

Panayiotopoulos syndrome and diffuse paroxysms as the first EEG manifestation at clinical onset: a study of nine patients

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Received May 12, 2014; Accepted February 08, 2015

ABSTRACT – *Aim.* To present a retrospective study of nine children with Panayiotopoulos syndrome associated with diffuse spikes and waves as the sole EEG manifestation at onset.

Methods. Charts of children with typical clinical criteria of Panayiotopoulos syndrome, electroclinically followed between February 2000 and February 2012, were reviewed.

Results. Among 150 patients who met the electroclinical criteria of Panayiotopoulos syndrome, we identified nine children who presented with the typical clinical manifestations but who, on EEG, only had diffuse paroxysms at onset that continued along the course of the syndrome. In three, in addition to the diffuse paroxysms, focal spikes appeared later. From a clinical point of view, other features were otherwise unremarkable. Diffuse spike-and-wave discharges were observed in all patients when awake and during sleep (100%). Later, three children also had focal spikes during sleep, which were occipital in one, frontal in one, and temporo-occipital in the remaining patient. Spikes were activated by sleep in all three cases. During disease evolution, no particular electroclinical pattern was observed. Two patients who received clobazam and carbamazepine, respectively, did not respond well to the drugs and valproic acid was added with excellent seizure control. Outcome was good.

Conclusions. We present evidence that patients with Panayiotopoulos syndrome may have diffuse discharges at onset as the sole EEG manifestation, which last throughout the course of the syndrome. In some, focal paroxysms developed later. The course was benign. In our group of patients, clinical features and evolution were similar to those of typical cases of Panayiotopoulos syndrome.

Key words: autonomic seizures, generalized paroxysms, spike and waves, occipital spikes, ictal vomiting, Panayiotopoulos syndrome

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In 1989, as reported in two studies with a long-term follow-up of patients, Panayiotopoulos brought to light a particular set of symptoms which he referred to as “benign nocturnal childhood occipital epilepsy” (Panayiotopoulos, 1989a, 1989b). One year earlier, Panayiotopoulos (1988) had emphasized vomiting as an ictal symptom in epileptic seizures in children.

Since then, important studies of children with this syndrome have been published (Caraballo *et al.*, 1997, 2000, 2007; Ferrie *et al.*, 1997, 2006; Oguni *et al.*, 1999; Kivity *et al.*, 2000; Verrotti *et al.*, 2000; Lada *et al.*, 2003; Covanis *et al.*, 2003; Ohtsu *et al.*, 2003; Durá-Travé *et al.*, 2008; Specchio *et al.*, 2010). The authors studied the variants of childhood epilepsies with occipital paroxysms (CEOP) based on a retrospective analysis of patients and confirmed the existence this early-onset variant.

The interictal EEG recording of Panayiotopoulos syndrome (PS) is characterized by occipital spikes in almost 75% of cases, but extraoccipital spikes, such as temporal and frontal spikes, are also observed (Panayiotopoulos, 1999; Caraballo *et al.*, 2007). Generalized spikes and waves may be recognized in approximately 15% cases (Panayiotopoulos *et al.*, 2012). Here, we present a retrospective study of nine children with PS associated with generalized spikes and waves as the only EEG manifestation at onset.

Methods

From February 2000 to February 2012, we evaluated 150 patients with PS in the Department of Neurology at our hospital; of whom only nine had generalized spike-and-wave paroxysms at onset.

The following inclusion criteria for PS were used:

- Autonomic manifestations, visual symptoms, and/or simple motor focal seizures, followed or not by impairment of consciousness, with or without secondary generalization;
- Normal neurological and mental state;
- Normal brain imaging;
- Diffuse paroxysms as the first EEG manifestation at clinical onset.

Patients with interictal functional occipital or extraoccipital spikes alone or in combination, a normal EEG with known mental or neurological deficits, typical electroclinical features of BCECTS, or Gastaut type of CEOP at onset were excluded.

We analyzed gender, age at onset, personal and family history of epilepsy, febrile seizures and migraines, duration and manifestations associated with seizures, circadian distribution and frequency of seizures, therapeutic response, and final outcome.

