

## Panayiotopoulos Syndrome- Revisited

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### Abstract

Paediatric epileptic syndromes are easily identified by the classical seizure semiologies and the electrical signatures of these epilepsies. However some of the less discussed entities can cause diagnostic confusion by their bizarre manifestations. One such scenario is that of a child presenting with ictal vomiting with or without autonomic manifestations. This intriguing epileptic phenomenology of Panayiotopoulos syndrome and its genesis is systematically explored in this review.

**Keywords:** Panayiotopoulos Syndromes; Seizure; Epilepsies

### Introduction

The childhood epilepsy syndrome of Panayiotopoulos is considered to be a seizure susceptibility syndrome which is intercalated between febrile seizures and benign childhood epilepsy with centro-temporal spikes (BCECTS) and probably represents a continuum of abnormal neuronal hyper-excitability that transfigures itself during the different phases of brain maturation [1]. The exclusive occurrence of this syndrome in the paediatric age group is reaffirmed by published reports till date, the classical age group being 2 - 6 years in both sexes. Family history of seizures, febrile seizures, SCN1 mutation and BCECTS are some of the putative associations of PS [2-4].

The objective of this review is to comprehensively discuss the clinical, electrographic, pathophysiological and therapeutic aspects of this pediatric epilepsy syndrome.

### Clinical Presentation

PS also known as early onset occipital lobe epilepsy of child hood is not a true occipital lobe epilepsy but rather a multifocal epilepsy personified by an uncompromisingly unique clinical picture. Autonomic seizures are the sine qua non of PS. The episodes usually begin with vomiting which can be protracted and laborious with severe retching often accompanied by other autonomic manifestations like pallor (which is typically observed in the peri-oral region) and diaphoresis. This may progress to a flaccid and unresponsive state lasting from minutes to sometimes over thirty minutes which evokes a sense of horror and helplessness for the witnessing parent(s). Ictal syncope is a term applied to this semiology and its minor forms where patient loses consciousness with autonomic accompaniments without other manifestations like version or tonic clonic movements akin to what we observe in a patient with other forms of syncope. It is not unusual for the pattern to evolve into a complex partial semiology with deviation of eyes and/or tonic/clonic movements. Yet another exemplary feature of AS is a profound mydriasis even apparent to the untrained eye. Although conventionally grouped under the class of occipital lobe epilepsies, visual hallucinations and headache are only rarely seen. Family history of seizures, febrile seizures, SCN1 mutation, BCECTS is some of the putative associations of PS [2]. Other less frequent features include cephalic aura, coughing often leading to vomiting, and hyper salivation [3-7]. The benign reputation of the entity is corrupted by the occurrence of cardio respiratory arrest in a small minority of cases. Sometimes the only symptom before the seizures set in is a sick or "unwell" feeling. PS is also often wrongly diagnosed as encephalitis, gastroenteritis and other mimicking diseases [8].

A predilection for the seizures to occur during sleep is documented by most authors with some reporting the autonomic manifestations especially vomiting also to follow this circadian pattern.

For simplicity, the cardinal features can be remembered as 4 P's: 1) Predominant seizure type is Autonomic seizures 2) Prolonged AS/retching lasting more than 30 minutes 3) Pallor 4) Pupillary changes.

In an analysis of 24 patients with ictal vomiting by Panayiotopoulos, benign childhood epilepsies especially those of occipital origin emerged as the leading cause [9]. The phenomenon in adults is considered to originate from the non-dominant temporal lobe and forms part of the complex partial semiology [10]. But ictal vomiting in the setting of PS has certain distinct characteristics: 1) prolonged retching, nausea and vomiting lasting several minutes 2) preserved/minimally impaired consciousness during the emetic phase of seizures 3) loss of consciousness following the episode with loss of tone (ictal syncope) along with other autonomic manifestations 4) vomiting and or autonomic seizures are the predominant seizure type 5) ictal vomiting/AS occur in the initial part of the seizure itself.

Neuropsychological and cognitive parameters are unaffected during the entire course of the illness which by itself is self-limiting. The children outlive their seizures and hardly ever have a seizure beyond the typical age group (AS have been reported in adolescents upto 14 years of age).

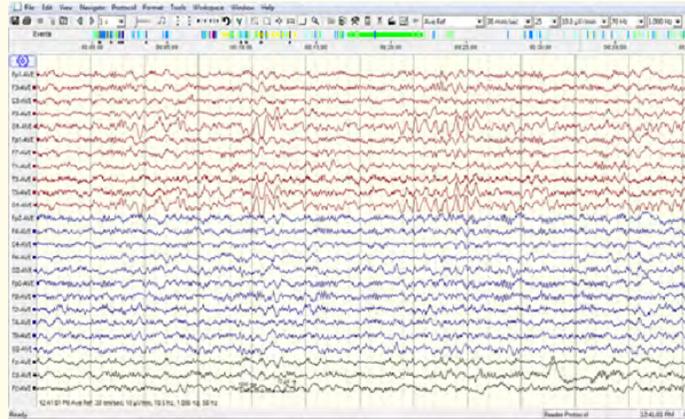
### **Electrographic features**

PS is unique among the epilepsies in that it results in AS irrespective of the lobar localization evidenced on electrography. Magnetoencephalographic studies have deciphered equivalent current dipole (ECD) clusters located along the banks of the parieto-occipital and calcarine sulci and rarely in the central sulcus [11-13]. EEG dipole analysis using a computer detection programme and automatic clustering analysis have shown very good stability of the dipole in PS patients along the same areas as opposed to symptomatic LREs [14]. Interictal surface EEG can show multifocal spikes originating from occipital, temporal, parietal and frontal areas [3-7,15].

