

## First Unprovoked Seizure: Clinical and Electrographic Aspects

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### ABSTRACT

**Objective:** To evaluate classification, EEG tracings and neuroimage following the first episode of unprovoked epileptic seizure in a pediatric population. **Methods:** Patients diagnosed with first episode of unprovoked epileptic seizure from May 2000 to May 2005 were included. All subjects were submitted to EEG and cranial CT in the first 72 hours after the event. Seizures were classified according to the ILAE classification criteria of 1981. **Results:** 387 patients, 214 (55.3%) male, average age 4.2 years. Neuropsychomotor development was normal in 315 (81.4%) patients. Seizure classification: 167 (43.15%) generalized, tonic-clonic being the most frequent of these (105/62.85%), followed by typical absence (22/13.17%), clonic (20/11.98%), tonic (13/7.78%) and atonic (7/4.19%). Focal seizures: 220 (56.85%), complex partial with secondary generalization as the most common of these (81/36.82%). EEG was normal in 208 (53.75%) cases. Brain atrophy was the most frequent abnormality on cranial CT. **Discussion:** The majority of the children had normal neurodevelopment after a first unprovoked epileptic seizure. Partial seizures were more frequent than generalized seizures. Early EEG identifies interictal paroxysms or focal slowing in virtually half the patients. **Key words:** first seizure, electroencephalogram, tomography.

### RESUMO

#### *Primeira crise epiléptica não-provocada: aspectos clínicos e eletrográficos*

**Objetivo:** Avaliar a classificação, resultados de EEG e de neuroimagem após a primeira crise epiléptica não-provocada em uma população pediátrica. **Metodologia:** Pacientes atendidos entre maio de 2000 e maio de 2005 com diagnóstico de primeira crise epiléptica não-provocada. Todos foram submetidos a EEG e tomografia de crânio nas primeiras 72 horas após o evento. As crises foram classificadas segundo a Classificação da ILAE, 1981. **Resultados:** 387 pacientes, sendo 214 (55.30%) do sexo masculino, com idade média de 4.2 anos. O desenvolvimento neuropsicomotor foi normal em 315 (81.40%) pacientes. Classificação das crises: 167 (43.15%) generalizadas, das quais a mais freqüente foi a crise tônico-clônica (105/62.85%), seguida pelas crises de ausência típica (22/13.17%), clônica (20/11.98%), tônica (13/7.78%) e atônica (7/4.19%). Crises focais: 220 (56.85%), sendo a crise parcial complexa com generalização secundária a mais freqüente (81/36.82%). EEG normal em 208 (53.75%) casos. A anormalidade mais observada na tomografia de crânio foi atrofia cerebral. **Conclusões:** A maioria das crianças apresentou desenvolvimento neuropsicomotor normal após a primeira crise epiléptica não-provocada. Crises parciais foram mais freqüentes que as generalizadas. EEG realizado precocemente identifica paroxismos interictais ou alentecimentos focais em praticamente metade dos pacientes.

**Unitermos:** primeira crise, etiologia, eletroencefalograma, tomografia.

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## INTRODUCTION

Epileptic seizures represent one of the most frequent manifestations of neurological impairment in the pediatric population. Epileptic seizures can manifest themselves as positive or negative motor, sensorial, psychic and autonomic phenomena. Various definitions for epileptic seizures have been postulated. The existence of synchronic, abnormal, sporadic and generally self-limited brain activity seems to be a consensus. An incidence rate of a first epileptic seizure is unknown and estimated at 25 to 40 thousand cases/year in the United States<sup>(1,2)</sup>.

Epileptic seizures are considered unprovoked whenever they occur in the absence of immediate precipitating factors such as cranial trauma, metabolic disturbances (hypocalcemia, hypernatremia, hyponatremia, hypomagnesemia, hypothyroidism, hypoglycemia, hyperglycemia), brain hypoxia and drugs (theophylline, isoniazid, clozapine, phenothiazines,  $\beta$ -lactam antibiotics, tricyclic antidepressants, selective serotonin reuptake inhibitors, acyclovir,  $\beta$ -blockers, cocaine). Epileptic seizures precipitated by febrile states are also excluded<sup>(3)</sup>.

This article aims to define the main epidemiological aspects of pediatric patients that present with the first unprovoked epileptic seizure, considering clinical data, classification of the seizures, electroencephalographic and neuroimage findings. To accomplish that, we studied a cohort of patients followed in a tertiary pediatric hospital in the South of Brazil.

## METHODS

All patients admitted at the Pediatric Neurology Unit of Pequeno Príncipe Hospital between May 2000 and May 2005 with the diagnosis of first unprovoked epileptic seizure were included. Neonates, children who reached our hospital more than 48 hours after the event and those with febrile seizures were excluded. Patients whose family members/caretakers and overview of medical chart did not provide information that allowed proper classification of the epileptic seizures were also excluded.

The Pediatric Neurology Unit of Pequeno Príncipe Hospital provides emergency and elective care of all children with neurological disturbances referred to this hospital. In 2004, 1210 patients were admitted for medical treatment and investigation of acute and chronic neurological diseases.

