Epileptic Disord 2012; 14 (4): 426-31

Video-EEG documented lengthy seizure in Panayiotopoulos syndrome: clinical manifestations may be inconspicuous

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Received July 4, 2012; Accepted September 19, 2012

ABSTRACT – A 4-year-old boy had an autonomic seizure of Panayiotopoulos syndrome during video-EEG recording. Interictal EEG showed multifocal spikes in the centrotemporal and left posterior regions. Ictal electrographic onset included fast rhythms in the left posterior regions progressing to a mixture of high-amplitude spikes and fast and slow rhythms, bilaterally. The clinical symptoms (sighing, arousal with eyes opening, eye-deviation, and emesis with possible alteration of consciousness) started two minutes after the electrographic onset. These symptoms were mild and their characterisation as epileptic seizure behaviour would have been difficult without the ictal EEG documentation. The clinical manifestations of the child's previous epileptic seizures were mainly from the Rolandic area. [*Published with video sequences*]

Key words: Panayiotopoulos syndrome, Rolandic epilepsy, ictal EEG, clinical manifestation, ictus emeticus

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Panayiotopoulos syndrome (PS) is a childhood-related syndrome rendering patients susceptible to autonomic seizures and autonomic status epilepticus (Ferrie *et al*., 2006; Ferrie *et al*., 2007). PS has been recognised by the ILAE (Berg *et al*., 2010) and confirmed in independent studies of over 700 children (Caraballo *et al*., 2007; Ohtsu *et al*., 2008; Hirano *et al*., 2009; Specchio *et al*., 2010a). PS affects around 13% of children, 3-6 years old, with one or more non-febrile seizure, and 6% of the age group 1-14 years (Panayiotopoulos, 2002). Onset is commonly between ages 3-6 years (76%) and usually presents with infrequent and lengthy seizures that mainly occur in sleep (70%). Clinical manifestations consist of an unusual seizure constellation of largely autonomic symptoms, alone or together with behavioural changes, unilateral

doi:10.1684/epd.2012.0536

deviation of the eyes, and other more conventional ictal symptoms. Commonly, the seizures start with autonomic manifestations (81%), which are mainly emetic (72%). Autonomic status epilepticus occurs in half of all patients.

The interictal EEG findings are variable, from normal to multifocal spikes, and also change significantly between serial EEGs. Occipital spikes are common but not necessary for diagnosis. Frontal or centro-temporal spikes may be the only abnormality. Generalised discharges may occur alone or together with focal spikes.

The level of misdiagnosis of PS is high because symptoms may be misinterpreted as encephalitis, cyclical vomiting syndrome, atypical migraine, and gastroenteritis (Covanis, 2006; Michael *et al*., 2010).

The ictal semiology of PS is based mainly on descriptions by patients and witnesses. This, together with the fact that seizures are mainly nocturnal, could explain the variations among authors regarding the prevalence of the various ictal symptoms. Furthermore, because of its unusual clinical manifestations, a few authors even now doubt its existence (Appleton *et al*., 2010), based on unsubstantiated evidence (Ferrie and Livingston, 2010). Ictal EEG and, in particular, video-EEG are used as the gold standard to clarify these matters. In PS, as is the case for Rolandic epilepsy, only 20 cases with reported ictal EEGs are available, due to the fact that patients have only single or rare seizures (Specchio *et al*., 2010b).

We present a case of a child with a video-EEG recording of an autonomic seizure of PS, demonstrating that ictal manifestations may be inconspicuous or misinterpreted as non-epileptic symptoms.

Case report

A boy, born in September 2007, had a lengthy epileptic seizure during an EEG after partial sleep deprivation in February 2012. Birth and development were normal and he had a normal MRI scan. His father had a single nocturnal seizure at age 10 years.