EEGs were performed while awake and asleep. Electrodes were placed according to the international 10-20

system. All patients underwent brain CT and MRI which were normal.

Between February 2000 and February 2012, nine patients who met the inclusion criteria were identified, and were followed to the present time. All patients were evaluated longitudinally, clinically and electroclinically, for two to eight years (mean: 4.5 years). A mean of 8 ± 3 EEGs were obtained for each patient. Clinical and EEG details of all patients were reviewed and unanimously agreed upon by all authors.

Results

Number of patients and gender

Six boys and three girls that met the inclusion criteria, specified in the methods section, were identified over a 12-year period between February 2000 and February 2012.

Age at onset

Age at first afebrile seizure ranged from 2.5 to 11 years, with a mean age of 5.5 and a median of 4 years.

Personal and family history of febrile convulsions, epilepsy and migraine

A family history of epilepsy was found in three cases (33.3%). Febrile seizures were reported in two (22.2%), and migraine in one (11%).

Ictal manifestations

Pallor was an ictal manifestation in all nine children (100%). Ictal vomiting was found in eight children (88.8%). Four (44.4%) and three (33.36%) patients also had nausea and retching, respectively. One patient (11%) presented with nausea without vomiting and one had a syncope-like symptom (11%). Eye and head deviation occurred in nine (100%), clonic focal seizures in one (11%), and secondary generalized seizures in five (55.5%). Consciousness was partially impaired in five (55.5%) patients at the end of the seizures.

According to parent reports, the duration of seizures was around five minutes. Four (44.4%) patients had a partial status epilepticus lasting for more than 30 minutes. In all patients, status epilepticus was characterized by pallor and/or vomiting, eye deviation, and impairment of consciousness, followed by unilateral or generalized motor seizures. In one patient, status epilepticus was the first manifestation of the syndrome. Seizures occurred during sleep in all nine children, but also while awake in five (55.5%).

No rolandic seizures or typical absences were observed in any of the patients.

Two patients (22.2%) had a single seizure and six (66.7%) had infrequent and sporadic seizures. The remaining child had weekly seizures.

Electroencephalographic findings

Diffuse spike-and-wave discharges were observed in all patients when awake and during sleep (100%) (*figures 1 and 2*). They occurred predominantly in anterior regions in seven patients (77.7%) and posterior regions in the other two (22.2%). In five patients, voltage asymmetry was observed. Later in the course of the syndrome, three patients also had focal spikes during sleep which were occipital in one, frontal in another, and temporo-occipital in the remaining patient (*figures 3 and 4*). Spikes were activated by sleep in all three cases and their pattern remained unchanged. The occipital spikes were not activated by eye closure. In all patients, response to intermittent photic stimulation was normal. No ictal EEG recordings were registered in any of the patients.

Treatment

Antiepileptic treatment with a single drug was started in seven patients (77.7%): valproic acid in four, carbamazepine in two, and clobazam in the remaining case. Two patients who received clobazam and carbamazepine, respectively, initially did not respond well, however, addition of valproic acid resulted in excellent seizure control.

Evolution

All seven patients treated had an excellent response to AEDs. The other two cases had isolated seizures and were therefore not treated. Seizures remitted within one year after onset despite persistent EEG abnormalities in five (55.5%). Antiepileptic treatment was discontinued in four of seven patients who remained seizure-free over a period of 2.5 to 11 years during follow-up. None of the patients developed an electroclinical picture compatible with epilepsy, with either typical absences or atypical evolution.

Discussion

In this study, we present children with typical clinical manifestations of PS who only had diffuse paroxysms on EEG at onset that continued along the course of the syndrome. In some, in addition to the diffuse paroxysms, focal spikes appeared later. From a clinical

point of view, presentation was comparable to the classic form of PS, with a benign course. During disease evolution, no particular electroclinical pattern was found in our nine patients. In view of the positive results based on this series of patients, valproic acid should be the first option to consider.

