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Original Article

Panayiotopoulos Syndrome: A Disorder Easily Misdiagnosed as Other Emergent Disorders in Children

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Objectives: The present study elucidated the clinical characteristics and outcomes of Panayiotopoulos syndrome (PS) in children and highlighted how easily PS can be confused with other neurological and non-neurological disorders given its typical and atypical presentations.

Methods: From 2012 to 2017, we enrolled 25 patients with PS, all of whom satisfied the following criteria: (a) ictal emetic symptoms (e.g., nausea, retching, and vomiting, alone or in combination; (b) onset age from 2 to 15 years; (c) normal development of neurological and mental states; (d) normal brain imaging, if performed; and (e) abnormal electroencephalogram (EEG). The patients were divided into two groups: typical presentations (impairment of consciousness, vomiting, nausea, pallor, miosis, and hypersalivation) and atypical presentations (less common symptoms of PS).

Results: We observed that on the basis of typical presentations, PS was most commonly misdiagnosed as encephalitis, gastroenteritis/GERD, syncope, and other seizure disorders and less commonly as septic shock, basilar migraine, or cyclic vomiting on the basis of atypical presentations.

Conclusions: This is the study of PS in Taiwan that demonstrated the misdiagnosis of PS cases as other emergent disorders on the basis of its typical and atypical presentations. This study demonstrated the misdiagnosis of PS cases as other emergent disorders on the basis of its typical and atypical presentations and raised awareness regarding this easily misdiagnosed epileptic syndrome.

Keywords: Panayiotopoulos syndrome; ictal; epilepsy; children; Taiwan

*** Section 1: What is already known on this subject**

1. The prevalence of Panayiotopoulos syndrome is approximately13% among children aged 3–6 years with one or more non febrile seizures and 6% among children aged 1–15 years.
2. Panayiotopoulos syndrome is an unusual epileptic syndrome characterized by not only seizure but also autonomic symptoms, such as nausea, retching, vomiting, and headache.

*** Section 2: What this study adds**

1. Our study elucidated the common and uncommon clinical characteristics of Panayiotopoulos syndrome in children.
2. This study demonstrated the misdiagnosis of PS cases as other emergent disorders on the basis of its typical and atypical presentations.

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1. Introduction

Panayiotopoulos syndrome (PS) is a common idiopathic, benign seizure disorder in children, which was recognized by the International League Against Epilepsy in 2001(1). The onset age of PS is typically from 1 to 15 years. Its prevalence is approximately13% among children aged 3–6 years with one or more non febrile seizures and 6% among children aged 1–15 years. In the general population, 2–3 children per 1000children may be affected (1). PS is characterized by nausea, retching, vomiting, headache, and seizure. In addition, visual symptoms include positive visual symptoms (sparks, flashes, and elementary, and complex visual hallucination) and negative visual symptoms (scotoma, hemianopsia, and amaurosis). These symptoms are easily confused with those of other paroxysmal disorders, such as gastroenteritis, migraine, motion sickness, syncope, and sleep terrors, as well as with those of critical neurological disorders, such as encephalitis, temporal lobe epilepsy (TLE), and intoxication (2). Interictal EEG revealed occipital spikes in approximately 75% of cases, and the cases were classified as a particular type of occipital lobe epilepsy; however, epileptiform activity arising from other or multiple areas was common, which leads to PS being considered as autonomic epilepsy (3, 4). The clarification of the clinical manifestation of PS is crucial for physicians treating epileptic patients. In this study, we investigated the clinical characteristics, EEGs, treatments, and outcomes of 25 children with PS. We focused on this rare autonomic seizure type and highlighted how easily PS can be misdiagnosed as other neurological and non-neurological disorders.

