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Periodic lateralized epileptiform discharges: association with seizures*

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The clinical features and EEGs of 45 consecutive patients (40 adults and 5 children) who had periodic lateralized epileptiform discharges (PLEDs) were reviewed to determine the relationship between seizures and PLEDs. Focal encephalitis and ischemic stroke were the most frequent underlying processes for adult patients. All of the children, but only six of the adults, had long-lasting cerebral disorders whereas the remaining adults had acute or subacute illness. There were 38 patients (84.4%) experiencing a seizure disorder. Twenty-six of them had their first seizure during their acute illness, as the pattern of PLED was encountered. Eight cases had status epilepticus, and seven of them had epilepsia partialis continua. Nineteen patients had a recent seizure in the day when PLEDs were observed but not during EEG recording; 12 patients had their seizures within 10 days before the observation of PLED. PLEDs were grouped into three categories with respect to their extensions: lateralized to one hemisphere ($n = 22$), localized in one region ($n = 17$) and being prominent over one side with contralateral spread ($n = 6$). The last group was found to be more closely associated with frequent seizures or status epilepticus than the other two groups. Our results showed that PLEDs were highly correlated with recent seizures in the majority of the patients. These EEG findings may be considered as a manifestation of an increased neuronal excitability caused by different etiologies; but not an ictal pattern.

Key words: EEG; epilepsy; seizure; periodic lateralized epileptiform discharges; periodic EEG activity.

INTRODUCTION

Periodic lateralized epileptiform discharges (PLEDs), first mentioned by Chatrian[1], are peculiar EEG patterns consisting of unilateral, focal spike or sharp wave complexes with a periodic appearance usually at a rate of 1–2 seconds. PLEDs are usually observed in association with acute or subacute structural lesions of the brain with different etiologies[2–7]. More rarely, however, a toxic metabolic cause or a chronic cerebral disorder is responsible for the occurrence of this unique EEG phenomenon[8–11]. PLED is frequently, but not always, accompanied by clinical seizures[2, 3, 6, 12]. Although its pathophysiology is unknown, in recent years there have been some reports considering PLED as an ictal EEG pattern[13–15].

In this study we reviewed clinical and EEG features of 45 patients with PLED, with special emphasis on the relationship between this typical EEG pattern and seizures.

PATIENTS AND METHODS

We retrospectively evaluated the EEGs and case records of the patients with PLEDs observed in our EEG laboratory over the past 15 years. PLEDs were defined as spike and/or sharp wave and slow wave complexes, which occur at approximately regular intervals and persist during the EEG recordings[4]. The EEGs were performed on 8-, 16- and 32-channel machines (Alvar and Medelec DG Compact) using the 10–20 International system of electrode placement. Recordings included both bipolar and referential montages with a mean duration of 20 minutes. Every EEG was reviewed by two experienced electroencephalographers (BB and AG) and a resident in joint sessions.

Forty-seven consecutive patients over 15 years showed PLEDs on the EEG during admission. All patients' hospital charts and documents from the emergency room were provided and their clinical findings

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Table 1: Etiology of PLEDs.

Adults	Cases with seizures		Cases without seizures	
CNS infections		11		3
Focal encephalitis[a]	10		2	
Tuberculous meningitis	1		—	
Creutzfeldt–Jakob Disease	—		1	
Cerebrovascular Disease		11		3
Ischemic stroke	8		1	
Intracerebral hemorrhage	—		2	
Cerebral venous occlusion	1		—	
Tuberculous vasculitis	2		—	
Neoplasm		5		—
Undetermined[b]		4		—
Focal cerebral lesion of unknown etiology		2		1
Children		5		—
Progressive neurodegenerative disorders	3		—	
Undetermined[b]	2		—	

[a] Two with pathologically proven herpes simplex encephalitis; 10 with probable herpes simplex encephalitis (clinically and/or MRI supported); [b] cases with cryptogenic partial epilepsy.

and available laboratory features were evaluated. Two of them were excluded, since they had some deficient data on the medical records and 45 were reviewed concerning the etiology, the history of seizures and neurological state on admission.

The group comprised 40 adults (aged between 19–80; mean age 49.5 ± 18.2) and 5 children (aged between 1.5–14). The group had 154 EEG recordings, 8 with a single EEG, 13 with two EEGs, the remaining cases with more than two EEGs (with a mean of 5 EEGs). PLEDs were grouped into three categories with respect to their extensions:

(1) Prominent over one side with a slight contralateral spread ($n = 6$) (Fig. 1).

