiame in 2; corticosteroids, ethosuximide, and clobazam in 1; the ketogenic diet and sulthiame in 1; and the ketogenic diet, clobazam, and ethosuximide in 1. Epilepsy surgery was performed with good results in 2 patients. In one of these patients, a partial lesionectomy

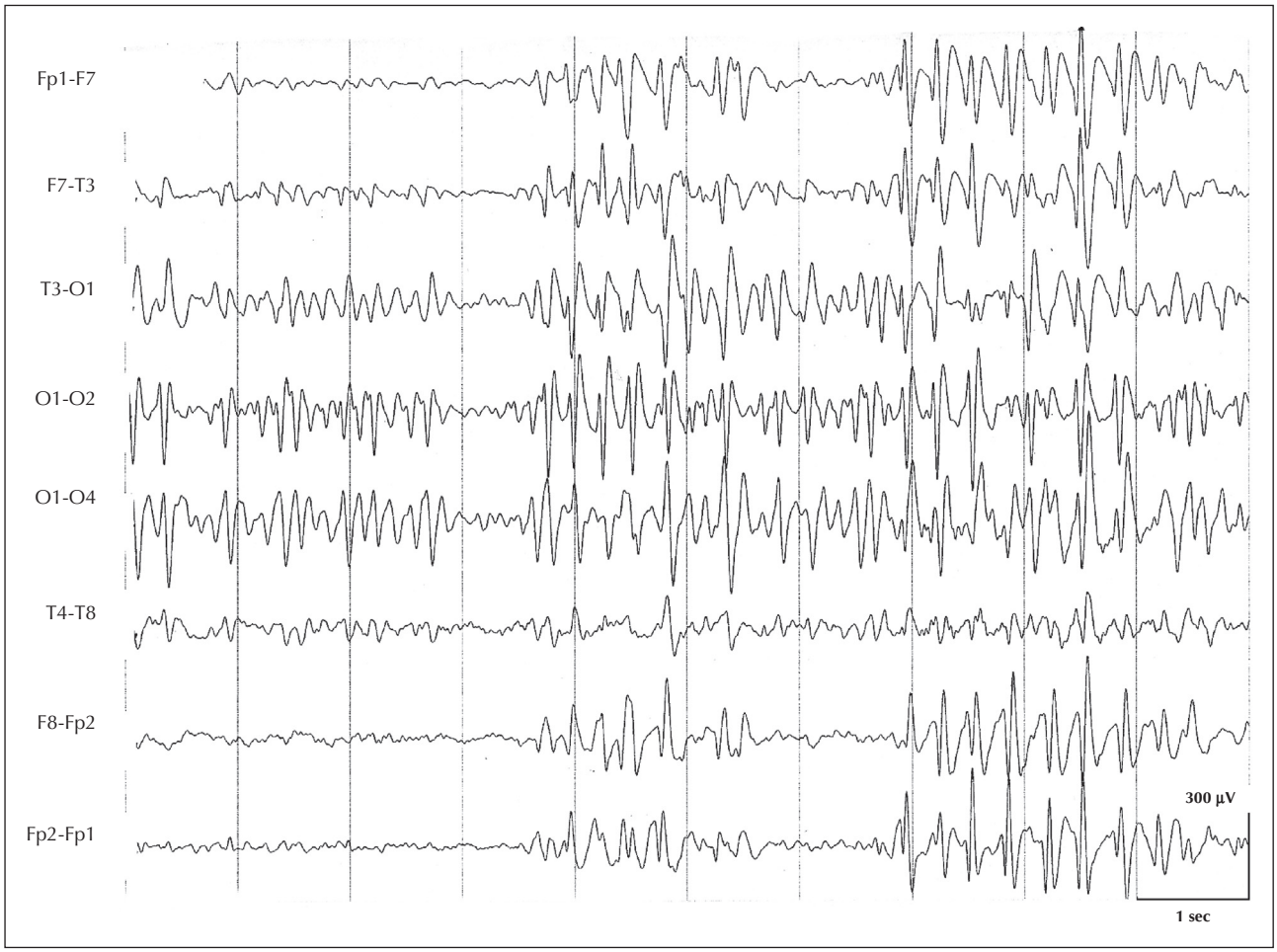

Figure 3. The same patient as in *Figure 2*. EEG recording during wakefulness shows occipital spikes and bilateral continuous spike-wave activity, clearly dominant in posterior regions.

was performed to avoid further motor deficit and in the other, who had unilateral PMG affecting the whole hemisphere associated with severe hemiparesis, a hemispherectomy was performed.

A partial response was observed in 15 patients using the following AEDs: sulthiame in 2 patients, valproic acid and ethosuximide in 2, clobazam and ethosuximide in 1, levetiracetam in 2, and diazepam in combination with sulthiame in 1.