2. Materials and methods

From 2012 to 2017, we enrolled 25 patients with PS , all patients diagnosed with PS were screened to confirm whether they fulfilled the study inclusion criteria, which were as follows: (a) ictal emetic symptoms(e.g., nausea, retching, and vomiting, alone or in combination; (b) onset age from 2 to 15 years; (c) normal development of neurological and mental states; (d) normal brain imaging, if performed; and (e) abnormal EEG (1, 5). By using the data of these patients, we recorded the family history of seizure disorders, history of febrile seizure, neurodevelopmental status, clinical features of seizures (including age at onset, circadian distribution, duration, total number and frequency of seizures, and semiology of seizures), findings of EEGs and neuroimages, and antiepileptic drugs used for treatment. Moreover, we divided the patients into two groups: typical presentations (such as impairment of consciousness, vomiting, nausea, pallor, miosis, and hypersalivation) and atypical presentations (less common symptoms of PS). We defined autonomic aura as a part of seizure including symptoms such as pallor, flushing, or cyanosis; mydriasis or miosis; cardiorespiratory or thermoregulatory changes; and incontinence of urine and/or feces. Motor seizures included partial convulsion, hemiconvulsion, and general convulsions of body.

3. Results

In total, 25 patients (9 boys and 16 girls) were enrolled in this study. The clinical characteristics of the patients are summarized in Table 1. The onset age ranged from 2.5 to 10 years (mean, 6.4 years). Only 1 patient had a family history of epilepsy, and 7 reported to have had febrile seizures previously. An analysis of the circadian distribution of seizure revealed that 8 (32%) patients had seizures only on awakening, 16 (64%) had seizures during sleep, and 1had seizures randomly. Status epilepticus occurred in eight patients. Twenty patients (80%) had only one seizure before treatment. After treatment, 15 (64%) attained seizure control for 2 years. After a 5-year follow-up, 13/19 (68%) patients exhibited negative EEG findings. The most common type of initial seizure was complex partial seizures, followed by partial seizures with secondary generalization and simple partial seizures. In general, motor seizures were observed in 15 (60%) and autonomic seizures or aura in 20 (80%).A total of 20 (90%) patients presented loss of consciousness at their first visit, followed by vomiting, eye deviation, and other motor seizures (Table 2). Furthermore, three patients with atypical presentations were initially misdiagnosed as having septic shock, basilar migraine, and cyclic vomiting. The seizure semiology of these children is

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Table 1. Demographic and clinical characteristics of 25 patients with Panayiotopoulos syndrome

Demographic and Clinical characteristics	Patients with Panayiotopoulos syndrome (n=25) (100%)
Gender(male/female)	9/16
Age at onset (mean, range, yr)	6.4 (2.5~10 y)
Family history of epilepsy	1
Family history of migraine	12 (48%)
History of febrile seizure	7 (28%)
Fever at the onset of seizure	6 (24%)
Circadian distribution of seizure	
Diurnal	8(32%)
Nocturnal	16(64%)
Random	1 (4%)
Duration	
< 3 mins	5 (20%)
3~29mins	11 (44%)
≥30 mins	9 (36%)
Frequency—before treatment	
Low	20 (80%)
Intermediate	4 (16%)
High	1 (4%)
Frequency-after 2-year treatment(n= 24)*	
Free	15/24 (62%)
Low	8/24 (33%)
Intermediate-high	1/24 (4%)
Total number of seizure-before treatment	
1	20 (80%)
>1	5 (20%)
Seizure type (first seizure)	
Simple partial seizure	2 (8%)
Complex partial seizure	8 (32%)
SPS/CPS with SG*	15 (60%)
Autonomic seizure or aura	20 (80%)
Headache	7 (28%)

Low: one seizure every 6 months, Intermediate: 1–2 seizure every 1–3 months, High: >1 seizure every month.
*SPS, simple partial seizures; CPS, complex partial seizures; SG, secondarily generalized.

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Table 2. Typical/atypical presentations of Panayiotopoulos syndrome and their initial diagnosis in our study

Typical presentations at first visit	Patients (n=22) (88%)	
Impairment of consciousness	20 (90%)	
Loss of muscle tone	11 (50%)	
Vomiting (1-3 times an hour)	16 (72%)	
Eyes deviation and other motor seizures	15 (68%)	
Pallor, miosis and hypersalivation	6 (27%)	
Atypical presentations at first visit	**Patients (n=3) (12%)**	**Tentative diagnosis at ER or by referral**
Tachycardia, high fever, cyanosis and hypotension	1 (4%)	Septic shock
Numbness, loss of consciousness and headache	1 (4%)	Atypical migraine (suspect to be basilar type)
Intense nausea and unremitting vomiting (>4 times an hour)	1(4%)	1(4%) Cyclic vomiting

ER, emergency room.