Surprisingly, this year already, we have identified five patients with PS and diffuse EEG paroxysms. One of these patients presented with autonomic status epilepticus, another had “syncope-like episodes”, and one had normal EEG at onset but showed diffuse spike-and-wave paroxysms 10 months later. The remaining two exhibited classic presentation. It would be interesting to consider whether this relatively high number of PS patients with diffuse EEG paroxysms, who were investigated during the preparation of this study and thus not included, is an incidental finding. Panayiotopoulos *et al.* (2012) stated that generalized paroxysms, as the sole EEG manifestation in children with PS, may occur in 4% of cases. In the most informative studies of patients with PS published, generalized paroxysms were found in 0% to 23.7% of cases (Ferrie *et al.*, 1997; Oguni *et al.*, 1999; Kivity *et al.*, 2000; Verrotti *et al.*, 2000; Lada *et al.*, 2003; Ohtsu *et al.*, 2003; Caraballo *et al.*, 2007; Durá-Travé *et al.*, 2008; Specchio *et al.*, 2010). In the literature, no reports of patients with PS who had only generalized discharges on EEG at onset have been published. This may be explained by the fact that, in different series of patients with PS published, this EEG feature, as a unique neurophysiological pattern, has not been considered as an inclusion criterion. It emphasizes that sometimes it is very important not to apply inclusion criteria that are too strict, not only from the clinical, but also from the EEG point of view, because, if this is the case, patients with PS with particular electroclinical features may be overlooked.

It is well known that in Rolandic epilepsy and occipital idiopathic epilepsy of Gastaut, generalized spike-and-wave discharges may occur (Panayiotopoulos *et al.*, 2012) and that, conversely, juvenile myoclonic epilepsy and epilepsy with absence seizures may present with focal EEG features (Thomas *et al.*, 2012). In addition, it has been widely acknowledged that idiopathic focal epilepsies of childhood and idiopathic generalized epilepsies may coexist at the same time or occur at different age periods in the same patient (Caraballo *et al.*, 2004, 2008; Dalla Bernardina *et al.*, 2005; Panayiotopoulos *et al.*, 2012), and types of focal and generalized epilepsies may occur in different members of the same family (Dalla Bernardina *et al.*, 2005; Panayiotopoulos *et al.*, 2012). These findings suggest a close genetic relationship between focal and generalized idiopathic epileptic syndromes.

Iannetti *et al.* (2009) identified a diffuse origin of the EEG discharges based on an ictal EEG record-

ing in a patient with PS. PS may be related to genetically-determined extensive cortical hyperexcitability, involving a specific system of the brain

(Koutroumanidis, 2007). This concept might explain the focal and diffuse electroclinical findings in children with PS.

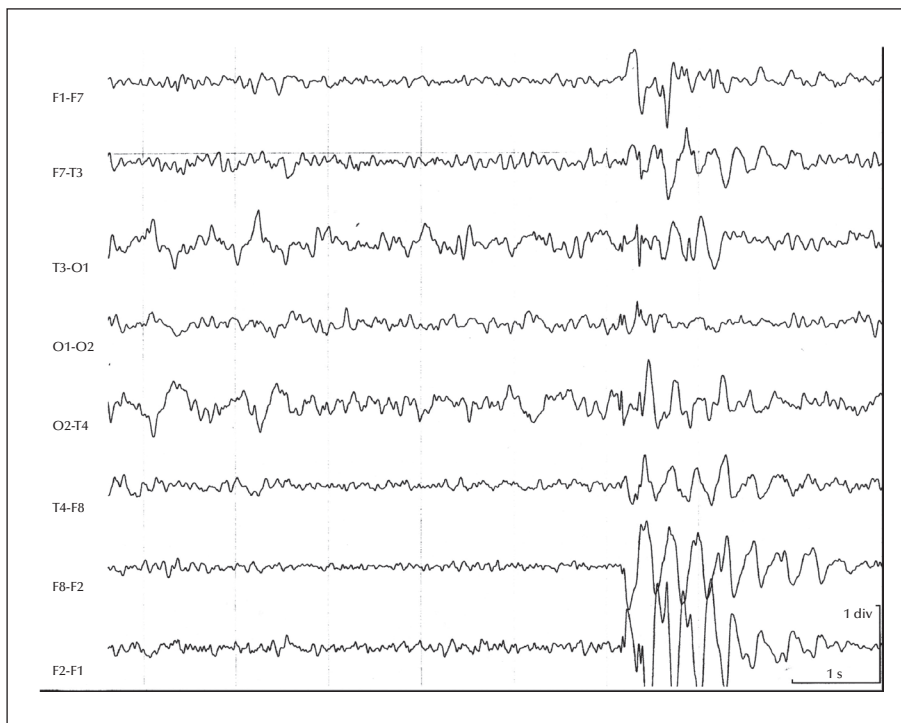


Figure 1. The interictal EEG recording during sleep shows diffuse spike-and-wave paroxysms.