Outcome

Average follow-up after the period of electroclinical change or onset of ESES/CSWS was 13.5 years (range: 3-20 years) for 43 children. ESES/CSWS disappeared after a time, ranging from 2 to 9 months. Seven patients had one or more relapses. At the last control, 3 patients remained seizure-free. One of them had undergone surgery. The EEG recordings showed isolated focal spikes in these 3 patients. Twenty-four patients had sporadic seizures, 5 had seizures every six months, 5 had two seizures a month, 3 had monthly seizures, and 3 had weekly seizures. The EEG in these 40 patients showed focal spikes in 25, multifocal spikes in 3, and bilateral asymmetric spikes in 12 patients.

In patients who became seizure-free and those who had a more than 75% seizure reduction, school performance and IQ improved significantly. They returned to baseline cognitive development. Cognitive deterioration remained unchanged in 5 patients (11%).

The remaining 10 patients with epilepsy without electroclinical changes or ESES/CSWS had sporadic seizures except one, who is currently seizure-free.

Discussion

The patients in this series had non-progressive encephalopathy or cerebral palsy, characterised by congenital hemiparesis associated with mental impairment and epilepsy. These patients frequently developed focal seizures with or without secondary

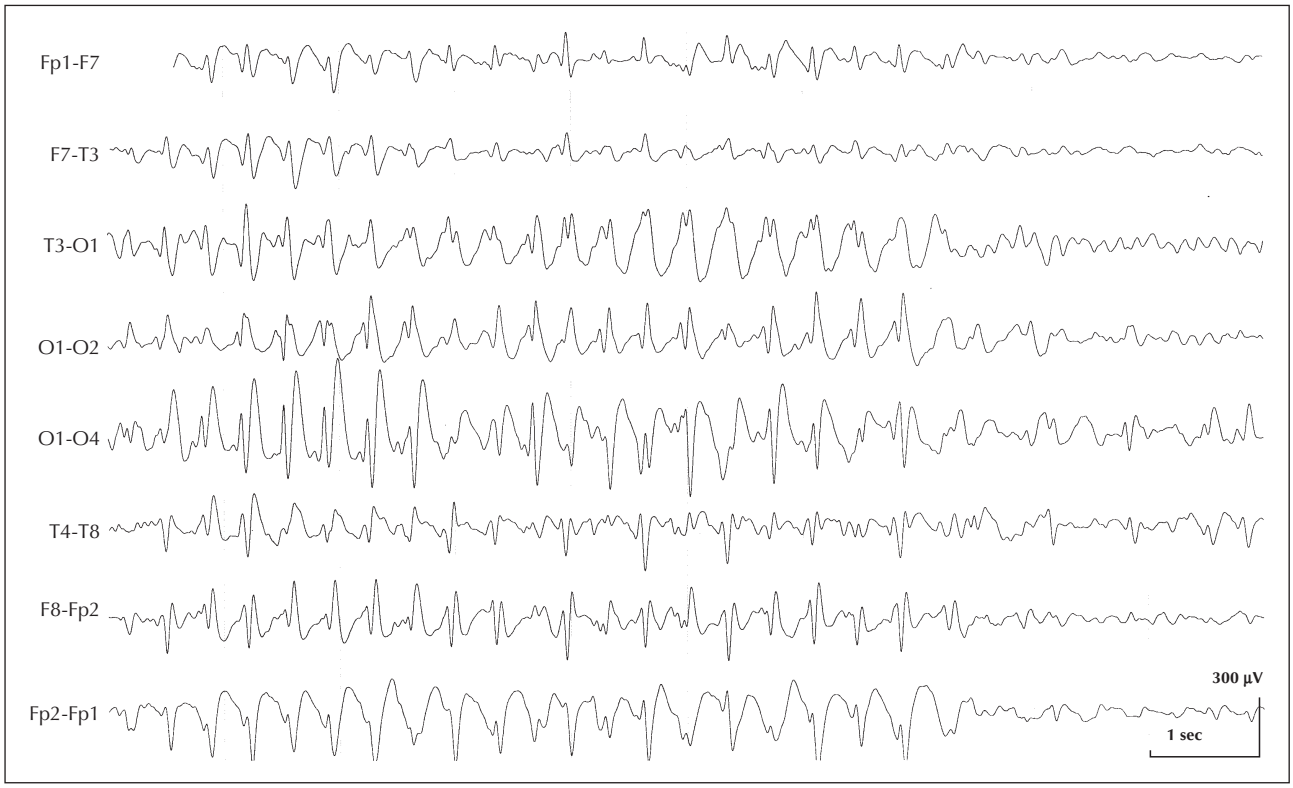

Figure 4. A 6-year-old boy with right fronto-parietal PMG.
The EEG recording during wakefulness shows asymmetric rhythmic bilateral spike-wave discharges with repetitive negative myoclonia, characterised by a sudden loss of muscle tone in the left upper limb when the patient extended both upper limbs in an antigravity position.

generalised tonic-clonic seizures, followed by a particular electroclinical pattern of negative and positive myoclonias, atypical absences, and an increase of focal seizures and ESES/CSWS, secondary to unilateral PMG, with relatively good outcome. The majority of these cases had mild, and less frequently, moderate, but never severe, spastic hemiparesis. The majority of the patients also had mild or moderate mental impairment. With regards to EEG findings, 43/53 of the patients had ESES/CSWS with more or less than 80% of the spike-wave index. If we consider more wide-reaching EEG inclusion criteria, all the cases with this particular electroclinical pattern may correspond to the ESES/CSWS syndrome. PMG is the most frequent structural cause of ESES/CSWS syndrome (Caraballo *et al*., 2013). In children with PMG, early recognition of this entity is important to adequately manage this particular type of epilepsy.