The EEG was planned following four epileptic seizures during sleep over a period of two years. The first couple of seizures were described as starting with left arm jerking, progressing to a generalised convulsion. The second seizure (eight months prior to the EEG) occurred when he was febrile and was associated with left-sided Todd's paralysis. The third seizure, five months later, was observed from the start and described as: "*It started with the left arm jerking up and down slowly, and then the right arm. He appeared unresponsive with eyes open, staring and vomiting a little. The episode lasted about 20 minutes and was stopped with rectal diazepam*." In the fourth seizure (one month prior to the EEG), "*lip smacking*" was noted. Also "*speech was slurred while recovering and he was very sleepy afterwards*". No medication was prescribed. The diagnosis of possible Rolandic epilepsy was considered by the referring paediatrician.

Clinical and EEG manifestations

The child had been partially sleep-deprived for the test. He was sick in the car on the way to the department, but appeared alert and well on arrival; the parents agreed that he should take the prescribed melatonin in order to help him sleep during the recording.

The boy was alert and cheerful at the start of the recording. The interictal EEG in the awake and sleep recording showed frequent high-amplitude multifocal spikes on a normal background. These localised independently to the right (maximal C4) and left (maximal C3) centrotemporal and left occipital electrodes (*figure 1 and video 1*). The right C4 spikes were more frequent and nearly continuous. The left posterior spike was not as frequent but of higher amplitude with maximal fluctuation between O1 and P3 electrodes. Photic stimulation and hyperventilation did not enhance the discharge.

An electroclinical seizure was recorded from stage 2 sleep (*figure 1 and video 2*). The onset of the electrical discharge was subtle with low-amplitude fast activity superimposed over the left posterior (maximal O1) background rhythms, leading to continuous focal high-amplitude fast spike-and-wave discharge that progressed over the left posterior cortex, later becoming bilateral. Interictal centrotemporal spikes continued on the right for around 20 seconds from ictal onset. When the clinical change appeared, two minutes from the electrical onset, the ictal abnormality of fast rhythms, spikes, and slow waves increased in amplitude and appeared more widespread, but remained of higher amplitude over the left posterior regions.

The first clinical manifestation occurred 2:06 minutes into the ictal discharge with a sigh, while the child was still asleep, lying on his left side. Twenty-four seconds later, he slowly opened his eyes and awoke. He nodded to his parents who were asking him if he was alright, and he outstretched his right arm towards them who were on his left side. He appeared slightly dazed and his parents continued to ask him how he was feeling; he answered appropriately by nodding his head slowly. He then correctly followed the instructions of the technician to turn on to his back and wave at the camera. While he waved, his eyes deviated to the right for around 10 seconds and he frowned, before turning his eyes towards his parents on his left side, but not