(2) Lateralized to one hemisphere ($n = 22$) (Fig. 2).

(3) Localized in one region ($n = 17$) (Fig. 3).

All relevant clinical and EEG features were compared to determine the correlation between PLEDs and seizures.

RESULTS

Final diagnoses of the patients with and without seizures are shown in Table 1. Central nervous system (CNS) infections and cerebrovascular disease (CVD) were the leading causes for the adult patients. Acute/subacute presentation at admission comprised 75.56% (34 patients) of the whole group. Long-standing cerebral disorders were present in only six adults whereas all the children had chronic cerebral disorders. Nine of the 11 patients with a chronic clinical course had an acute episode during admission. These acute episodes, which were also the reason for admission, consisted of increased seizure frequency or occurrence of status epilepticus and were followed by a deterioration in neurological state associated with seizures.

There were 38 patients (84.4%) with a history of seizures. Twenty-six (57.7%) had new onset of seizures during their acute illness, resulting in admission to the hospital. There were only seven patients who had never experienced clinical seizures. Partial seizures either simple/complex (11 patients) or with secondary generalization (17 patients) were the most frequently encountered seizure types, followed by generalized convulsions without known focal onset (8 patients) and infantile spasms (1 patient). In one patient the seizure type could not be determined. In five patients with complex partial seizures, the clinical origin of the seizure could not be lateralized. In 15 patients, PLEDs were contralateral to the clinical seizure origin and in another 5 patients the first side affected clinically was contralateral to the prominent side of the bilateral PLEDs. In the last three patients PLEDs were ipsilateral with seizures, but, in two of them, other epileptic abnormalities in the EEG concordant with the clinical seizure origin could be demonstrated.

Seven patients suffered from epilepsia partialis continua (EPC) and one patient had complex partial status epilepticus during admission. The patient with complex partial status epilepticus due to focal encephalitis recovered and his seizures were controlled with antiepileptic therapy. Two patients with EPC also had focal encephalitis; one of them died and the other patient recovered with mild neurological deficits and used antiepileptic therapy. One patient with EPC had tuberculous menengitis and died in spite of therapy.

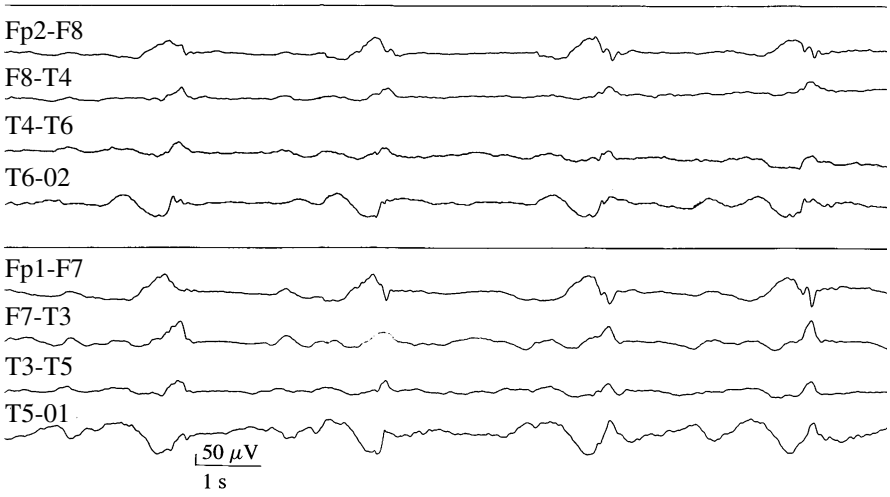

Fig. 1: A 52-year-old woman with herpes simplex encephalitis. She had epilepsia partialis continua on the right side, which did not resolve after treatment with IV clonazepam, phenytoin and phentobarbitone. She died in the intensive care unit 3 days after this EEG recording demonstrating PLED over left hemisphere with a contralateral spread.

Table 2: Association of extension of PLEDs with seizures and status epilepticus in 31 cases[a].

	Seizures (*n*)[b]	Status Epilepticus (*n*)[b]
Localized PLED	11 (6)	1 (1)CPSE
Lateralized PLED	14 (7)	3 (2)EPC
PLED prominent over one side with contralateral spread	6 (6)	4 (4)EPC

[a] In seven patients, the temporal relationship of seizures and PLED could not be exactly determined and in another seven patients there were no seizures (number in brackets); [b] indicates the number of patients who had seizures or status epilepticus on the *same day* as PLED. CPSE, complex partial status epilepticus; EPC, epilepsia partialis continua.

