

Children with Rolandic spikes and ictal vomiting: Rolandic epilepsy or Panayiotopoulos syndrome?

Athanasios Covanis, Christina Lada, Konstantinos Skiadas

Received January 31, 2003; Accepted June 5, 2003

ABSTRACT – Centrottemporal spikes are the EEG marker of Rolandic epilepsy, while ictus emeticus is one of the main seizure manifestations of Panayiotopoulos syndrome. Ictus emeticus has not been reported in Rolandic epilepsy. Out of a population of 1340 children with focal afebrile seizures we studied 24 children who had emetic manifestations in at least one seizure and centrottemporal spikes in at least one EEG. They were of normal neurological status and had a follow-up of at least two years after the last seizure. All children had sleep EEG following sleep deprivation. Two groups of patients were identified. Group A (12 patients) with EEG centrottemporal spikes only and group B (12 patients) with centrottemporal spikes and spikes in other locations. In 21 patients, ictal emetic manifestations culminated in vomiting and in three only nausea or retching occurred. The commonest presentation was ictus emeticus at onset followed by deviation of the eyes or staring, loss of contact and floppiness. In 79%, seizures occurred during sleep. Autonomic status epilepticus occurred in 37.5%. The mean age at onset was 5.3 years. Overall analysis of the clinical and EEG data points out that the vast majority of these patients primarily suffer from Panayiotopoulos syndrome. Twenty patients (83%) had ictal semiology typical of Panayiotopoulos syndrome, but five also had concurrent Rolandic symptoms and four later developed pure Rolandic seizures. The other four patients (17%) had typical Rolandic seizures with concurrent ictus emeticus. These findings suggest a link between Rolandic epilepsy and Panayiotopoulos syndrome, the two most important phenotypes of the benign childhood seizure susceptibility syndrome.

KEY WORDS: Rolandic spikes, ictal vomiting, ictus emeticus, Rolandic epilepsy, Panayiotopoulos syndrome, autonomic status.

Panayiotopoulos syndrome (PS) is a recently recognised, idiopathic childhood focal epilepsy [1-5]. PS is a benign childhood susceptibility, in some manifesting with ictal autonomic symptoms. Ictus emeticus (nausea, retching, vomiting), occurring in 70% of the seizures, is often the first symptom at onset. PS is common, affecting around 6% of children with seizures [2-6]. Interictal EEG shows spikes from

any electrode location although occipital and frontal spikes predominate. One third of the patients do not have occipital spikes [4-7]. Onset in ictal EEG may be posterior [8], and less often anterior [9, 10]. It is for these reasons that descriptive names of PS, such as "early onset benign childhood epilepsy with occipital spikes" [11] or "early onset benign childhood occipital lobe epilepsy" [1], are unsatisfac-

Correspondence:

A. Covanis
Director of Neurology Department
Agia Sophia Children's Hospital
11527-Goudi-Athens
Greece
Tel: + 302107751637
Fax: + 302107705785
E-mail: graaepil@otenet.gr

tory as recently detailed by Martinovic [10].

Benign childhood epilepsy with centrotemporal spikes (Rolandic epilepsy) is another idiopathic childhood focal epilepsy manifesting mainly with hemifacial seizures and ictal oropharyngolaryngeal symptoms [12-15]. Centrotemporal spikes are the EEG markers of Rolandic epilepsy. Of the autonomic symptoms hypersalivation is common [6] but ictal vomiting has not been previously reported in Rolandic epilepsy.

We studied the occurrence of ictal vomiting in children with centrotemporal spikes in their EEG.

Patients and methods

The study is based on patients seen in the Epilepsy Center of Agia Sophia Children's Hospital in Athens. The Epilepsy Center has both in- and outpatient clinical and EEG facilities for children with seizures. The hospital is one of the three major pediatric hospitals in Athens and a referral center for the central and southern mainland of Greece.

For the purpose of this study, we reviewed the medical records of 1340 children with single or recurrent focal seizures seen during the last 18 years [4].