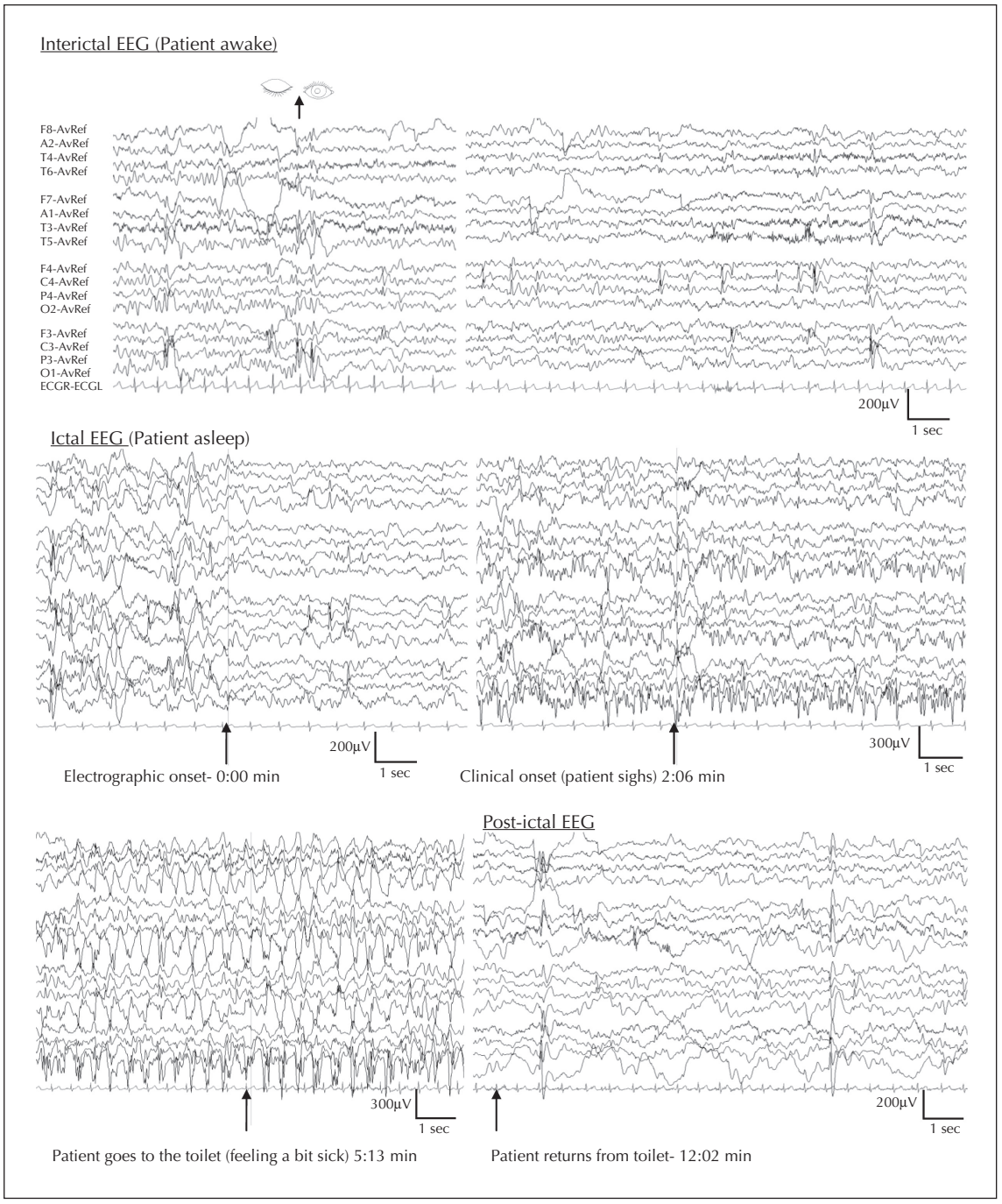

Figure 1. EEG samples showing the interictal EEG with eye closure (upper section), the ictal onset and progression of the seizure (middle section), and the postictal EEG (lower section). An average montage was used to display the EEG activity with one ECG channel showing heart rate.

looking directly at them. Also, intermittently, his eyes deviated to the right (away from his parents), and he sighed a couple of times and frowned.

At 3:52 minutes into the seizure, he complained that his "*tummy hurt*" and wanted to go to the toilet. His mother asked him if he was going to be sick, he was unsure but again asked to go to the toilet. During this period, he correctly answered simple questions regarding his age and about his brother (*video 3*). He also gave his age using his fingers. However he continued to appear languid with eyes fixed to the right, occasionally sighing and frowning. At 5:13 minutes into the seizure (still showing seizure activity, bilaterally), the recording was stopped in order to allow the child to

go to the toilet. He walked to the toilet accompanied by his father. He vomited a little, felt better, and was able to walk back in to the recording room noticeably more alert and smiling, though he was still sleepy and felt a little sick. By the time the EEG recording was resumed 6:46 minutes later, there was no ictal seizure activity but the EEG background was moderately slow, especially posteriorly, on the left more than the right (with infrequent multifocal spikes), as the child appeared drowsy (*figure 1 and video 4*). The recording continued for a couple of minutes and he was then left to go back to sleep and awoke 2-3 hours later when, after initially appearing sleepy, he quickly became more alert and reported feeling better. He had something to eat before going home.

There was no change in his breathing pattern during the seizure, at least as seen on video. The ECG rate was calculated retrospectively from 10-second samples at different stages of the recording, as follows: resting rate (awake; 90-110 bpm), sleep (90-100 bpm), electrographic ictal onset (90-100 bpm), clinical onset (patient sighed; 90-100 bpm), opening eyes (90-100 bpm), answering questions (110-120 bpm), going to the toilet (120-130 bpm), returning from the toilet (100-110 bpm), and at the end of the recording (awake/drowsy; 90-100 bpm).