Blood samples of all subjects were drawn on admission, and routine laboratory studies were performed. Complete blood count, glycemia, serum sodium, potassium, calcium and magnesium were analyzed in order to exclude possible metabolic disturbances that could either precipitate or contribute to the event.

All patients were submitted to EEG with minimal duration of 20 minutes. Electrodes were positioned according to the International 10-20 System. Whenever necessary, sleep was induced by chloral hydrate. All EEG tracings were obtained either in 21 channel NEUROTEC digital equipment or 8 channel BERGER analogical equipment. The EEG was performed within the first 48 hours that followed the first unprovoked epileptic seizure. The exam was analyzed by two neurophysiologists certified by the Brazilian Association of Clinical Neurophysiology.

Previously elaborated clinical charts containing epidemiological data, birth conditions (type of birth, gestational age, Apgar scores at the first and fifth minutes), development hallmarks, classification of the epileptic seizure according to the International League Against Epilepsy<sup>(4)</sup> (ILAE-1981), estimated duration of the seizure, EEG and CT were filled in by two researchers (PBNL e SCV).

The data obtained by this comprehensive compilation are the result of a five-year experience of a pediatric neurology department at a tertiary hospital located in the South of Brazil. These data were tabulated, analyzed and compared to the available literature.

## RESULTS

Between May 2000 and May 2005, 387 patients were diagnosed with first unprovoked epileptic seizure at the Pediatric Neurology Unit of Hospital Pequeno Príncipe; 214 (55.30%) were male. Their age varied from 68 days to 14.4 years (average 4.2 years). The neuropsychomotor development was considered normal in 315 (81.40%) patients.

According to the Classification Criteria for Epileptic Seizures of the International League Against Epilepsy<sup>(4)</sup> (ILAE – 1981), 167 (43.15%) patients had generalized and 220 (56.85%) focal seizures. Among the subjects with generalized seizures, 105 (62.85%) had tonic-clonic generalized seizures, 22 (13.17%) had typical absences, 20 (11.98%) had clonic seizures, 13 (7.78%) had tonic seizures and 7 (4.19%) had atonic seizures. Among those diagnosed with focal seizures, 81 (36.82%) had complex partial seizures with secondary generalization, 56 (25.45%) had complex partial seizures, 30 (13.64%) had simple partial seizures with secondary generalization, 23 (10.45%) had simple partial seizures evolving to complex partial seizures, 17 (7.73%) had simple partial seizures and 13 (5.91%) had simple partial seizures evolving to complex partial seizures with secondary generalization.

EEG recordings were normal in 208 (53.75%) patients. Interictal epileptiform activity was recorded in 111 (28.68%) patients, 41 with generalized and 70 with focal projection. Asymmetric tracing due to focal slowing was observed in 68 (17.57%) of the exams.

CT scans were normal in 273 (70.54%) patients, showed volumetric reduction of the cerebral hemispheres compatible with cerebral atrophy in 35 (9.04%), focal hypodense lesions in 24 (6.20%), hydrocephaly in 23 (5.94%), calcified lesions suggestive of neurocysticercosis in 20 (5.17%), bilateral white matter hyperintense signal in 7 (1.81%) and malformations of the cortical development such as lissencephaly/pachygyria in 5 (1.29%) patients.

**Table 1.** Results in absolute and percentual values.

	n	%
<b>Epidemiological data</b>		
Total of patients	387	100.00
Male gender	214	55.30
Female gender	173	44.70
Normal NPMD	315	81.40
Delayed NPMD	72	18.60
<b>Classification of the epileptic seizure</b>		
Generalized seizure	167	43.15
GTCS	105	62.85
Typical absence seizure	22	13.17
Clonic seizure	20	11.98
Tonic seizure	13	7.78
Atonic seizure	7	4.19
Partial seizure	220	56.85
CPS with secondary generalization	81	36.82
CPS	56	25.45
SPS with secondary generalization	30	13.64
SPS evolving to CPS	23	10.45
SPS	17	7.73
SPS evolving to CPS and GTCS	13	5.91
<b>EEG tracings</b>		
Normal	208	53.75
Focal interictal paroxysmic activity	70	18.09
Generalized interictal paroxysmic activity	41	10.59
Focal slowing	68	17.57
<b>Cranial CT</b>		
Normal	273	70.54
Volumetric reduction of the cerebral hemispheres	35	9.04
Focal hypodense lesions	23	5.94
Calcified circumscribed lesions	20	5.17
White matter hypersignal	7	1.81
Lissencephaly/pachygyria	5	1.29

NPMD – neuropsychomotor development; GTCS – generalized tonic-clonic seizure; SPS – simple partial seizure; CPS – complex partial seizure.