A review of patients with hemiparetic cerebral palsy showed that in 7% of the cases, it was associated with unilateral cortical dysplasias (Wiklund *et al*., 1991). PMG is the most common cause of congenital hemiplegia (Barkovich, 2010; Caraballo *et al*., 2007).

In our series, most cases were sporadic and only one was familial. Inheritance of PMG, including both cases of affected parents and siblings, has been suggested in several reports (Yoshimura *et al*., 1998; Bartolomei *et al*., 1999; Caraballo *et al*., 2000), most commonly through X-linked transmission. Chang and co-workers (2006) identified four families in which unilateral right-sided PMG, based on MRI, was present in more than one individual, with pathological confirmation in one. These findings strongly suggest that unilateral PMG can have a germline genetic aetiology (Chang *et al*., 2006).

Bilateral continuous or subcontinuous spike-wave discharges during slow-wave sleep with higher voltage over the dysplastic areas indicate a mechanism of secondary bilateral synchrony (SBS), presumably correlating with atypical absences and epileptic negative myoclonus causing gait instability (Dalla Bernardina *et al*., 1989, 1996). Kobayashi and co-workers (1992, 1994) suggested that SBS implies an initial diffusion of discharges through the corpus callosum, with or without intervention of centro-encephalic structures, during generalisation. Spencer and co-workers (1985) also hypothesized about mesencephalic/diencephalic mechanisms for SBS (Spencer *et al*., 1985).

Polymicrogyric abnormalities are often more widespread than can be shown by MRI and an