Inclusion criteria

- a. Definite ictal emetic manifestations in at least one seizure
- b. EEG centrotemporal spikes (CTS) in at least one EEG. CTS could occur alone or together with spikes in other locations. Background EEG should be normal in all except postictal records
- c. Normal development and neurological state, and neuroimaging if performed
- d. Follow-up at least two years after the last seizure.

Exclusion criteria

- a. Abnormal neurological signs, brain imaging or background EEG
- b. Inadequate description of seizures
- c. Children seen only once, not having an EEG or not having adequate follow-up.

Clinical criteria of benign childhood epilepsy with CTS as defined by the ILAE [12] were not considered to be inclusion criteria.

All authors reviewed the clinical and EEG data; only patients for whom a unanimous agreement was reached were included. We analyzed gender, age at onset of seizures, ictal symptomatology, circadian distribution, duration and frequency of seizures, therapeutic response, final outcome, family history of epilepsy and EEG findings.

Investigations

Most patients had brain neuroimaging (computed tomography, magnetic resonance imaging and, rarely, both), which, as requested by inclusion criteria, was normal.

All children had EEG studies, often supplemented with sleep EEG after sleep deprivation. Our practice is to repeat EEG yearly until normalization of the sleep record. The sleep record is repeated twice, at short intervals, for confirmation before therapy is discontinued. Subsequently, the patients are assessed yearly for relapses. Most of the patients had serial EEG for years, even after seizure remission.

Definitions

- *Centrotemporal spikes* are defined as very high amplitude sharp and slow wave complexes, unilateral or independently bilateral in the central and midtemporal areas, exaggerated by sleep.
- *Occipital spikes* are defined as spikes localized in the occipital electrodes irrespective of amplitude. Occipital paroxysms are repetitive occipital spikes of high amplitude usually occurring when the eyes are closed.
- *Autonomic seizures* consist of episodic, altered autonomic function of any type at onset or as the sole manifestation of an epileptic event. These may be objective, subjective or both. They must be distinguished from secondary (indirect) effects on the autonomic system by other seizure symptoms [16].
- *Autonomic status epilepticus* is an autonomic seizure that lasts for more than 30 minutes [6].

Results

Twenty four (1.8%) of the 1340 patients with focal, afebrile seizures fulfilled the inclusion criteria. Fifteen were boys. The patients were divided in two groups according to EEG findings: group A comprised 12 patients with CTS only. Group B comprised 12 patients whose EEG had CTS and additional spikes in other locations.

Clinical characteristics of patients are shown in *table 1*.

Family history of seizure or epilepsy

Family history in first degree relatives was positive for febrile seizures in two cases (8%) and for epilepsy in one (4%). Twin siblings of two patients did not have seizures.

Clinical manifestations

According to the inclusion criteria, all 24 patients had ictus emeticus manifestations, which in 21 culminated in vomiting; in three they were limited to nausea or retching. The commonest presentation found in 20 patients was onset with ictus emeticus, followed by deviation of the eyes or starring, loss of contact and floppiness. Half of them ended with convulsions. Ictal vomiting could be mild or severe, short or prolonged, occurring at onset or during the progression of the seizure, once or repeatedly. Pallor was commonly reported. In 19 children (79%) seizures occurred only during sleep.

Table I. Clinical characteristics in each group

Male/Female	Group A (n = 12) 5/7	Group B (n = 12) 10/2	Total (n = 24) 15/9
Age at 1 st seizure (years)	5.7 ± 2.8 (1.2-12.5)	4.9 ± 1.6 (2.5-7.5)	5.3 ± 2.3
Age at last seizure (years)	7.8 ± 3.0 (2.5-13)	7.2 ± 2.5 (4.2-12)	7.5 ± 2.7
No of seizures/patient	3.2 ± 1.6 (1-6)	4.7 ± 2.9 (1-10)	4 ± 2.4
Autonomic status	6/12	3/12	9/24

