

## A Study of 43 Patients with Panayiotopoulos Syndrome, a Common and Benign Childhood Seizure Susceptibility

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**Summary:** *Purpose:* To determine prevalence, clinical, EEG features, and prognosis of Panayiotopoulos syndrome and to examine the proposition that clinical manifestations are more important than EEG findings.

*Methods:* We analyzed retrospectively the clinical and EEG records of 1,340 children with one or more focal seizures seen in the last 18 years, supplemented with a prospective study from 1998. Panayiotopoulos syndrome was defined by clinical criteria, mainly ictal emesis, irrespective of EEG findings.

*Results:* We analyzed 43 of 90 patients with Panayiotopoulos syndrome who were seizure free >2 years. Girls predominated. Mean age at first seizure was 5 years. Seizures consisted mainly of autonomic manifestations; ictal emesis was often the first symptom, culminating in vomiting in 86%. Of nonautonomic manifestations, lateral eye deviation was the most common; visual symptoms were exceptional. Impairment of consciousness ensued in all seizures, half of which ended with hemi or

generalized convulsions. Nearly 46.5% of cases had at least one seizure >30 min, constituting autonomic status epilepticus. Seizures during sleep (84%) were more common than those in wakefulness. EEG showed occipital spikes in 29 patients. Of the other 14 cases, five had extraoccipital abnormalities or brief generalized discharges, and nine had normal awake and sleep EEG. Prognosis was excellent. All 43 children have been free of seizures for  $\geq 2$  years, 53% having a single seizure, and 47%, an average two to three seizures.

*Conclusions:* Panayiotopoulos syndrome is common and needs wider recognition. EEG shows occipital or extraoccipital abnormalities, is normal in one third of patients, and does not determine clinical manifestations or prognosis, which is excellent despite the high prevalence of lengthy seizures. **Key Words:** Children—Autonomic seizures—Epilepsy—Prognosis.

Panayiotopoulos syndrome (PS; susceptibility to early-onset benign childhood seizures with mainly autonomic symptoms) (1) is a common childhood epileptic syndrome described by Panayiotopoulos (2–5), confirmed world-wide (6–10), newly officially recognized (11), and recently attracting interest beyond that of epileptologists (1,12). Prevalence of PS may be high, probably affecting ~13% of children 3–6 years old with one or more nonfebrile seizures and 6% of the age group from 1 to 15 years (2,5). It is the second most frequent benign syndrome of childhood after rolandic epilepsy, which primarily affects 15% of children at a peak onset at age 7–9 years (13,14). Another epileptic syndrome categorized with PS and rolandic epilepsy is the Gastaut-type childhood occipital epilepsy (11), manifesting with frequent and brief visual seizures. However, this is rare, of uncertain prognosis, and markedly different from PS,

despite common interictal EEG manifestations of occipital spikes (5).

The key clinical features of PS are infrequent, often single, focal seizures comprising an unusual constellation of autonomic, mainly emetic, symptoms, behavioral changes, and other more conventional ictal clinical manifestations such as unilateral deviation of the eyes and convulsions (1,2,5–10,12). The full emetic triad (nausea, retching, vomiting) culminates in vomiting in 74% of the seizures; in others, only nausea or retching occurs, and in a few, emesis may not be apparent. Other autonomic manifestations include pallor, flushing or cyanosis, mydriasis or miosis, cardiorespiratory and thermoregulatory alterations, incontinence of urine and/or feces, hypersalivation, cephalic sensations, and modifications of intestinal motility (5). More recognizable conventional seizure symptoms often ensue, and half of them end with hemiconvulsions or generalized convulsions. Two thirds occur during sleep.

The seizures usually last for 5–15 min, but half of them are prolonged, sometimes for hours, constituting autonomic status epilepticus. Even after the most severe seizures and status, the patient recovers within a few

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hours. Prognosis is excellent (1,2,5,8,10). Lengthy seizures and status do not have any adverse prognostic significance, and the risk of developing epilepsy in adult life is probably no more than that of the general population (5). One third of patients (27%) have a single seizure only, and another half (47%) have two to five seizures. Only 5% have >10 seizures, but outcome is again favorable. Remission usually occurs within 1 to 2 years from onset. Multifocal spikes that predominate in the posterior regions characterize the EEG (5).