Another patient who had chronic epilepsy had CVD due to tuberculous vasculitis. Two patients with EPC had acute ischemic CVD; one of them had undergone carotid endarterectomy the previous day and also had diabetes mellitus. After control of the seizures with antiepileptic drugs, these two patients recovered with mild deficits. The last patient with EPC had Alper's disease with a progressive course.

The temporal relationship between PLED and seizures were exactly determined in 31 of the 38 patients who ever had seizures. Nineteen of them suffered from seizure(s) within 24 hours of PLED observation, six had seizures one day prior to the recording of the EEG and the remaining 6 had seizures within the previous 10 days.

Six patients, with PLED prominent over one side with contralateral spread, had either EPC (4 patients) or frequent seizures (2 patients) on the same day as PLED, regardless of etiology or clinical presentation (Table 2) (compare Fig. 1 with 2 and 3).

DISCUSSION

Our results are similar to the data combined from relevant reports which show that PLEDs are usually associated with acute/subacute presentation of the underlying process of the disease[11]. In patients with chronic cerebral disorders we usually found an acute episode (clinically increasing seizures) when PLEDs were observed. Westmoreland *et al.*[9] reported six patients with chronic epilepsy who had persistent PLEDs in their interictal EEGs. Among our cases with chronic disease, only two patients (4.4% of the main group) had PLEDs without acute-subacute exacerbation, which emphasizes the rarity of PLED in chronic cerebral disorders.

In our series PLEDs were associated with occurrences of seizures as mentioned in previous reports[1,5]. The seizures that occur in patients with PLEDs consist of partial (focal) sensorimotor seizures, as well as generalized seizures and complex partial status epilepticus and epilepsia partialis continua (EPC)[1,3,6,12]. EPC is a special type of localization-related motor epilepsy and represents a rare type of partial status epilepticus. A variety of acute and chronic cerebral lesions may be responsible for EPC[16]. Schomer emphasized that the onsets of EPC and PLEDs have many clinical overlapping features and these two conditions are more alike than dissimilar[17]. A parsimonious explanation for the association of EPC and PLEDs is that both represent partial status[15].

Schrader *et al.*[12] reported 20 of the 24 patients with PLEDs had seizures, 7 had focal motor alone, 10 had focal motor with secondary generalization, and 3 had generalized seizures without any observed focal features. Twelve patients had their first seizure when their

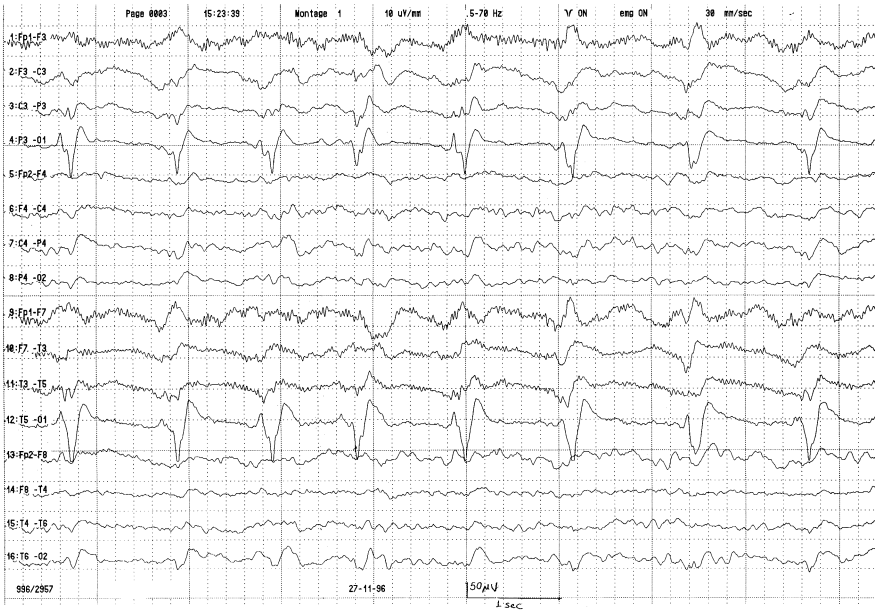

Fig. 2: A 58-year-old man with left middle cerebral artery territory infarction. He had frequent simple partial, motor seizures on the right side. His EEG showed PLED lateralized to the left hemisphere. The seizures were stopped with antiepileptic therapy.