Discussion

This child fulfils the diagnostic criteria of PS which occurs in children with normal neurodevelopment but with at least one autonomic epileptic seizure and at least one abnormal EEG with focal spikes (Koutroumanidis *et al*., 2012). The recorded seizure could only be classified as an autonomic seizure, which, by definition, is "*characterised by altered autonomic function of any type at seizure onset or in which manifestations consistent with altered autonomic function are prominent (quantitatively dominant or clinically important), even if not present at seizure onset. The altered autonomic function may be objective or subjective or both*" (Ferrie *et al*., 2007).

The video-EEG recording of the autonomic epileptic seizure of this child adds to the literature of previous reports which include 20 recorded autonomic seizures in PS (Beaumanoir, 1993; Vigevano and Ricci, 1993; Vigevano *et al*., 2000; Oguni *et al*., 2001; Demirbilek and Dervent, 2004; Koutroumanidis *et al*., 2005; Parisi *et al*., 2005; Battaglia *et al*., 2007; Iannetti *et al*., 2009; Specchio *et al*., 2010b; Gonzalez-Duarte *et al*., 2011). For details, see the recent report and detailed review by Specchio *et al*. (2010b). All these recorded seizures occurred while the children were asleep. The onset of the electrographic ictal discharge was mainly occipital (seven cases) or frontal (seven cases). The first clinical manifestation, which appeared long after the electrographic onset (1-10 minutes), usually consisted of opening of the eyes as if the children were waking up. There were no other abnormal seizure movements such as tonic or clonic movements, or eyes rolling or flickering. At this stage, usually the children responded, often correctly, to simple questions. On many occasions, tachycardia was the first objective sign when ECG was recorded. Vomiting was a common ictal symptom occurring at any stage of the seizures but not as the first clinical manifestation. Seizures associated with ictal vomiting did not have any particular localisation or lateralisation. Vomiting occurred mainly when the ictal discharges were more diffuse than localised. Sometimes only retching without vomiting occurred and on a few occasions vomiting did not occur. Other autonomic manifestations included mydriasis, pallor, cyanosis, tachypnea, hypersalivation, and perspiration at various stages of the ictus. Of non-autonomic manifestations, deviation of eyes to the right or left occurred before or after vomiting without any apparent EEG localisation; this was present in seizures starting from the occipital or frontal regions.

In our case, the clinical manifestations during the ictal electrographic discharge were, in order of appearance: a sigh, eyes opening upon awakening, eye deviation, and nausea and vomiting with probably some mild alteration of consciousness. The parents commented that although they felt something was wrong with their child, they did not recognise the event as a seizure. After being told that this episode with minor clinical change was an epileptic seizure, there was considerable parental anxiety, consistent with the findings of Valeta (2005) for benign childhood epilepsies and mainly PS.

A sigh was the first ictal clinical manifestation with no other apparent change in respiratory rhythm. Sigh is a respiratory manifestation which has been reported only as a postictal symptom in temporal lobe epilepsy (Foldvary *et al*., 1997). It presents commonly during sleep and can also present in sleep in normal people and infants. It is probably generated in the respiratory network in the pre-Botzinger complex of the medullary respiratory network (Schwarzacher *et al*., 2011). Subsequent symptoms were eyes opening and awakening, during which the child was very responsive and able to correctly answer the various questions asked by the technician and parents, similar to any child immediately after normal awakening from sleep. Consciousness probably remained intact during the whole seizure, though some mild confusion could not be excluded. Eye deviation to the right was clearly an abnormal symptom, but this was not associated with any other eyeball or eyelid clonic or tonic movements. The final symptoms were nausea, retching, and vomiting. The child was able to walk to the toilet to vomit and

on return, six minutes later, he looked and behaved normally. At this stage, the ictal EEG discharge had also ceased.

The recorded seizure started from the left occipital region, though his interictal EEG also showed numerous centrotemporal spikes which continued even after the onset of the ictal electrographic discharge.