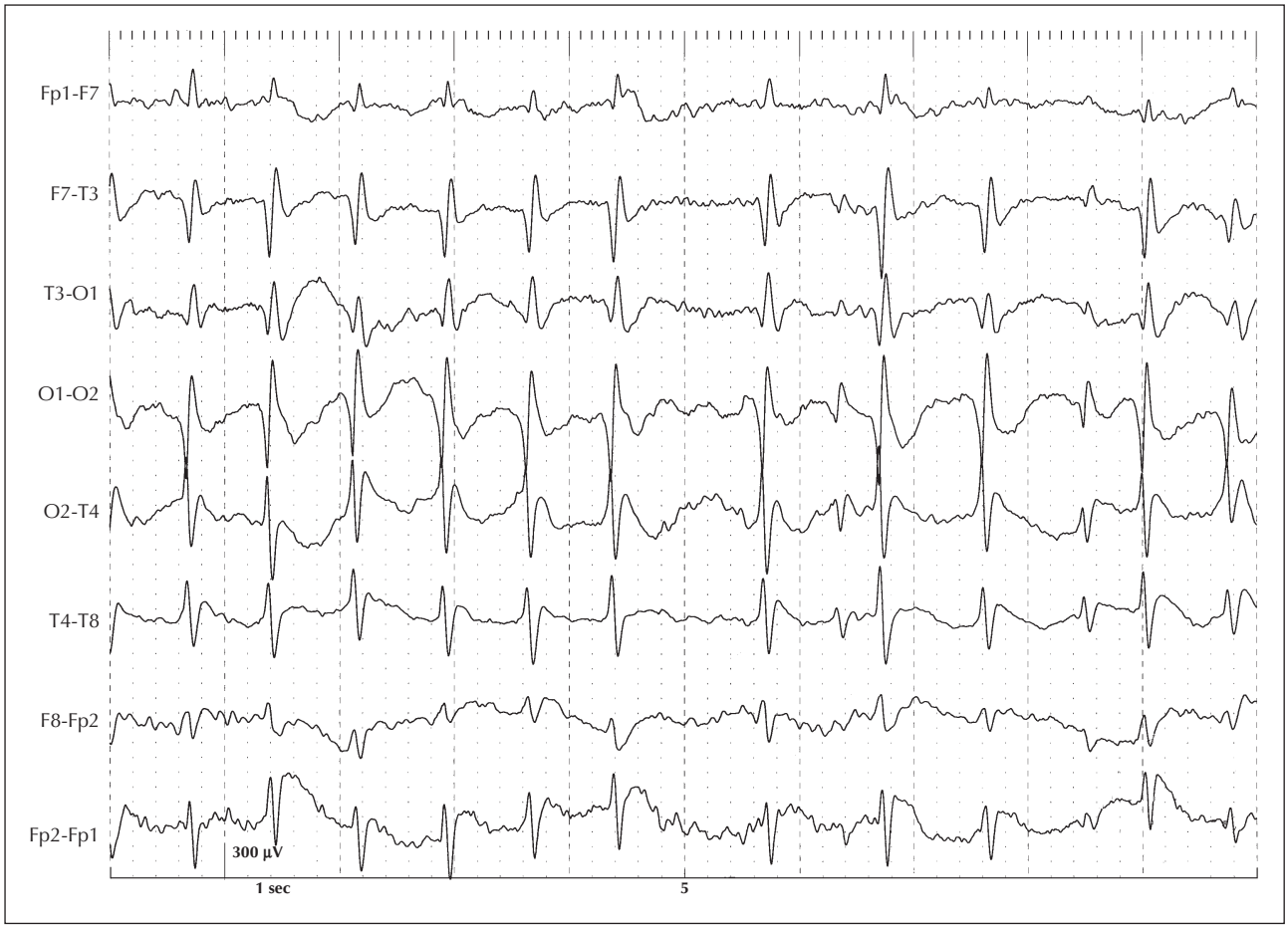

Figure 5. Slow sleep EEG recording shows asymmetric continuous spike-wave activity dominant in the left hemisphere.

extensive area of cortical abnormality may facilitate SBS. Enhanced excitation arising from the abnormal cortex in PMG and reduced inhibitory activity in the cortical surface surrounding PMG can trigger hypersynchronous neuronal discharges. For the majority of patients with unilateral PMG who develop status of epileptic negative myoclonus, the location of cortical dysplasia is fronto-temporal, which may explain the phenomenon of SBS.

Brain CT and particularly MRI are necessary to identify PMG in detail, and also search for other types of lesion that may be associated in the same patients. Unilateral PMG is most frequently located in the fronto-temporal regions and less frequently in the parieto-occipital regions. CT may show periventricular calcifications associated with PMG. These findings may suggest an infection with cytomegalovirus. An encephalomalacic lesion and/or porencephalic cyst associated with PMG may occur in the same patient and could represent a vascular phenomenon. Brain MRI may also show other types of malformation of cortical development, such as schizencephaly (SCHZ) and nodular periventricular heterotopia.

Previously, we published cases with a unilateral porencephalic cyst, with a similar electroclinical picture. However, in these cases, the cortical region surrounding the porencephalic lesion showed a polymicrogyric cortex which accounted for the electroclinical findings (Caraballo *et al*., 2007). This particular electroclinical pattern associated with unilateral PMG has not been described for other types of malformation of cortical development. In addition, we compared the electroclinical features of patients with unilateral PMG and closed-lip SCHZ. Both conditions are secondary to abnormal cortical organisation. Nevertheless, the patients with closed-lip SCHZ never developed electroclinical features due to SBS (Caraballo *et al*., 2004). The fact that continuous or subcontinuous spikes and waves during slow sleep due to SBS were found to be associated with unilateral PMG, but not with cases with other cortical malformations, may suggest that a unique anatomo-functional system is involved. A series of children with prenatal or perinatal unilateral thalamic injuries associated with symptomatic CSWS or sleep slow-wave over-activation were reported (Monteiro *et al*., 2001; Guzzetta *et al*.,