In most of the reported studies on PS, selection of patients is based on EEG criteria of occipital spikes (6–8,10), which are not specific and not a prerequisite for PS (2,4,15).

## METHODS

### Study sample and participants

The study is based on patients seen in the Epilepsy Center of Agia Sophia Children's Hospital in Athens. The Epilepsy Center has in- and outpatient clinical and EEG facilities for children with seizures. The consultant and associates of the Epilepsy Center are qualified pediatric neurologists with a special interest in epilepsies and EEG. 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 purposes of this study, we reviewed the medical records of 1,340 children with single or recurrent focal afebrile seizures seen in the last 18 years. We have also initiated a prospective study of PS from 1998.

### Inclusion and exclusion criteria

Inclusion criteria were strictly clinical, irrespective of EEG findings: (a) ictal emetic symptoms (nausea, retching, vomiting, alone or in combination); (b) onset from age 1 to 12 years; (c) normal development, neurologic and mental state; (d) normal brain imaging if performed; and (e) normal background EEG, except for postictal records.

We excluded patients (a) with abnormal neurology, brain imaging, or background EEG; (b) with inadequate description of seizures; or (c) seen only once or not having an EEG

We analyzed gender, age at onset of seizures, ictal symptoms, circadian distribution, duration and frequency of seizures, therapeutic response, final outcome, personal and family history of epilepsy, and EEG findings in patients. Most patients had brain neuroimaging [brain computed tomography (CT) scan, magnetic resonance imaging (MRI), and rarely both], which by definition of criteria was normal.

### Investigations

All children had EEG studies, and most (38 of 43) had at least one EEG performed during sleep and wakefulness; two patients had only awake, and another three, only sleep EEG. Hyperventilation and intermittent photic

stimulation were tested according to a standard protocol, although this was not always possible for some younger children. Most of the patients had serial EEGs for years, even after seizure remission. The number of EEGs per patient ranged from one to 11 (mean,  $4 \pm 2$ ).

Occipital spikes are defined as spikes localized in the occipital electrodes irrespective of amplitude and frequency. Occipital paroxysms are repetitive occipital spikes of high amplitude, usually occurring when the eyes are closed.

### Sample for analysis and follow-up

All authors reviewed the clinical and EEG data; only patients for whom a unanimous agreement was reached were included. Ninety (6.7%) of the 1,340 patients with focal seizures met the criteria for PS. Outcome and the final analysis were assessed only for 43 of them that had  $\geq 2$  years of follow-up after the last seizure.

The other 47 children with PS were excluded from the final analysis for the following reasons: (a) 20 had <2 years of follow-up after their last seizure; (b) 24 had seizures with ictal vomiting in at least one seizure per patient, but other manifestations were typical of rolandic epilepsy; all had EEG centrotemporal spikes accentuated by sleep and 12 additional spikes in other regions; and (c) three had "atypical" features. These three atypical cases were (a) an otherwise normal girl with a normal brain CT scan had three seizures typical of PS (onset at sleep with vomiting, gradual loss of contact, gaze deviation to the left, followed 15 min later by left hemiconvulsions) between age 3.5 and 5 years. At age 7 years while still taking carbamazepine (CBZ), frequent (one to two per day), brief seizures developed with visual illusions of macropsias, mainly of humans. EEG showed occipital paroxysms; (b) an otherwise normal boy with normal brain CT scan initially had benign neonatal seizures followed by two febrile seizures at 15 months and 3 years; at age 6 years, he had a single seizure in sleep, beginning with vomiting and left gaze deviation for a few minutes; his first EEG at age 3 years was normal, but the subsequent seven EEGs from 3.5 to 7 years showed occipital paroxysms; (c) an otherwise normal girl with normal brain CT scan had seizures typical of PS that started at age 1.5 years; she continued having seizures (~16) up to age 11 years despite treatment with CBZ or combined with valproate (VPA) or vigabatrin (VGB). She had been free of seizures for the last 1.5 years. Her EEGs showed typical occipital paroxysms blocked by eye opening. Follow-up of the 43 patients analyzed ranged from 2 to 17 years (mean  $\pm$  SD,  $6.5 \pm 3.8$ )

## RESULTS

### Sex and age at onset

Of 43 patients with PS included in the analysis, girls (67%) predominated (Table 1). Age at onset was from 2 to 12 years (mean  $\pm$  SD,  $5.3 \pm 2.2$ ).