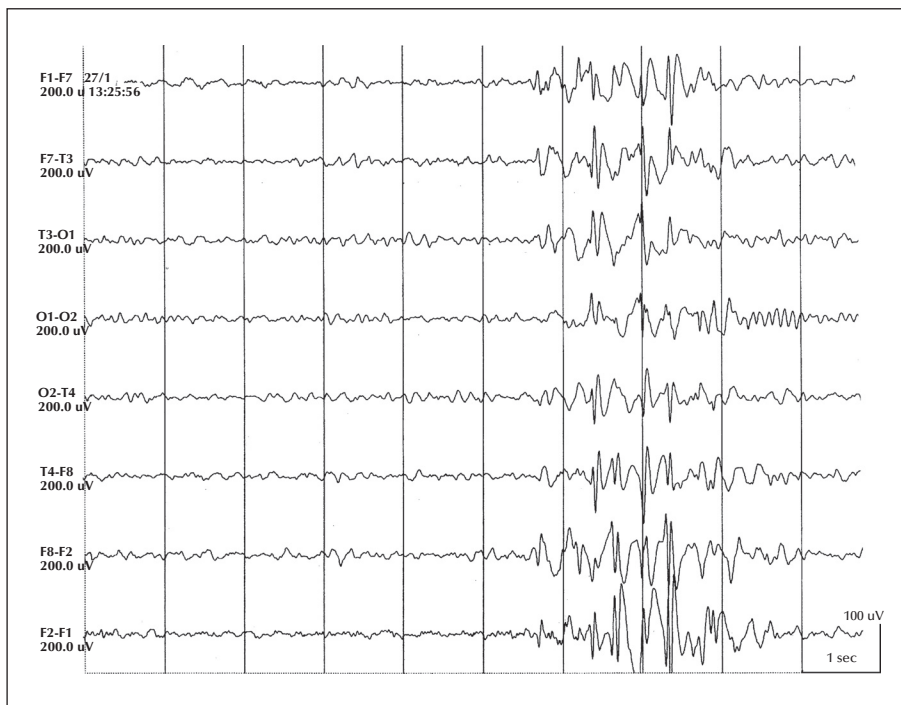


Figure 2. The interictal EEG recording when awake shows asymmetric and irregular diffuse spike-and-wave paroxysms.