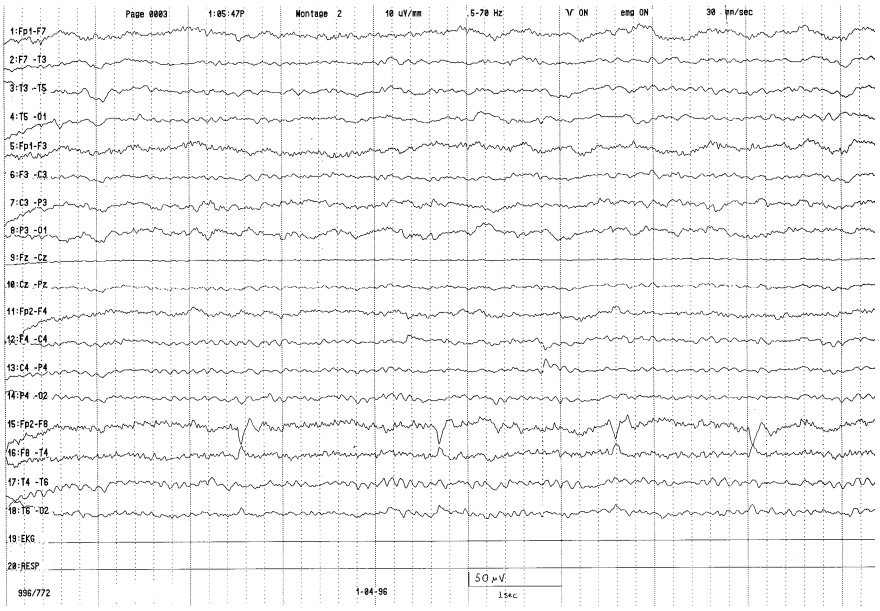

Fig. 3: A 37-year-old woman with herpes simplex encephalitis. She had no seizures. Her EEG showed PLED localized to the right frontotemporal region. After 12 days she recovered with IV acyclovir treatment.

PLEDs were found[12]. Their results are similar to our observations in a larger group.

The extension of PLED is also important regarding the association with seizures. Our results showed that PLEDs which appeared prominent over one side but with a slight contralateral spread had a stronger relationship with recent frequent seizures/status epilepticus than very strictly localized PLEDs. This phenomenon was not observed before. It remains questionable if this group represents another entity or a continuing spectrum with other forms of PLED. Terzano's report of seven geriatric patients with confusion as an epileptic phenomenon included an EEG example which also showed spread to the other hemisphere, which supports our finding[14].

Our coincidental finding that all the five children with PLEDs had a chronic cerebral disorder may indicate that the growing brain has somewhat different pathophysiologic adjustment; but the small number of children in our study makes the validity of our inter-

pretation suspect. Raroque *et al.*[18] reported that in a series of 18 children there were no significant clinical differences between PLEDs in children and adults, which contradicts the results of other reports[19,20].

Significant controversies still exist regarding the underlying pathophysiologic processes of PLED. In recent years case reports with PET and SPECT showed hypermetabolism and hyperperfusion in PLED foci, respectively[8,15]; but these findings are a reflection of increased neuronal activity rather than a specific marker of a seizure. The role of the associative basal ganglia circuit in the generation of periodic phenomenon was proposed with the description of a case with PLEDs confined to synchronized sleep which were not affected by surgical manipulation of the motor basal ganglia circuit[21].

Nei *et al.*[22] reported recently that PLEDs are the only EEG feature related to poor outcome in status epilepticus independent of etiology. Snodgrass[23] found that most of the EEGs with PLEDs were obtained within the first 4 days of seizure activity or status epilepticus and they postulated that the EEG phenomenon of PLEDs could be considered a part (late phase) of the status epilepticus. In our opinion PLEDs can be considered an activity, intimately associated with recent seizures, which is a manifestation of increased neuronal excitability caused by different etiologies. It is important to note that in our series and in a previous report[12], 1 in 6 of the patients had never experienced seizures. Little is known about the underlying mechanism causing periodic discharges and the retrospective nature of our clinical study, like all the other reports on this topic, do not allow definite conclusions; but PLEDs are observed in neurological practice as a substantial matter and the clinician must have a basic knowledge and understanding of these peculiar EEG phenomena. Future experimental studies should focus on the role of cellular mechanisms underlying periodicity.

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