Classification of patients according to seizure type

a. Fourteen patients (58%) only had seizures typical of Panayiotopoulos syndrome that is seizures characterized by ictus emeticus, deviation of the eyes or eye opening and impairment of consciousness. Seven belonged to group A and 7 to group B. One case from group A and two from group B had concurrent oropharyngolaryngeal manifestations. Of two additional patients (8%) with this type of seizure, one experienced febrile status epilepticus at the age of 7 years and the other, a single afebrile motor seizure.

b. Four cases (17%) initially had the above type of seizures (two with and two without Rolandic features) followed by the occurrence of typical Rolandic seizures after a period of 3 months to 3 years. The two patients with Rolandic features belonged to group A.

c. Four cases (17%) had only typical Rolandic seizures with concurrent ictal vomiting (three cases) or nausea (1 case). One patient belonged to group A and three patients to group B.

Duration of seizures

Duration of seizures varied from 1 minute to 2 hours. In 12 patients duration was < 5 minutes and in three ranged 5-20 minutes. The other nine patients had lengthy seizures, over 30 minutes.

Autonomic status epilepticus

Nine patients (38%) had seizures lasting longer than half an hour (range: 30-120 minutes; mean 45 minutes); constituting autonomic status epilepticus (ASE). Six were from group A and three from group B. ASE occurred once in six patients, twice in two and three times in one patient. This last patient did not have brief seizures. In five cases, ASE was the first seizure, and in the rest a single epileptic event. Ictal vomiting (six patients) or nausea (one patient) were the main manifestations at the beginning of ASE. Another child started with hypersalivation, eye and head deviation, but vomiting occurred only near the end of the status. In the remaining child, emetic symptoms were apparent at onset. Eye deviation or staring, floppiness and unresponsiveness ensued in all instances but only two ended with generalized convulsions. Age at status was 2.5-13 years (mean ± SD = 6.4 ± 2.9).

Number of seizures

Four (17%) of the total 24 patients had a single seizure. Group A: Eleven patients had 1-6 seizures (mean ± SD = 3 ± 2). The remaining patient was a girl with many seizures between 5 and 10 years of age. Her brain CT and MRI scan were normal and she has been now seizure-free for 8 years.

Group B: All 12 patients had 1-10 seizures (mean ± SD = 5 ± 3).

Seizures during febrile illness

Three children (13%) developed seizures during febrile illnesses at the age 5 to 8 years. This happened once in two cases and seizures were described as generalized tonic-clonic, lasting 5 minutes in one and 30 minutes in the other. In both cases this was their last epileptic event and happened while on carbamazepine. The third child had two febrile focal clonic seizures lasting 10 minutes at the age of 5 and 8 years and two afebrile seizures at eight and 10 years.

EEG findings

Each patient had on average 5 ± 3 EEGs ranging from 1 – 14. EEG follow-up ranged from 6 months to 9 years (mean ± SD = 5 ± 3 years). Only two patients had a single EEG. According to the inclusion criterias all patients had one or more EEGs with centrottemporal spikes accentuated by sleep. These were bilateral in 14 cases (58%) with shifting side emphasis over the years of EEG monitoring, right-sided in seven (29%) and left-sided in three (13%). All 12 patients in Group B also had occipital epileptiform activity in the same or another record. No other epileptiform abnormalities were found. Nine had repetitive occipital spike morphologically identical to centrottemporal spikes and activated by sleep, two had classical occipital paroxysms blocked by eye opening and one had small and infrequent occipital spikes. In six cases with adequate EEG follow-up, occipital spikes were found only in a single record, between the ages of 4 to 9 years, while centrottemporal spikes occurred consistently between the ages of 3.5 to 12 years.

Eleven patients (belonging to both groups) were followed-up until normalization of awake and sleep records in repeated examinations. EEG normalization oc-

curred after a seizure-free period of one month to 5 years (mean \pm SD = 3.2 ± 2.2 years) and at an age from 6 to 16 years.

Treatment and prognosis

Follow-up ranged from two to 14.5 years (mean \pm SD = 7 ± 4.2 yrs). According to the inclusion criteria, all patients were seizure-free for at least two years after their last seizure.