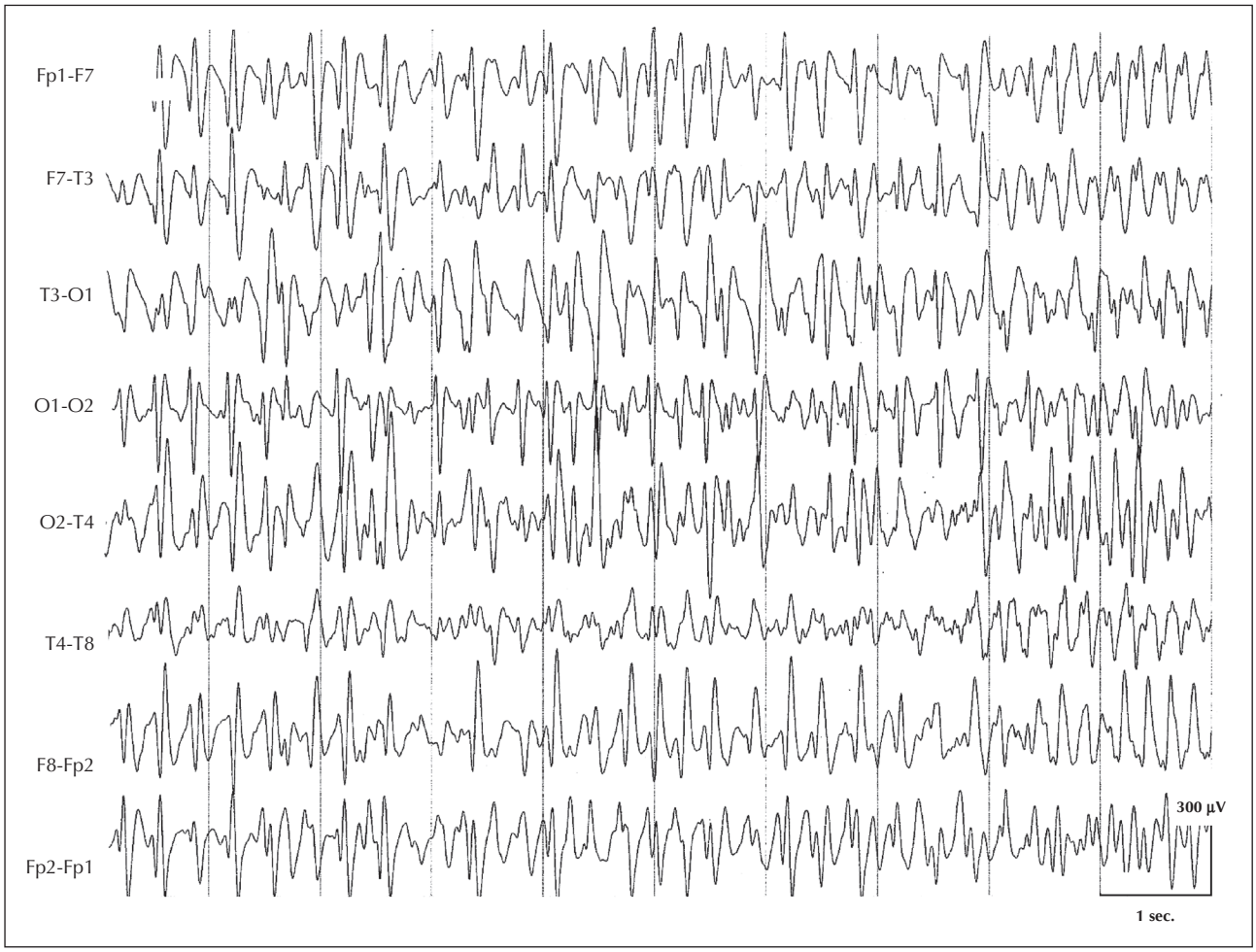

Figure 6. EEG recording during slow sleep shows diffuse continuous spike-waves.

2005; Kelemen *et al*., 2006). CSWS was also detected in children with shunted hydrocephalus, suggesting involvement of thalamo-cortical circuitries (Veggiotti *et al*., 1998; Ben-Zeev *et al*., 2004; Caraballo *et al*., 2008).

In cases with unilateral PMG without hemiparesis and mental impairment, the distinction between cryptogenic or idiopathic focal epilepsy with SBS may be more difficult. However, brain MRI findings will confirm the diagnosis.

Care should be taken in the selection of AED treatment. A probable association between certain AEDs and the appearance of continuous spike-wave activity with negative myoclonus has repeatedly been reported in children with benign childhood epilepsy exposed to carbamazepine, phenobarbital, phenytoin, and even valproate (Caraballo *et al*., 1989; Pratz *et al*., 1998; Guerrini *et al*., 1998b). This phenomenon has also been described in association with topiramate (Montenegro and Guerreiro, 2002). The majority of these cases were exposed to AEDs, effective against focal seizures, prior to the peculiar evolution of their epilepsy. In our experience, after the onset of continuous or subcontinuous electroclinical manifestations, the best results are initially obtained with valproic acid, benzodiazepines, and ethosuximide, either in monotherapy or in combination. Oguni and co-workers (1998) and Capovilla and co-workers (1999) stated that ethosuximide is the drug of choice to treat negative myoclonus. We also consider sulthiame to be a good option, both for non-lesional and unilateral PMG (Caraballo *et al*., 2007; Fejerman *et al*., 2012). Corticosteroid therapy may be an alternative (Caraballo *et al*., 2007). In cases refractory to these drugs, valproic acid, levetiracetam, and/or corticosteroids should be considered.

In refractory cases with hemiparesis and extensive unilateral PMG, total or subtotal hemispherectomy could be useful. In the planning for the surgical strategy, it should be considered whether the epileptogenic zone extends beyond the polymicrogyric lesion (Chassoux *et al*., 2008. Any surgical approach to treat epilepsy, secondary to PMG, should be viewed with extreme

Table 2. Electroclinical change in 43 of 53 cases with epilepsy and unilateral PMG.