**TABLE 1.** *Panayiotopoulos syndrome: clinical characteristics*

No. of patients, 43
Female/male, 29/14 (67%)
Family history, 3 (7%) of 43
Personal history of febrile seizures: 2 (4.4%) of 43
Incidence of PS seizures with fever, 2 (4.4%) of 43
Age at first seizure, 2–12.5 y (mean $\pm$ SD, 5.3 $\pm$ 2.2)
Age at last seizure: 2–12.7 y (mean $\pm$ SD, 5.6 $\pm$ 2.2)
No. of seizures per patient: 1–6 (mean $\pm$ SD, 2 $\pm$ 1.3)
No. of patients with a single seizure, 23 (53%) of 43
Duration of follow-up: 2–17 yr (mean $\pm$ SD, 6.5 $\pm$ 3.8)

PS, Panayiotopoulos syndrome.

### Personal and family history of seizures

Of first-degree relatives, one child had a relative with febrile convulsions, and another child, a relative with a single seizure. Additionally, the brother of a boy with PS had a history of two lengthy episodes ~30 min of loss of consciousness and postural tone at age 4 years after falling from a swing and while watching TV. His EEGs from age 4 to 9 years showed bilateral occipital paroxysms, which subsequently disappeared. In the group of 20 patients with PS without long follow-up, there was a pair of sibs who both had a single lengthy >30 min seizure typical of PS at ages 4 and 9 years. Conversely, in the total group of 90 patients with PS, there were two pairs of twins with only one sibling having PS, whereas the other never had a seizure up to late teen-age.

Of the personal history, only two (4.4%) children had febrile seizures.

### Clinical manifestations

Clinical seizure characteristics are shown in Table 2. The data refer to the first seizure only, because subsequent seizures were often modified with rectal diazepam (DZP) or other antiepileptic medication (AED).

Thirty six (84%) patients had their seizures either at

**TABLE 2.** *Panayiotopoulos syndrome: seizure characteristics*

Sleep related, 36 (84%) of 43
Longer than 30 min, 22 (51.1%) of 43
Ictal vomit, 37 (86%) of 43
Ictal nausea, 4 (9%) of 43
Lateral gaze deviation, 24 (55.8%) of 43
Impairment of consciousness, 43 (100%) of 43
Evolution of hemiconvulsions, 9 (20%) of 43
Evolution to generalized convulsions, 13 (30.2%) of 43
Pallor, 8 (18.6%) of 43
Perioral cyanosis, 8 (18.6%) of 43
Incontinence of urine, (19.2%) of 43
Incontinence of feces, 2 (4.6%) of 43
Retching, 1 (2.3%) of 43
Hypersalivation, 5 (11.6%) of 43
Dysarthria, 2 (4.6%) of 43
Visual loss, 1 (2.3%) of 43
Visual hallucinations, 1 (2.3%) of 43
Hystagmus, 2 (4.6%) of 43
Ictal headache, 2 (4.6%) of 43

the beginning of nocturnal sleep or near arousal or during an afternoon nap (three patients). Recurrent seizures of the same patient usually occurred at the same sleep state.

Thirty-seven (86%) patients had ictal vomiting, which often was the first apparent symptom. The other six had nausea or retching, which did not culminate in vomiting. Deviation of the eyes was reported in 24 patients. This was unilateral in all but two, whose eyes turned upward. Ipsilateral head deviation occurred in nine of them simultaneously or after the eye deviation.

Impairment of consciousness described as confusion of various degrees to complete unresponsiveness happened in all seizures but usually in the progress of the ictus. Often the children were fully aware at seizure onset, complaining of nausea and wanting to be sick; impaired consciousness from the beginning was reported in 11 of them in nocturnal seizures.

The seizures evolved to convulsions in 22 (51%) patients, usually after other prolonged ictal manifestations for >30 min (19 seizures). Convulsions were generalized in 13 patients either from the onset or after hemiconvulsions and unilateral in nine. Of four patients with adequate relevant information, hemiconvulsions were ipsilateral to the deviation of the eyes in two and contralateral in the other two.