Of the 24 patients, 17 were treated; mainly with carbamazepine alone (15 patients) or combined with sodium valproate (one patient) or lamotrigine (one patient).

Ten patients had relapse seizures, which were of short duration, during treatment. Two relapsed with fever and one during carbamazepine withdrawal; in all three patients this was their last seizure. All children with relapses during treatment have now been in remission for at least 2 years and 6 of them are unmedicated.

Prognosis of autonomic status epilepticus

Nine patients with ASE had a 2-12 years follow-up (mean \pm SD = 6 ± 3.6 years). The active course of seizures in these patients was from one month to 7.5 years (mean \pm SD = 3 ± 2.9 years). Seven cases were followed by repeated EEGs until normalization of awake and sleep records; that happened between the age of 10 to 16 years (mean \pm SD = 11.6 ± 3.2 years).

Discussion

The 24 patients in this report have according to the inclusion criteria EEG features of Rolandic epilepsy and a prevalent clinical feature of Panayiotopoulos syndrome. Where should these patients be classified? Overall analysis of the clinical and EEG data points out that the vast majority of these patients primarily suffer from Panayiotopoulos syndrome. Thus, based on ictal manifestations, three groups emerged. Firstly, the majority (67%) had ictal semiology typical of PS. Secondly, 17% with initial seizures typical of PS later developed typical Rolandic seizures. Thirdly, 17% had typical Rolandic seizures with concurrent ictus emeticus. Of 18 patients with seizures typical of PS, five (28%) also had concurrent Rolandic symptoms as previously reported [6, 7, 17].

Occurrence of autonomic status epilepticus was very high (37%) and in all cases symptomatology was typical of Panayiotopoulos syndrome. None of the 13 instances of ASE in nine patients had the form of status epilepticus described in patients with Rolandic epilepsy [12-15].

It appears that clinical manifestations do not depend on whether the EEG centrottemporal spikes occur alone or with occipital spikes. Although the number of patients is small, the two groups did not differ in age at first and last seizure, duration of active seizure period, seizure type and

incidence of autonomic status epilepticus. Further, of the majority group with seizures typical of PS, half of them had CTS alone and the other half CTS and occipital spikes.

Prognosis was excellent irrespective of clinical and EEG features. All but one patient had fewer than ten seizures in total with four of them having a single seizure. Only one patient had many seizures before remission at the age of 10 years. All patients were free of seizures for at least 2 years from their last seizure. However, 10 of 17 treated patients (59%) had relapse seizures, which in some cases were the last clinical event.

Our findings corroborate and extend previous reports documenting overlapping features of Panayiotopoulos syndrome with Rolandic epilepsy [2-7, 17-21] and the EEG variability of PS regarding spike localizations [2-7, 20, 21]. Thus, we have confirmed that in children with PS occipital spikes may not be present and seizures may associate symptoms reminiscent of Rolandic Epilepsy. Some children with PS may later present with typical Rolandic seizures.

In addition to confirming previous research, the present study is unique in that it observed that the clinical manifestations of Panayiotopoulos syndrome may occur in children with centrottemporal spikes alone (half of our cases) without other occipital or extra-occipital spikes. Further, four of our patients (16%) had solely Rolandic seizures with concurrent ictus emeticus. One of them had centrottemporal spikes only and the other three had additional occipital spikes. This has not been previously reported.

Our findings and those of other authors [2-7, 17-21] suggest a pathogenetic links between Panayiotopoulos syndrome and Rolandic epilepsy which are the two main phenotypes of a benign childhood seizure susceptibility syndrome [14, 22]. □

References

1. Engel J, Jr. A proposed diagnostic scheme for people with epileptic seizures and with epilepsy: Report of the ILAE Task Force on Classification and Terminology. *Epilepsia* 2001; 42: 796-803.
2. Ferrie CD, Grunewald RA. Panayiotopoulos syndrome: a common and benign childhood epilepsy. *Lancet* 2001; 357: 821-3.
3. Koutroumanidis M. Panayiotopoulos syndrome: a common benign but underdiagnosed and unexplored early childhood seizure syndrome. *Br Med J* 2002; 324: 1228-9.
4. Lada C, Skiadas K, Theodorou V, Covanis A. A study of 43 patients with Panayiotopoulos syndrome: A common and benign childhood seizure susceptibility. *Epilepsia* 2003; 44: 81-8.
5. Ohtsu M, Oguni H, Hayashi K, Funatsuka M, Imai K, Osawa M. EEG in children with early-onset benign occipital seizure susceptibility syndrome: Panayiotopoulos syndrome. *Epilepsia* 2003; 44: 435-42.