Number and gender of cases	27 Male; 16 Female
Localisation of unilateral PMG	Fronto-temporal: 25 Fronto-temporo-parietal: 5 Parieto-occipital: 13
Affected hemisphere	Right: 24 Left: 19
Median age at worsening of epilepsy	5 years (R: 2-9.5 years)
Type of seizure	Negative and positive myoclonus Atypical absences Frequent focal seizures with or without SGTCS
EEG findings	CSWS > 80% 29 patients CSWS < 80% 14 patients
AEDs used	CLB, ETS, STM, ETS+VPA, LVT
Other treatments	Corticosteroids, KD, surgery

VPA: valproic acid; CLB: clobazam; ETS: ethosuximide; STM: sulthiame; LVT: levetiracetam; KD: ketogenic diet.

caution, and restricted to highly selected cases, given that: the outcome of seizures is favourable in most cases; the polymicrogyric cortex may retain its functional properties, at least in part; and its removal carries a high risk of producing neurological deficits (Guerrini and Barba, 2011).

With a careful selection of AEDs, a relatively benign course of epilepsy in patients with hemiparesis associated with unilateral PMG has repeatedly been reported (Caraballo *et al*., 1992, 1997, 2004; Aicardi, 1994; Guerrini *et al*., 1996).

Response to change of treatment is initially good for the majority of patients, but the evolution can vary. A significant number of patients may show one or more relapses of the same electroclinical picture. The seizures usually remit completely before adolescence and only a few patients continue with sporadic seizures after this period of age. Even though epilepsy in patients with cortical dysplasia is frequently refractory to AEDs, the majority of cases with unilateral PMG show a favourable outcome. Nevertheless, some of the patients in our series continued with seizures and we consider that the prognosis of epilepsy in patients with PMG is not as benign as that of idiopathic focal epilepsy in childhood, however, outcome is more favourable compared to epilepsy secondary to other types of cortical dysplasia.

Conclusion

In a patient presenting with congenital hemiparesis, particular electroclinical features characterised by negative myoclonus, absences, and focal motor seizures with continuous or subcontinuous spikes or spike-waves during slow-sleep, unilateral PMG should be considered. Brain MRI is mandatory in order to confirm this cortical malformation.

We believe it is important to recognise this particular association between focal PMG conditioning contralateral hemiparesis and the appearance of epilepsy with peculiar evolution, including one or more periods of frequent inhibitory seizures as an epileptic negative myoclonus expressing the SBS phenomenon.

In our study, the most commonly used treatments were clobazam, ethosuximide, and sulthiame, alone or in combination. In refractory cases, high-dose steroids were administered.

The prognosis of these patients with malformation of cortical development is relatively benign and thus adequate management may avoid cognitive deterioration and surgical intervention. □

Disclosures.
None of the authors have any conflict of interest to disclose.

References

Aicardi J. Epilepsies characterized by simple partial seizures. In: Aicardi J, ed. *Epilepsy in children*. 2nd Edition. New York: Raven Press, 1994, p. 130-64.

Aligianis I, Morgan N, Mione M, *et al*. Mutations of the catalytic subunit of RAB3GAP cause Warburg Micro syndrome. *Nat Genet* 2005; 37: 221-3.

Baala L, Briault S, Etchevers HC, *et al*. Homozygous silencing of T-box transcription factor EOMES leads to microcephaly with polymicrogyria and corpus callosum agenesis. *Nat Genet* 2007; 39: 454-6.

Barkovich AJ, Kuzniecky R, Dobyns W, Jackson G, Becker L, Evrard P. A classification scheme for malformations of cortical development. *Neuropediatrics* 1996; 27: 59-63.

Barkovich AJ, Kuzniecky R, Jackson G, Guerrini R, Dobyns W. Classification system for malformations of cortical development: update 2001. *Neurology* 2001; 57: 2168-78.

Barkovich AJ. Current concepts of polymicrogyria. *Neuroradiology* 2010; 52: 479-87.

Barkovich AJ, Guerrini R, Kuzniecky RI, Jackson GD, Dobyns WB. A developmental and genetic classification for malformations of cortical development: update 2012. *Brain* 2012; 135: 1348-69.

Bartolomei F, Gavaret M, Dravet C, Guerrini R. Familial epilepsy with unilateral and bilateral malformations of cortical development. *Epilepsia* 1999; 40: 47-51.

Ben-Zeev B, Kivity S, Pshitizki Y, Watemberg N, Brand N, Kramer U. Congenital hydrocephalus and continuous spike wave in slow-wave sleep: a common association? *J Child Neurol* 2004; 19: 129-34.

Brooks A, Bertoli-Avella A, Burzynski G, *et al*. Homozygous nonsense mutations in *KIAA1279* are associated with malformations of the central and enteric nervous systems. *Am J Hum Genet* 2005; 77: 120-6.

Capovilla G, Beccaria F, Veggliotti P, Rubboli G, Meletti S, Tassinari CA. Ethosuximide is effective in the treatment of epileptic negative myoclonus in childhood partial epilepsy. *J Child Neurol* 1999; 14: 395-400.

Caraballo R, Fontana E, Micheliza B, *et al*. Carbamazepina, assenze atipiche crisi atoniche e stato di PO continua del sonno (POCS). *Boll lega It Epil* 1989; 66/67: 379-81.