## DISCUSSION

The diagnosis of an epileptic seizure depends essentially on both clinical history and description of the event. Not all paroxysmic events that cause increase or reduction of the muscle tone, change in consciousness or behavior originate in the cerebral cortex. Paresthesias,

episodic loss of consciousness, tremors, muscle jerks and dystonic postures frequently do not correspond to ictal events, even though they may clinically simulate focal or generalized epileptic seizures<sup>(5)</sup>. Many paroxysmic events of nonepileptic origin such as sleep disorders, syncope, gastrointestinal reflux, nonepileptic myoclonus, conversion, somatization, psychogenic seizures among others, may reproduce epileptic seizures in the pediatric age group<sup>(5,6)</sup>. Studies demonstrate that about 1/3 of the patients referred to epilepsy investigation centers were diagnosed with nonepileptic paroxysmic events after video-EEG monitoring<sup>(7)</sup>.

For study purposes, epileptic seizures are divided into generalized, simple partial, complex partial and partial with secondary generalization. In generalized seizures, extensive areas of both cerebral hemispheres are involved from the start, whereas partial seizures characteristically have ictal beginning restricted to a group or circuit of neurons<sup>(4)</sup>. The precise description of the outset of the event is essential for the accurate classification of the seizure. Even so, the distinction between generalized and focal is often impossible after the first unprovoked seizure in childhood.

The first episode of unprovoked epileptic seizure in children is frequently improperly classified and its etiology often remains obscure. Velásquez and Ramirez studied the etiological aspects of the first epileptic seizure in different pediatric age groups and found that in children under 1 year the most common etiologies were central nervous system infections and metabolic disturbances. Between 1 and 5 years, central nervous system infections along with cranial trauma were responsible for the majority of seizures. In children aged 6 to 12 neurocysticercosis and brain tumors prevailed<sup>(8)</sup>. We emphasize that the exclusion of an immediate precipitating factor is critical for the diagnosis of a first unprovoked epileptic seizure.

All children included in our study were evaluated by pediatric neurologists during their stay at our hospital. The description of the event was checked by more than one doctor with more than one family member/caretaker granting a precise classification of the seizure. Partial seizures predominated (56.85%). Most of the subjects had a normal neuropsychomotor development. Among those with delayed neuropsychomotor development or signs of focal cerebral lesions in the neurological examination, partial seizures with secondary generalization prevailed. All children who presented with atonic or tonic seizures had delayed neuropsychomotor development. Clinical examination focusing on language skills, motor and sensory functions, eye movement, pupillary and facial symmetry after the first episode of epileptic seizure is of great importance, even in patients with no neurological deficit<sup>(9)</sup>.

Routine blood exams of patients admitted to emergency units, diagnosed with first episode of epileptic

seizure, is a debatable issue among authors. Even though some stress their importance, other studies demonstrate that they do not contribute significantly either to etiological diagnosis or to therapeutical follow-up<sup>(10,11)</sup>. The routine workup for patients with first episode of unprovoked epileptic seizure at the emergency room of Pequeno Príncipe Hospital includes complete blood count, sodium, potassium, calcium, magnesium, glycemia, EEG and cranial CT. Blood exams are particularly important in children under 6 months, when metabolic disturbances contribute to a considerably large portion of the epileptic seizures<sup>(8,10,11)</sup>.

In our study, little over half of the EEGs done within 48 hours of the first unprovoked epileptic seizure were normal. Interictal paroxysmic activity (focal or generalized) was found in 28.68% of subjects. Although the EEG results are relevant in attempting to predict recurrence, 35 to 57% of children with first normal EEG tracings will have recurring epileptic seizures<sup>(3,12)</sup>.

According to Shinnar et al.<sup>(13)</sup>, abnormalities on the EEG following an unprovoked epileptic seizure are related to a 54% chance of recurrence, while normal EEG correlates with 25% recurrence rates. EEG is an easy to perform, low cost exam with minimum risks that should be done as soon as possible after a first unprovoked epileptic seizure<sup>(14)</sup>.

CT is the most used neuroimage routine investigation method after a first unprovoked epileptic seizure. In our series, the great majority (70.54%) of patients had normal cranial CT. The most frequently observed abnormality was volumetric reduction of the cerebral hemispheres, followed by hypodense and calcified lesions. In our study, we observed a greater percentage of abnormal cranial CT when compared to the literature. Between 5 and 10% of neurologically normal children who present with a first episode of unprovoked epileptic seizure have altered neuroimage exams<sup>(15,16)</sup>, which greatly raises the risk of recurrence of the epileptic seizure<sup>(17,18)</sup>. It is well established that MRI has greater sensibility and specificity in detecting brain lesions that are potentially related to epileptic seizures. However, since this is not a routine image exam performed in all patients following a first episode of unprovoked epileptic seizure, it has not been included in this study.

The data presented allow us to conclude that most of the patients had a normal neuropsychomotor development at the time of the first unprovoked epileptic seizure. Partial seizures predominate. Tonic and atonic seizures strongly relate to neuropsychomotor delay. Early EEG is able to identify abnormalities (interictal paroxysms or focal slowing) in about half of the patients. Cranial CT is capable of detecting abnormalities in about 20% of the subjects. The assessment of prognosis after a first unprovoked

epileptic seizure depends on a series of factors that include semiological characteristics of the seizure, medical history of the child, genetic aspects and the results of subsidiary exams.

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