Another interesting finding is that, previously, the child had had other epileptic seizures with mainly clinical manifestations of focal motor seizures from the Rolandic area, however, there was not a single element of Rolandic involvement in the recorded autonomic seizure, either at ictal EEG onset or with regards to clinical symptoms. This is consistent with the notion that PS and Rolandic epilepsy share a close pathogenetic relationship (Panayiotopoulos, 2002). Indeed, autonomic seizures of PS may present with clinical symptoms of Rolandic epilepsy, moreover, the same child may independently have both typical Rolandic and autonomic seizures (Panayiotopoulos, 2002; Covanis *et al*., 2003; Caraballo *et al*., 2007; Ohtsu *et al*., 2008; Specchio *et al*., 2010a).

This video-EEG documented seizure indicates that some children with PS may have inconspicuous clinical manifestations that may be overlooked by parents, suggesting that the prevalence of PS may be higher than is currently estimated. □

Legends for video sequences

Video sequence 1.

Interictal recording: the patient is alert, pointing to pictures around the room, with closing of the eyes.

Video sequence 2.

Ictal and clinical onset of seizure: the patient is asleep at electrographic onset and clinical onset (a sigh) follows before the patient opens his eyes and reaches for his parents for comfort.

Video sequence 3.

Ictal EEG: the patient is asked simple questions during the seizure, which he is able to answer appropriately, he then complains that his "tummy hurts" and asks to go to the toilet.

Video sequence 4.

Postictal EEG: the patient returns from the toilet appearing more alert and smiling.

Key words for video research on www.epilepticdisorders.com

Syndrome: Panayiotopoulos syndrome
Etiology: idiopathic
Phenomenology: autonomic seizure; vomiting (ictal)
Localization: not applicable

Acknowledgements and disclosures.
We are very grateful to the parents of this child for allowing us to use the medical history and video-EEG footage for this publication. None of the authors has any conflict of interests to disclose. Dr. Panayiotopoulos declared *"Paid consultancy with UCB Pharma, the manufacturers of Keppra and Vimpat"*.

References

Appleton RE, Tedman B, Preston T, Foy T. Panayiotopoulos syndrome: a debate. *Epileptic Disord* 2010; 12: 91-2. doi: 10.1684/epd.2010.0299

Battaglia D, Martinelli D, Perrino F, *et al*. Ictal video-EEG and atypical evolution in a child with Panayiotopoulos syndrome. *Boll Lega It Epil* 2007; 136-137: 51-4.

Beaumanoir A. Semiology of occipital seizures in infants and children. In: Andermann F, Beaumanoir A, Mira L, Roger J, Tassinari CA. *Occipital seizures and epilepsies in children*. London: John Libbey and Company Ltd, 1993: 71-86.

Berg AT, Berkovic SF, Brodie MJ, *et al*. Revised terminology and concepts for organization of seizures and epilepsies: Report of the ILAE Commission on Classification and Terminology, 2005-2009. *Epilepsia* 2010; 51: 676-85.

Caraballo R, Cersosimo R, Fejerman N. Panayiotopoulos syndrome: a prospective study of 192 patients. *Epilepsia* 2007; 48: 1054-61.

Covanis A. Panayiotopoulos syndrome: a benign childhood autonomic epilepsy frequently imitating encephalitis, syncope, migraine, sleep disorder, or gastroenteritis. *Pediatrics* 2006; 118: e1237-e2143

Covanis A, Lada C, Skiadas K. Children with Rolandic spikes and ictal vomiting: Rolandic epilepsy or Panayiotopoulos syndrome? *Epileptic Disord* 2003; 5: 139-43.

Demirbilek V, Dervent A. Panayiotopoulos syndrome: video-EEG illustration of a typical seizure. *Epileptic Disord* 2004; 6: 121-4.

Ferrie CD, Livingston JH. Panayiotopoulos syndrome: learning lessons from atypical cases. *Epileptic Disord* 2010; 12: 92-4. doi: 10.1684/epd.2010.0299

Ferrie C, Caraballo R, Covanis A, *et al*. Panayiotopoulos syndrome: a consensus view. *Dev Med Child Neurol* 2006; 48: 236-40.