Caraballo R, Kochen S, Cersósimo R, Fejerman N. Unilateral pachygyria with congenital hemiplegia and peculiar type of epilepsy (Abstract). *Pediatr Neurol* 1992; 8: 398.

Caraballo R, Cersósimo R, Fejerman N. Un tipo particular de epilepsia en pacientes con hemiparesia congenita asociada a polimicrogiria o paquigiria unilateral. *Rev Neurol (Barc)* 1997; 25: 1058-63.

Caraballo R, Cersósimo R, Fejerman N. A particular type of epilepsy in children with congenital hemiparesis associated with unilateral polymicrogyria. *Epilepsia* 1999; 40: 865-79.

Caraballo R, Cersósimo R, Mazza E, Fejerman N. Focal polymicrogyria in mother and son. *Brain Dev* 2000; 22: 336-9.

Caraballo R, Cersósimo R, Fejerman N. Unilateral closed-lip schizencephaly and epilepsy: a comparison with cases of unilateral polymicrogyria. *Brain Dev* 2004; 26: 151-7.

Caraballo R, Cersósimo R, Fejerman N. Symptomatic focal epilepsies imitating atypical evolutions of idiopathic focal epilepsies. In: Fejerman N, Caraballo R, eds. *Benign focal epilepsies in infancy, childhood and adolescence*. Montrouge (France): John Libbey Eurotext, 2007, p. 221-39.

Caraballo RH, Bongiorni L, Cersosimo R, Semprino M, Espeche A, Fejerman N. Epileptic encephalopathy with continuous spikes and waves during sleep in children with shunted hydrocephalus: a study of nine cases. *Epilepsia* 2008; 49: 1520-7.

Caraballo R, Veggiotti P, Kaltenmeier M, *et al*. Encephalopathy with status epilepticus during sleep or continuous spikes and waves during slow sleep syndrome: a multicenter, long-term follow-up study of 117 patients. *Epilepsy Res* 2013; 105: 164-73.

Colamaria V, Grimau R, Sgro V, *et al*. Epilepsia focale con statu di punta-onda continua in sonno lento: asterixis critico in soggeto con emipachigiria. *Bol Lega It Epil* 1989; 66/67: 233-5.

Colamaria V, Franco A, Zamponi N. Emiplegia congenita, alterazioni corticale ed epilepssia. *Bol Lega It Epil* 1991; 74: 169-70.

Chang BS, Apse K, Caraballo R, *et al*. A familial syndrome of unilateral polymicrogyria affecting the right hemisphere. *Neurology* 2006; 66: 133-5.

Chassoux F, Landre E, Rodrigo S, *et al*. Intralesional recordings and epileptogenic zone in focal polymicrogyria. *Epilepsia* 2008; 49: 51-64.

Dalla Bernardina B, Fontana E, Michelizza B, Colamaría V, Capovilla G, Tassinari C. Partial epilepsies in childhood bilateral synchronization, continuous spike-waves during slow sleep. In: Manellis J, Bental E, Loeber N, Dreiffus F, eds. *Advances in Epileptology: XVIIth Epilepsy International Symposium*. New York: Raven Press, 1989, p. 295-302.

Dalla Bernardina B, Pérez-Jiménez A, Fontana E, *et al*. Electroencephalographic findings associated with cortical dysplasias. In: Guerrini R, Canapicchi R, Zifkin B, Andermann F, Roger J, Pfanner P, eds. *Dysplasias of cerebral cortex and epilepsy*. Philadelphia: Lippincott-Raven Publishers, 1996, p. 235-45.

Dobyns WB, Mirzaa G, Christian SL, *et al*. Consistent chromosome abnormalities identify novel polymicrogyria loci in 1p36.3, 2p16.1-p23.1, 4q21.21-q22.1, 6q26-q27, and 21q2. *Am J Med Genet A* 2008; 146A: 1637-54.

Fejerman N, Caraballo R, Cersosimo R, Ferraro SM, Galicchio S, Amartino H. Sulthiame add-on therapy in children with focal epilepsies associated with encephalopathy related to electrical status epilepticus during slow sleep (ESES). *Epilepsia* 2012; 53: 1156-61.

Glaser T, Jepeal L, Edwards JG, *et al*. PAX6 gene dosage effect in a family with congenital cataracts, aniridiaanophtalmia and central nervous system defects. *Nat Genet* 1994; 7: 463-71.

Guerrini R, Dravet C, Raybaud C, *et al*. Epilepsy and focal gyral anomalies detected by MRI: electroclinic, morphological correlations and follow-up. *Dev Med Child Neurol* 1993; 34: 706-8.

Guerrini R, Pammeggiani M, Bureau M, *et al*. Localized cortical dysplasia: good seizure outcome after sleep-related electrical status epilepticus. In: Guerrini R, Canapicchi R, Zifkin B, Andermann F, Roger J, Pfanner P, eds. *Dysplasias of cerebral cortex and epilepsy*. Philadelphia: Lippincott-Raven Publishers, 1996, p. 329-36.