Autonomic manifestations, other than nausea or vomiting, were relatively common, usually at seizure progress. These were incontinence of urine (19.2%), pallor (18.6%), perioral cyanosis (18.6%), hypersalivation (11.6%), and less frequently, incontinence of feces and ictal headache (4.6%) (Table 2).

Two patients had nystagmus, witnessed by pediatricians, at the end of lengthy seizures. Blinking without other convulsive manifestations was reported in one patient. Visual symptoms were described in two patients. One patient in only one of three seizures complained of visual loss during the course of it. The other patient had two seizures in wakefulness; in one, reported seeing “a grey circle with a white moon in it,” and in the other, a “stool.” Ictal headache was reported only once at the onset of a seizure with visual hallucinations. Both of these children received no treatment, and they have now been seizure free for 7 and 8 years.

### Misdiagnosis

Six patients were misdiagnosed as having encephalitis (three children), head injury (one) or gastroenteritis (two). Of the cases diagnosed as encephalitis, one had a febrile disease when the seizure occurred, another had fever postictally only, and the last patient had two post-ictal EEGs with lateralizing posterior abnormal background of slow waves.

### Treatment

Twenty-two (51%) patients received CBZ (12 patients), oxcarbazepine (OCBZ; two patients), VPA (three

patients), and phenobarbital (PB; four patients). One patient was treated with a combination of two drugs.

Three patients relapsed while receiving treatment (one of them with fever). Of the 20 patients who had status as the first seizure, 12 received treatment (four of them after seizure relapse). The remaining eight patients with status did not receive treatment; of them, two had further seizure relapse.

### Prognosis

This was excellent, with half (53%) of the patients having a single seizure in a long follow-up of 2–17 years (mean  $\pm$  SD,  $6.5 \pm 3.8$ ). In total, the number of seizures ranged from one to six, with a median of two (mean  $\pm$  SD,  $2 \pm 1.3$ ). Fourteen of the 22 treated patients are currently not receiving treatment, and none of them relapsed after drug discontinuation. Age at last seizure was from 2 to 13 years (mean  $\pm$  SD,  $5.6 \pm 2.2$ ).

### Electroencephalographic findings

Despite similar clinical manifestations, there was a significant EEG variability from normal to abnormal EEGs with occipital or extraoccipital spikes or even brief generalized discharges with or without focal spikes.

#### Normal EEG

Nine (21%) patients with typical clinical features of PS had completely normal EEGs despite two to four repeated recordings per patient performed during sleep and wakefulness. These nine children had one to three seizures each (mean,  $2 \pm 1$ ) with an earlier onset at 2 to 6.5 years (mean,  $4.3 \pm 1.4$ ) than that of the total group. Five of them had lengthy seizures over half an hour, and in four, this was a singular event. Four had their first EEGs within the first or second postictal day, and five, during a period of 1 month to 1 year after their first seizures. Their last EEG was performed from 1.5 month to 12 years after the last seizure. Five received treatment for 0.5–6 years either because of seizure relapse (two cases) or because the first seizure was prolonged (three cases). All of them have now not had treatment for 4.5–11 years.

#### EEG with occipital spikes

Occipital was the most common EEG spike localization recorded in 29 (67%) patients, but only nine had the classic occipital paroxysms inhibited when eyes were open (Fig. 1). Of the other 20 patients, 46% had occipital spike and slow-wave complexes or small-amplitude occipital spikes that were rare or frequent; there was no demonstrable attenuation by eye opening or this was not tested either because it appeared mostly during sleep or because the children were too young to cooperate. Occipital spike-and-wave or occipital paroxysms were unilateral in 13 patients (right sided in seven and left sided in six) and bilateral in 16 patients (usually synchronous, with right-side preponderance in six, left-side preponder-

ance in four, and without clear lateralization in six patients). Seven (24%) of the 29 patients with occipital spikes also had additional epileptiform abnormalities in the initial or subsequent records. These were rolandic spikes in three, multifocal spikes in two, and brief bursts of generalized 3-Hz spike-and-wave discharges with photosensitivity in two cases.

#### EEG with epileptiform abnormalities other than occipital spikes

Five (12 %) patients never had occipital spikes despite three to six EEGs per patient. Instead, there were rolandic spikes in two patients (Fig. 1) or rare, brief bursts of generalized 3- to 3.5-Hz spike-and-wave discharges and photosensitivity in three patients (Fig. 1).