Table 3. EEG features and migration of the focal spikes in patients with Panayiotopoulos syndrome

Panayiotopoulos syndrome (n=25)	First EEG					Final EEG (5 year follow-up)			
	O	F	C	T	P	O	F	T	N
	20	1	1	2	1	5	1	-	13

F,frontalarea;N,normalEEG;O,occipitalarea;P,parietalarea;T,temporal area.

summarized in Table 3.

EEG findings

The EEG findings and the evolution of focal spikes on the serial EEGs in all25 patients are presented in Table 3. Paroxysmal abnormalities including high-voltage spike waves, sharp waves, and diphasic spikes followed by slow waves were recorded. The final EEG after the 5-year follow-up in 19 patients was normal in 13 patients and revealed focal spikes in 6(5 located in the occipital areas and 1 in the frontal area).

Treatment and prognosis

All but 1children received antiepileptic therapy. The majority (80%) of these children received monotherapy. In total, 24 patients received antiepileptic therapy for at least 2years, and 15 were seizure free for 2 years. Moreover, 8 patients exhibited a low frequency of seizure (1 seizure every 6 months); only 1 patient had a seizure per month. In all, 19 patients were followed up for 5years, and 13 successfully withdrew from the antiepileptic drugs after attaining seizure freedom for 2 years.

Example cases

Case 1. A girl had her first nocturnal seizure at age of 5 years. Her mother described the symptom as an initial headache followed by vomiting, eye deviation to the left side, and focal tonic-clonic seizure on the right side for several minutes. The present event started with fever, vomiting, sweating, and a pale appearance and then evolved into convulsive status epilepticus; thus, encephalitis was initially suspected.

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Figure 1. A girl had her first nocturnal seizure at age of 5 years. She had febrile seizures twice between 3 and 4 years of age. Interictal EEG revealed occipital polymorphous spikes on the right side (arrows). Five seizures with headaches and ictal emeticus recurred within the following 2 years. The fifth seizure lasted for 1 hour. The occipital spikes were persistent even after a 2-year therapy.



Figure 2. A 7-year-old girl had her first seizure during sleep with initial vomiting, followed by eye deviation and general motor seizure. No oral drooling or mouth deviation occurred. Initial EEG revealed bilateral spikes on the central areas (arrows). Seizure within initial ictal vomiting followed by eye deviation and general motor seizure occurred five times after the first seizure. After treatment, the seizures were under control, and the girl was seizure free for 2 years.

However, her fever subsided immediately after seizure remission. Series investigations including spinal tapping with normal cerebral fluid examination yielded a very low chance of inflammation. Her intelligence was normal. She had febrile seizures twice between 3 and4 years of age. Interictal EEG revealed occipital polymorphous spikes on the right



Figure 3. A 7-year-old girl developed status epilepticus at midnight during sleep and was admitted to the intensive care unit. Initially, she was diagnosed as having encephalitis; however, her consciousness recovered shortly. The interictal EEG revealed focal spikes and waves on the frontal areas, followed by slow waves of 2–3 Hz (arrows).

side (Figure 1). Magnetic resonance imaging (MRI) was normal. Valproic acid was administered at 250mg twice per day. However, five seizures with headaches and ictal emeticus recurred within the following 2 years. The fifth seizure lasted for 1hour. The occipital spikes were persistent even after a 2-year therapy.

Case 2. A 7-year-old girl had her first seizure during sleep with initial vomiting, followed by eye deviation and general motor seizure. No oral drooling or mouth deviation occurred. Her intelligence was normal. She previously had febrile seizure. Initial EEG revealed bilateral spikes on the central areas (Figure 2) and occipital spikes in the same EEG recording. She was treated with carbamazepine at 50 mg twice per day. Seizure within initial ictal vomiting followed by eye deviation and general motor seizure occurred five times after the first seizure. After treatment, the seizures were under control, and the girl was seizure free for 2 years.