Guerrini R, Genton P, Bureau M, *et al*. Multilobar polymicrogyria, intractable drop attack seizures, and sleep-related electrical status epilepticus. *Neurology* 1998a; 51: 504-12.

Guerrini R, Belmonte A, Genton P. Antiepileptic drug-induced worsening of seizures in children. *Epilepsia* 1998b; 39: S2-10.

Guerrini R, Parrini E. Neuronal migration disorders. *Neurobiol Dis* 2010; 48: 39-48.

Guerrini R, Barba C. Polymicrogyria and schizencephaly. In: Shorvon S, Andermann F, Guerrini R, eds. *The causes of epilepsies: common and uncommon causes in adults and children*. Cambridge: Cambridge University Press, 2011, p. 311-29.

Guzzetta F, Battaglia D, Veredice C, *et al*. Early thalamic injury associated with epilepsy and continuous spike-wave during slow sleep. *Epilepsia* 2005; 46: 889-900.

Jaglin XH, Poirier K, Saillour Y, *et al*. Mutations in the beta-tubulin gene TUBB2B result in asymmetrical polymicrogyria. *Nat Genet* 2009; 41: 746-52.

Kelemen A, Barsi P, Gyorsok Z, Sarac J, Szucs A, Halász P. Thalamic lesion and epilepsy with generalized seizures, ESES and spike-wave paroxysms - Report of three cases. *Seizure* 2006; 15: 454-8.

Kobayashi K, Ohtsuka Y, Oka E, Ohtahara S. Primary and secondary bilateral synchrony in epilepsy: differentiation by stimulation of interhemispheric small time differences during short spike-wave activity. *Electroencephalogr Clin Neurophysiol* 1992; 83: 93-103.

Kobayashi K, Nishibayashi N, Ohtsuka Y, Oka E, Ohtahara S. Epilepsy with electrical status epilepticus during slow sleep and secondary bilateral synchrony. *Epilepsia* 1994; 35: 1097-103.

Kuzniecky R, Barkovich J. Malformations of cortical development and epilepsy. *Brain Dev* 2001; 23: 2-11.

Leventer R, Martin C, Gajecka M, Shaffer L. Consistent chromosome abnormalities identify novel polymicrogyria loci in 1p36.3, 2p16.1-p23.1, 4q21.21-q22.1, 6q26-q27, and 21q2. *Am J Med Genet A* 2008; 146A: 1637-54.

Monteiro JP, Roulet-Perez JP, Davidoff V, Deonna T. Primary neonatal thalamic haemorrhage and epilepsy with continuous spike-wave during sleep: a longitudinal follow-up of a possible significant relation. *Eur J Paediatr Neurol* 2001; 5: 41-7.

Montenegro MA, Guerreiro MM. Electrical status epilepticus of sleep in association with topiramate. *Epilepsia* 2002; 43: 1436-40.

Oguni H, Uehara T, Tanaka T, Sunahara M, Hara M, Osawa M. Dramatic effect of ethosuximide on epileptic negative myoclonus: implications for the neurophysiological mechanism. *Neuropediatrics* 1998; 29: 29-34.

Palmini A. Disorders of cortical development. *Curr Opin Neurol* 2000; 13: 183-92.

Pratz JM, Garaizar C, García-Nieto ML, Madoz P. Antiepileptic drugs and atypical evolution of idiopathic partial epilepsy. *Pediatr Neurol* 1998; 18: 402-6.

Roll P, Rudolf G, Pereira S, *et al*. SRPX2 mutations in disorders of language cortex and cognition. *Hum Mol Genet* 2006; 15: 1195-207.

Sertié AL, Sossi V, Camargo AA, Zatz M, Brahe C, Passos-Bueno MR. Collagen XVIII, containing an endogenous inhibitor of angiogenesis and tumor growth, plays a critical role in the maintenance of retinal structure and in neural tube closure (Knobloch syndrome). *Hum Mol Genet* 2000; 9: 2051-8.

Spencer SS, Spencer DD, Williamson PD, Mattson RH. Effects of corpus callosum sections on secondary bilaterally synchronous interictal EEG discharges. *Neurology* 1985; 35: 1689-94.

Veggiotti P, Beccaria F, Papalia G, Termine C, Piazza F, Lanzi G. Continuous spikes and waves during sleep in children with shunted hydrocephalus. *Childs Nerv Syst* 1998; 14: 188-94.

Yoshimura K, Hamada F, Tomoda T, Wakiguchi H, Kurashige T. Focal pachy-polymicrogyria in three siblings. *Pediatr Neurol* 1998; 18: 435-8.

Wiklund L, Uvebrant P, Flodniar K. Computed tomography as an adjunct in etiological analysis of hemiplegic cerebral palsy: children born at term. *Neuropediatrics* 1991; 22: 121-8.