#### EEG evolution

Ten patients with abnormal EEGs were followed up until normalization of their records, which occurred at age 3.5 to 14 years (mean, 8.4 years) and from 1 month to 7 years (mean, 3.3 years) after their last seizure. Eight of them had occipital abnormalities (including a patient with additional multifocal spikes), and two had only rolandic spikes.

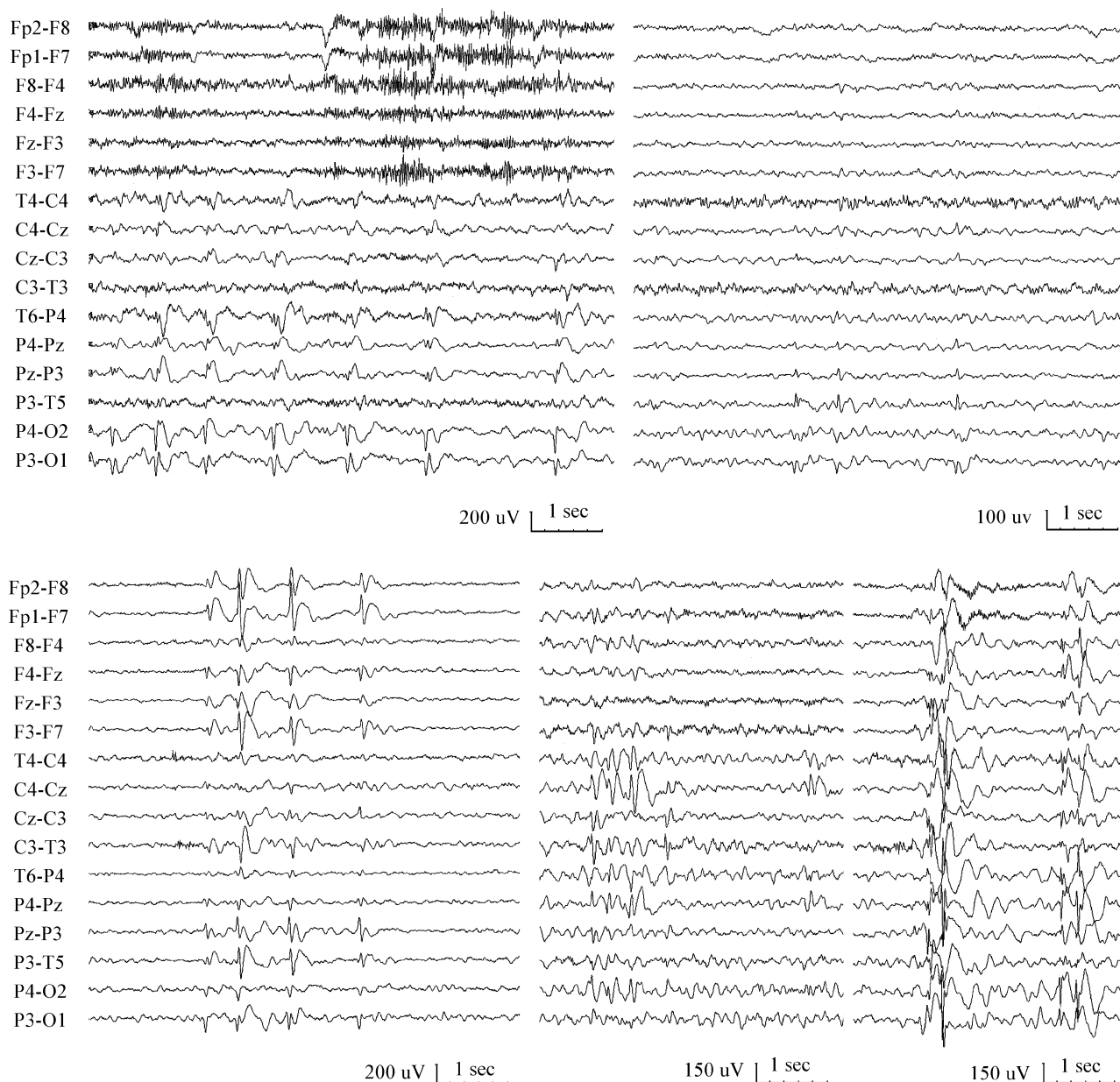
## DISCUSSION

The findings corroborate and extend previous reports documenting PS as a common and benign childhood epileptic syndrome primarily manifesting with autonomic seizures and autonomic status epilepticus (1,2,5–10). In addition to confirming previous research, the present study is unique in that it observed that clinical manifestations are more important than EEG in diagnosing PS. We analyzed definite cases of PS based on clinical criteria only, irrespective of EEG manifestations. The reason for this is that all but two (2,7) of other studies (6,8–10,16–18) are based on EEG manifestations of occipital spikes (6,8,10,16,18), which are erroneously considered a prerequisite for PS (11).

Exact prevalence of PS is unknown, ranging from none in epidemiologic studies (12) to 6% of children age 0–15 years with one or more seizures and probably ~13% in the age group 3–6 years (5). We confirm that PS has a high prevalence of 6.7% in children with focal seizures, although we included only typical cases with a definite diagnosis of PS and excluded others because of inadequate information, atypical presentations, seen only once, or not having an EEG. We did this purposefully because we were interested in the pure form of PS. Further studies are required to assess atypical cases that were beyond the limitations of this report.

Many of our findings with minimal variations confirm that PS is a clinically uniform syndrome with mainly autonomic manifestations and particularly ictal emesis (1,2,6–8,10). Emetic symptoms may not culminate to vomiting (14%). Other autonomic manifestations such as

### EEG variability in Panayiotopoulos syndrome



**FIG. 1.** EEG variability of Panayiotopoulos syndrome in five of the 43 patients. Despite similar clinical features, the interictal EEG is different with occipital paroxysms (upper left), small and scattered occipital spikes (upper right), repetitive multifocal spikes (lower left), extraoccipital spikes only (lower middle), and brief generalized discharges (lower right). EEGs also may be consistently normal (see text).