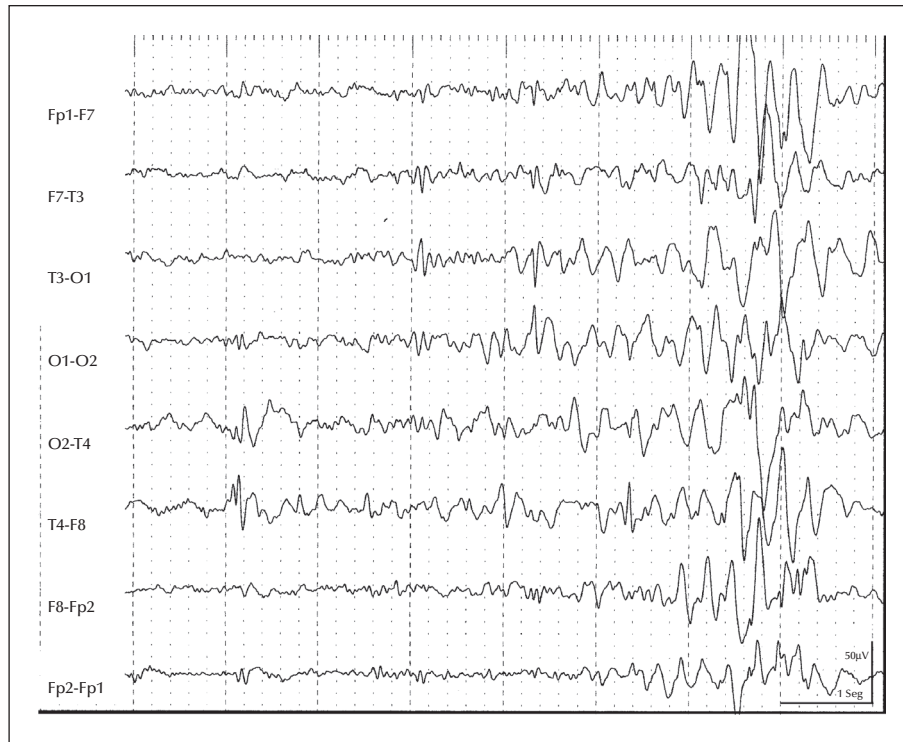


Figure 3. The interictal EEG recording during sleep shows multifocal spikes and diffuse spike-and-wave discharges.

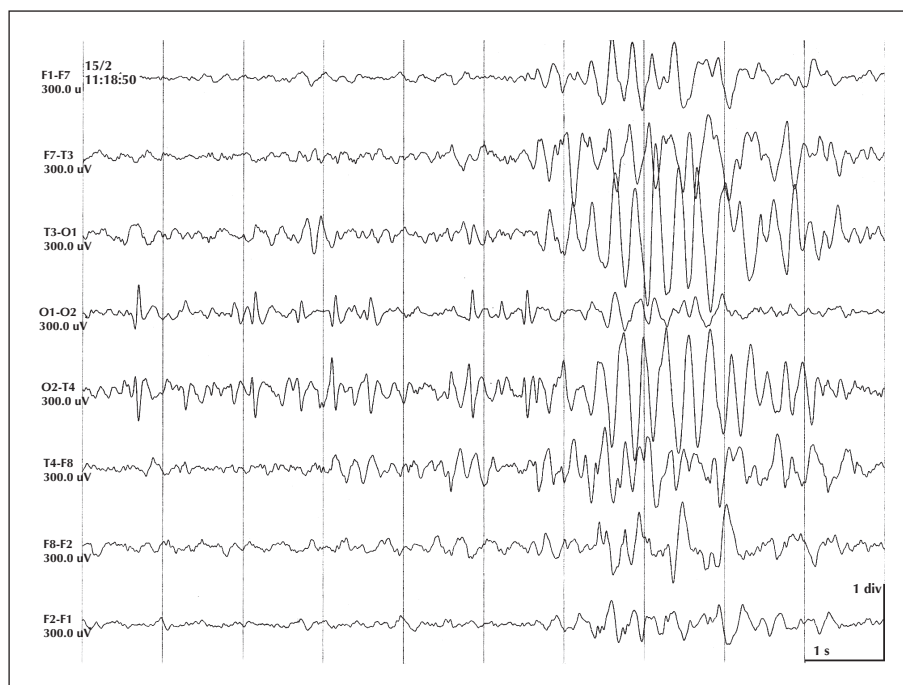


Figure 4. The interictal EEG recording during slow sleep shows diffuse spike-and-wave discharges and right occipital spikes.

Conclusion

In this retrospective study, we identified patients with typical clinical manifestations of PS who had diffuse discharges at onset as the sole EEG manifestation, which lasted throughout the course of the syndrome. In some, focal paroxysms developed later. Our group of patients had the same clinical features and evolution as typical cases of PS. Until now, no particular electroclinical evolution has been identified for these patients. Further studies should be performed to confirm these findings in order to manage these patients accordingly. □

Supplementary Data.

Summary didactic slides are available on the www.epilepticdisorders.com website.

Disclosures.

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

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TEST YOURSELF



- (1) What are the main clinical manifestations of Panayiotopoulos syndrome?
- (2) What are the most frequent EEG findings in patients with Panayiotopoulos syndrome?
- (3) Are diffuse discharges at onset the sole EEG manifestation in patients with Panayiotopoulos syndrome?

Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, www.epilepticdisorders.com, under the section "The EpiCentre".