6. Panayiotopoulos CP. *Panayiotopoulos syndrome: A common and benign childhood epileptic syndrome*. London: John Libbey, Company, 2002.
7. Panayiotopoulos CP. Vomiting as an ictal manifestation of epileptic seizures and syndromes. *J Neurol Neurosurg Psychiatr* 1988; 51: 1448-51.
8. Vigevano F, Lispi ML, Ricci S. Early onset benign occipital susceptibility syndrome: video-EEG documentation of an illustrative case. *Clin Neurophysiol* 2000; 111 Suppl 2: S81-6.
9. Oguni H, Hayashi K, Imai K, Hirano Y, Mutoh A, Osawa M. Study on the early-onset variant of benign childhood epilepsy with occipital paroxysms otherwise described as early-onset benign occipital seizure susceptibility syndrome. *Epilepsia* 1999; 40: 1020-30.
10. Martinovic Z. Panayiotopoulos syndrome or early-onset benign childhood occipital epilepsy. *Epilepsia* 2002; 43: 1268-72.
11. Taylor I, Scheffer IE, Berkovic SF. Occipital epilepsies: identification of specific and newly recognized syndromes. *Brain* 2003; 126: 753-69.
12. Commission on Classification and Terminology of the International League Against Epilepsy. Proposal for revised classification of epilepsies and epileptic syndromes. *Epilepsia* 1989; 30: 389-99.
13. Aicardi J. *Epilepsy in children*. New York: Raven Press 1994.
14. Panayiotopoulos CP. Benign childhood focal seizures and related syndromes (benign childhood seizure susceptibility). In: Panayiotopoulos CP, ed. *A clinical guide to epileptic syndromes and their treatment*. Oxford: Bladon Medical Publishing 2002: 89-113.
15. Dalla Bernardina B, Sgro M, Fejerman N. Epilepsy with centro-temporal spikes and related syndromes. In: Roger J, Bureau M, Dravet C, Genton P, Tassinari CA, Wolf P, eds. *Epileptic syndromes in infancy, childhood and adolescence (3rd ed)*. London: John Libbey, Co Ltd 2002: 181-202.
16. Burgess RC. Autonomic signs associated with seizures. In: Luders HO, Noachtar S, eds. *Epileptic seizures. Pathophysiology and clinical semiology*. New York: Churchill Livingstone 2000: 631-41.
17. Caraballo R, Cersosimo R, Medina C, Fejerman N. Panayiotopoulos-type benign childhood occipital epilepsy: a prospective study. *Neurology* 2000; 55: 1096-100.
18. Ferrie CD, Beaumanoir A, Guerrini R, et al. Early-onset benign occipital seizure susceptibility syndrome. *Epilepsia* 1997; 38: 285-93.
19. Guerrini R, Belmonte A, Veggiotti P, Mattia D, Bonanni P. Delayed appearance of interictal EEG abnormalities in early onset childhood epilepsy with occipital paroxysms. *Brain* 1997; 120: 343-6.
20. Panayiotopoulos CP. Extraoccipital benign childhood partial seizures with ictal vomiting and excellent prognosis. *J Neurol Neurosurg Psychiatry* 1999; 66: 82-5.
21. Panayiotopoulos CP. *Benign childhood partial seizures and related epileptic syndromes*. London: John Libbey, Company Ltd, 1999.
22. Panayiotopoulos CP. Benign childhood partial epilepsies: benign childhood seizure susceptibility syndromes. *J Neurol Neurosurg Psychiatry* 1993; 56: 2-5.