pallor or cyanosis and urine incontinence are very common. Of nonautonomic manifestations, unilateral deviation of the eyes is the most frequent (56%), but this often occurs after the ictal emesis. Visual hallucinations or other visual symptoms are exceptional (5%) and not a consistent symptom in recurrent seizures. Half (46.5%) of the seizures last for more than half an hour, constituting autonomic status epilepticus. Despite prolonged duration, only half (50%) of the seizures end with hemiconvulsions (20%) or generalized convulsions

(30%). Ictal nystagmus has not been previously reported in PS (5). This was reliably witnessed by physicians in two of our patients toward the end of lengthy seizures while the children were unresponsive, without any other convulsive features. Epileptic nystagmus is a rare ictal event usually considered a sign of lesional epilepsy (19). Our patients did not differ from the other cases of PS in any other respect. They both had a single seizure, have been seizure free for 5–7 years though unmedicated, and had normal brain scans.

Sleep is the main precipitating factor, with 84% of the seizures occurring soon after the child goes to sleep or in the early hours of the morning. Fever may be a rare precipitating factor if not coincidental; two cases of our patients had typical PS seizures during a febrile illness. This may be significant regarding differential diagnosis from encephalitis or febrile seizures, which are usually generalized convulsions. These cases also are different from other patients with PS, in whom fever may develop as a consequence of thermoregulatory disturbances during or immediately after the attacks (5). Prognosis is excellent, with half of the children having only one seizure and rarely more than six recurrences (1–3,5–8,10–17). Recurrent prolonged attacks resistant to AEDs are rare, but these also have good prognosis (5,20,21). Lengthy seizures do not appear to have adverse effects; the children are normal after a few hours' sleep. This contradicts basic teaching that prolonged seizures are often associated with brain damage; even febrile seizures, if lengthy, carry a worse prognosis and are associated with a higher risk for developing "epilepsy" in later life (22).

Misdiagnosis is a significant management problem, adversely affecting thousands of children with PS (5,23,24); encephalitis, migraine, cardiogenic syncope, gastroenteritis, and dehydration are the most common errors. PS is well known to Greek pediatricians, yet three of our patients were diagnosed and treated as having encephalitis.