Ferrie CD, Caraballo R, Covanis A, *et al*. Autonomic status epilepticus in Panayiotopoulos syndrome and other childhood and adult epilepsies: a consensus view. *Epilepsia* 2007; 48: 1165-72.

Foldvary N, Lee N, Thwaites G, *et al*. Clinical and electrographic manifestations of lesional neocortical temporal lobe epilepsy. *Neurology* 1997; 49: 757-63.

Gonzalez-Duarte A, Norcliffe-Kaufmann L, Martinez J, *et al*. Cardiovascular and neuroendocrine features of Panayiotopoulos syndrome in three siblings. *Epilepsy Behav* 2011; 21: 296-300.

Hirano Y, Oguni H, Funatsuka M, Imai K, Osawa M. Neurobehavioral abnormalities may correlate with increased seizure burden in children with Panayiotopoulos syndrome. *Pediatr Neurol* 2009; 40: 443-8.

Iannetti P, Spalice A, Rocchi V, Verrotti A. Diffuse onset of ictal electroencephalography in a typical case of Panayiotopoulos syndrome and review of the literature. *J Child Neurol* 2009; 24: 472-6.

Koutroumanidis M, Rowlinson S, Sanders S. Recurrent autonomic status epilepticus in Panayiotopoulos syndrome: video/EEG studies. *Epilepsy Behav* 2005; 7: 543-7.

Koutroumanidis M, Ferrie CD, Valeta T, Sanders S, Michael M, Panayiotopoulos CP. Syncope-like epileptic seizures in Panayiotopoulos syndrome. *Neurology* 2012; 31: 463-7.

Michael M, Tsatsou K, Ferrie CD. Panayiotopoulos syndrome: an important childhood autonomic epilepsy to be differentiated from occipital epilepsy and acute non-epileptic disorders. *Brain Dev* 2010; 32: 4-9.

Oguni H, Hayashi K, Funatsuka M, Osawa M. Study on early-onset benign occipital seizure susceptibility syndrome. *Pediatr Neurol* 2001; 25: 312-8.

Ohtsu M, Oguni H, Imai K, Funatsuka M, Osawa M. Early-onset form of benign childhood epilepsy with centrotemporal EEG foci: a different nosological perspective from Panayiotopoulos syndrome. *Neuropediatrics* 2008; 39: 14-9.

Panayiotopoulos CP. *Panayiotopoulos syndrome: a common and benign childhood epileptic syndrome*. London: John Libbey & Company, 2002.

Parisi P, Ferri R, Pagani J, Cecili M, Montemitro E, Villa MP. Ictal video-polysomnography and EEG spectral analysis in a child with severe Panayiotopoulos syndrome. *Epileptic Disord* 2005; 7: 333-9.

Schwarzacher SW, Rub U, Deller T. Neuroanatomical characteristics of the human pre-Botzinger complex and its involvement in neurodegenerative brainstem diseases. *Brain* 2011; 134: 24-35.

Specchio N, Trivisano M, Di Ciommo V, *et al*. Panayiotopoulos syndrome: a clinical, EEG, and neuropsychological study of 93 consecutive patients. *Epilepsia* 2010a; 51: 2098-107.

Specchio N, Trivisano M, Claps D, Battaglia D, Fusco L, Vigevano F. Documentation of autonomic seizures and autonomic status epilepticus with ictal EEG in Panayiotopoulos syndrome. *Epilepsy Behav* 2010b; 19: 383-93.

Valeta T. Parental attitude, reaction and education in benign childhood focal seizures. In: Panayiotopoulos CP. *The epilepsies: seizures, syndromes and management*. Oxford: Bladon Medical Publishing, 2005: 258-61.

Vigevano F, Ricci S. Benign occipital epilepsy of childhood with prolonged seizures and autonomic symptoms. In: Andermann F, Beaumanoir A, Mira L, Roger J, Tassinari CA. *Occipital seizures and epilepsies in children*. London: John Libbey & Company Ltd, 1993: 133-40.

Vigevano F, Lispi ML, Ricci S. Early onset benign occipital susceptibility syndrome: video-EEG documentation of an illustrative case. *Clin Neurophysiol* 2000; 111: S81-6.