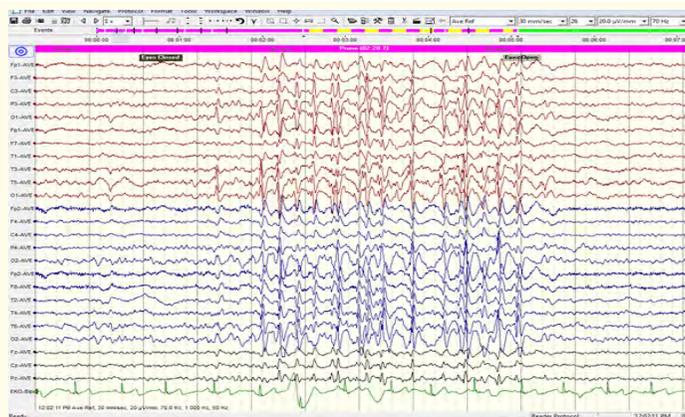
Significant spread of activity from these foci of origin to other lobes was distinctly observed in a neurophysiological study which analyzed the temporal and spatial dynamics of spikes [16]. The frontal ictal activity can spread to the insular cortex and then travel to the autonomic centers located in the brainstem especially the medulla. A temporal focus can also recruit the autonomic nuclei by travelling via the hypothalamus. This is substantiated by the observation that the ictal origin on the EEG predates the first clinical symptoms by upto several minutes thus explaining the dissociation between interictal EEG and clinical seizure semiology [17-20].

In a video polysomnography recording conducted by Parisi, *et al.* in a patient with PS and some atypical features like visual aura, the electrographic onset was documented to precede the ictal vomiting by 11 minutes. During the initial phase patient had exclusive occipital fast spikes with tachycardia, accompanied by 3 Hz spike and wave activity located occipitally to begin with and then showing diffuse spread with the sole manifestation of ictal tachycardia. After 10 minutes of onset the patient had focal motor manifestations with predominantly frontal theta and then remarkably as the vomiting set in, all the discharges disappeared giving way to post ictal low voltage activity in the frontal regions [19]. So it is evident from these ictal recordings, source analysis and serial MEG studies that, the interictal spikes represent areas of cortical hyper-excitability existing in a developing brain and not a persistent epileptogenic focus [16-20].

Another common but non-specific finding is the presence of occipital paroxysms referring to runs of spikes/sharp waves in the occipital region. The characteristic fixation off sensitivity referring to disappearance of these discharges on visual fixation is a curious phenomenon seen in PS as well as in other occipital lobe epilepsies both benign and symptomatic (Figure 1). Generalized discharges occipital slowing and photo paroxysmal response can also be observed in a small subset of cases (Figure 2). The multifocal discharges giving way to rolandic spikes is a peculiar observation which underpins the link between the epileptic syndromes of childhood [21].



**Figure 1:** EEG in a 6 year old boy with PS showing occipital intermittent rhythmic delta activity.



**Figure 2:** Fixation off sensitivity marked by the appearance of posterior dominant spike wave activity immediately after eye closure.

## Neuroimaging

A normal MRI is the usual but not the universal finding in patients with PS. Incidental abnormalities like gliosis, developmental anomalies or cortical malformations are rarely encountered.

## Differential diagnosis

The deceptive semiology bewilders many a clinician who ends up making the erroneous diagnoses of migraine, encephalitis, GERD or psychiatric illness [8]. Idiopathic childhood occipital epilepsy occurs in a slightly higher age group and is typified by the presence of ictal headache, elementary visual hallucination especially circular and colourful patterns along with pursuit like eye versions, ictal nystagmus and rarely lid myoclonia, palinopsia and autoscopia. Autonomic manifestations are not a feature of this syndrome. The association of PS with BCECTS has been well recognized and an electrographic and clinical overlap can exist between the two in a small percentage of cases.

## Management

Pharmacotherapy in PS is optional depending on the severity of symptoms and their impact on the family. Carbamazepine is the most commonly used agent but there is insufficient evidence to prefer one anti-epileptic drug over other. Reassurance and psychological support are especially important.

## Conclusion

Panayiotopolous syndrome is clinically recognizable and eminently treatable epilepsy of early childhood. The prototypical presentation is that of autonomic seizures and ictal vomiting with or without focal or multifocal EEG abnormalities. Counselling of parents along with initiation of appropriate anti-epileptic drugs is recommended for the efficient management of this benign syndrome.

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