In our patients, girls (67%) outnumbered boys, but cumulative data of 344 patients (5–8,10) indicate that both sexes are equally affected. Although PS is considered a genetically determined predisposition to childhood seizures (5), the occurrence of epilepsies in first-degree relatives was very low in our study. This may partly reflect the predominantly retrospective character of our study. Others reported a higher incidence of 7–30% (6–8), but this needs evaluation in future prospective studies. Panayiotopoulos also found that epilepsies are infrequent among relatives of children with PS and emphasized on a high prevalence of abnormal births. Similarly, prevalence of febrile seizures among children with PS varied in the reported series from 13% (5) to 45% (7), as opposed to only 4.4% in our study. PS in the same family is exceptional. Caraballo et al. (8) reported two pairs of siblings among 62 patients with PS. Similarly, we found two pairs of siblings with PS.

### Diagnostic procedures

By definition, PS affects otherwise normal children with normal brain imaging, if this is performed. EEG is the most useful diagnostic procedure. However, it should be emphasized that PS should not be equated with occipital spikes or occipital epilepsy. In the original study of Panayiotopoulos of 21 otherwise normal children with

ictal vomiting, occipital spikes occurred in 12 (57%); the others had extraoccipital spikes (five), infrequent brief generalized discharges (one), or consistently normal EEG (three) (2,5,15). Subsequent attention was focused on the predominant group of occipital spikes and occipital paroxysms (3,6,8–10,16,18–21) with which PS was associated by a descriptive name "early onset benign childhood epilepsy with occipital paroxysms" (3,6,9,10–16–18,21). Even in recent studies, occipital spikes are a mandatory inclusion criterion (8,10), and some even exclude small occipital spikes (10). Occipital spikes are nonspecific EEG abnormalities often found in children without seizures and even in 1% of normal children (13,25).

Only recently it became apparent that the clinical manifestations of PS are the same irrespective of EEG localizations (1,4,5,7). This point is documented in our study with frequent awake and sleep EEGs. Only 29 (67%) of 43 patients had at least one EEG with occipital spikes, and these often were small, occurred with other epileptiform abnormalities or were seen once only; occipital paroxysms were even rarer (nine patients). Conversely, the other 14 (33%) consistently had normal EEGs (nine patients) or epileptiform abnormalities other than occipital spikes (five patients). We particularly stress the high prevalence of normal EEG (21%); a finding that has not been previously adequately addressed. A normal EEG compounded with the unusual for seizures clinical manifestations of PS may be a significant factor for misdiagnosis. Our results also indicate that children with normal EEGs or initially normal EEGs with delayed appearance of spikes may differ from the others with PS because of earlier onset and smaller total number of seizures (17).

Occipital spikes or other functional spikes and brief generalized discharges may appear short or long after a seizure and are more likely to be seen in serial EEGs also including sleep EEGs (5,17). This point is exemplified by two of our patients. One with a single lengthy >5-h seizure at age 10 years had three normal EEGs from age 10 to 11 years during wakefulness and sleep, but another EEG at age 12 showed random small occipital spikes. Another patient only once 2 days after a single seizure, had an abnormal EEG with occipital paroxysms; many other subsequent EEGs were normal.

Spikes may appear only once in one of series of EEGs or may persist after clinical remission for many years until the mid-teens (5,17). Frequency, location, and persistence of functional spikes do not determine clinical manifestations, duration, severity and frequency of seizures, or prognosis (5).

### Pathophysiology

The clinical and EEG features of PS in this study support the view that there is a maturation-related diffuse

cortical hyperexcitability (5,23). This diffuse epileptogenicity may be unequally distributed, predominating in one area, which is often posterior. The preferential involvement of emetic and the autonomic systems in general may be attributed to epileptic discharges generated at various cortical locations and influencing vulnerability to children's emetic centers and the hypothalamus (5,23). Certainly our findings do not support the currently held official view (11) that PS is "occipital epilepsy": (a) of all clinical manifestations, only deviation of the eyes may originate from the occipital regions, but this rarely is the first symptom; visual symptoms are exceptional and not consistent in recurrent seizures; (b) interictal occipital spikes may never occur; and (c) ictal EEG documented posterior or anterior onset (7).

### Limitations of the study

This study has several methodologic limitations. Foremost, this is a primarily retrospective study with strict inclusion criteria limited to typical presentations of PS, probably underestimating the prevalence of PS and ignoring atypical presentations. We also may have been overcautious with atypical cases of PS that we did not include in the final analysis. However, these may be of significant interest; thus 24 of our patients had ictal vomiting concomitant with other typical rolandic features. Further, an additional patient with seizures typical of PS later developed frequent visual seizures typical of Gastaut-type childhood occipital epilepsy (11,13). Another patient initially had benign neonatal seizures, then developed febrile convulsions, and later had seizures typical of PS. These cases probably illustrate the links of PS with rolandic and other focal benign childhood seizures in the same nosologic category of a benign childhood seizure susceptibility syndrome, which is maturation dependent (13,26).

We also excluded from the final analysis one patient (case c in the Methods) because of frequent seizures, although this probably represents a more severe form of PS that also has a good prognosis (20,21).

We also probably erroneously did not categorize as having PS the brother of a patient with PS. He had two lengthy seizures of loss of consciousness and postural tone but no emetic or other autonomic manifestations. Similar cases have been previously reported (16), probably manifesting with pure ictal syncope (loss of consciousness and of postural tone), which is another intriguing feature of PS (5,23).

Further prospective studies are needed to address these areas of uncertainty.

### Clinical practice implications

Despite high prevalence and often striking clinical manifestations that may last for hours, PS remains practically unknown by the general pediatricians because it is conspicuously absent from all relevant pediatric publica-

tions. In view of the high rate of misdiagnosis of PS, this results in avoidable morbidity and costly hospital admissions (1,5,24). Pediatricians were made aware of febrile seizures and rolandic epilepsy through appropriate publications, practice parameter guidelines, and public awareness campaigns. Pediatricians were receptive and made excellent use of this knowledge in their roles as advocates for children and families. This also is expected with PS, which is now well documented from around the world.

### Management

There are no practice parameters guidelines for the management of PS. Ours are similar to those issued by Panayiotopoulos in 2001 (1), based on appropriate modifications of practice parameter guidelines for febrile seizures (27).

### Immediate management

Control of the seizure is paramount. In the rare occasions that the child is febrile, treatment of possible fever and mainly of the underlying illness also is important. One third (30%) of the seizures are relatively brief and self-limited. They subside spontaneously within 2–10 min. The other two thirds (70%) have long-lasting seizures (>10 min) or status epilepticus (>30 min to hours), which are a genuine pediatric emergency. These should be appropriately and vigorously treated as for status epilepticus (28,29). Early, usually parental, is more effective than late emergency treatment (29). Parents of children with recurrent seizures should be advised to place the child on its side or stomach on a protected surface and administer a preparation of rectal benzodiazepine (BZD). In an emergency facility, the child's airway should be kept clear, oxygenation maintained, and intravenous or rectal AED given to halt the seizure. A BZD is probably the first choice.

Whether antiemetic drugs may be useful for repetitive ictal vomiting should be addressed. The child may be dehydrated, and this should be appropriately managed.

### Prophylactic management

The great majority with PS do not need AED treatment even if they have lengthy seizures or have more than two recurrences. There is no increased risk of subsequent epilepsy or neurologic deficit. These risks are small, and the potential side effects of drugs appear to outweigh the benefits.

However, prophylactic treatment may be desired if a child has multiple recurrences (only ~5% exceed 10 seizures) and in the unlikely event of parental insistence.

Continuous prophylaxis consists of daily medication with any AED with proven efficacy in partial seizures. Although there is no evidence of superiority among monotherapy with PB, CBZ, VPA, or no treatment in PS, most authors prefer CBZ (6).

### Parental attitude and education

The traumatizing, sometimes long-lasting effect on parents, even of a benign seizure, has been well documented in febrile seizures (22,30). This is even worse in PS, in which seizures may last for many hours, compounded by physicians' uncertainty regarding diagnosis, management, and prognosis. Seizures in PS, like febrile convulsions, despite their excellent prognosis, are a dramatic experience of usually young age and inexperienced parents, who often think that their child is dead or dying.

Parents of young children should have general information by the family doctor regarding PS (5). Parents who have watched their child during a seizure need specific information to avoid long-term reactions.

Supportive family management includes education about PS and specific instructions about emergency procedures for possible subsequent seizures (5).

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