Case 3. A7-year-old girl developed status epilepticus at midnight during sleep and was admitted to the intensive care unit. Initially, she was diagnosed as having encephalitis; however, her consciousness recovered shortly. Her intelligence was normal. He had febrile seizure at the age of 3 years. The interictal EEG revealed focal spikes and waves on the frontal areas, followed by slow waves of 2–3 Hz (Figure 3). The MRI was normal. She was treated with

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oxcarbazepine, and no seizure recurred for 1 year.

Case 4: A 4-year-old boy was admitted to our emergency room (ER) for sudden onset of vomiting accompanied by cyanosis, tachycardia, and fever up to 39 °C. He had one episode of febrile convulsions at the age of 1 year. At the ER, he gradually lost consciousness and exhibited eye deviation to the right side. An hour after his arrival, his body temperature increased to 39.9°C, oxygen saturation dropped to 85%, blood pressure was 66/30 mmHg, respiratory rate was 39/min, and heart rate was 200/min. Fluid resuscitation was performed, high flow oxygen was started, and he was transferred to the pediatric intensive care unit. A series of investigations, including complete blood count, serum electrolytes, blood gases, serum electrolytes panel, and glucose levels was within normal ranges. Blood and urine cultures were normal. Brain computed tomography (CT) and MRI urgently performed at the ER were unremarkable. However, he regained consciousness after 2 h, and the fever subsided shortly without any antipyretics use; in addition, his blood pressure, oxygen saturation, respiratory rate, and heart rate were back to normal without further medical support. The interictal EEG revealed occipital polymorphous spikes on the right side. We administered levetiracetam (20mg/kg/day) to him during the entire hospitalization period, and the medication was continued for 3 days after discharge. The manifestation during the episode was similar to that observed in a septic shock. However, the rapid recovery, normal investigations, and previous history of similar episodes ruled out septic shock. At the 2-month, 6-month, and 1-year follow-up, he was asymptomatic and had a normal neurological examination.

Discussion

PS is characterized by its special seizure semiology as autonomic symptoms and is often confused with or misdiagnosed as other nonepileptic conditions such as atypical migraine, gastroenteritis, encephalitis, cyclic vomiting, andsyncope.[2] Moreover, the appearance of PS could be more variable. Typical presentations of PS include impairment of consciousness, loss of muscle tone, vomiting, eye deviation, nausea or retching, pallor, miosis, and hypersalivation.[1] With a thorough understanding of PS, particular "atypical" presentations were observed and taken seriously (6). In this study, three patients exhibited atypical presentations of PS, and they were misdiagnosed as having septic shock, atypical migraine (basilar migraine), and cyclic vomiting.

Some atypical presentations in PS, such as those observed in our cases, have attracted less attention. Mujawar et al. reported a case of a 3.5-year-old boy with PS who presented with status epilepticus and ictal cardiorespiratory arrest requiring cardiopulmonary resuscitation for revival (7). Coincidentally, another 4-year-old girl experienced life-threatening bradycardia twice, which eventually resulted in severe respiratory acidosis requiring intubation and ventilator support.8 Despite the relatively low frequency, such life-threatening events entail the consideration or reevaluation of the need to treat children with PS.

The exact pathogenesis of PS remains unclear. A functional MRI study of the syndrome demonstrated that the regional dipole seeding in spike-related blood oxygen level-dependent clusters originated from the lateral and inferior occipital lobe and then spread to the lateral temporal lobe, thus suggesting that epileptic activity originated in the lateral occipital area (9-11). However, although most brain MRIs of PS were unremarkable, brain lesions such as neuroepithelial cyst, right occipital encephalomalacia and an arachnoid cyst located in the cisterna magna, and colpocephaly have been reported to be associated with PS, thus suggesting that a solid lesion could also act as the focal generator of PS (11.12).

To accurately diagnose PS, other autonomic nervous system (ANS) diseases and TLE that present autonomic seizures must be investigated (Table 4) (13-18). In TLE, autonomic symptoms are typically much less pronounced and occur toward the end rather than at the beginning of the seizure (19). However, notably, these autonomic crises may be relevant to sudden unexpected death in epilepsy regardless of PS or TLE (7,20). In the present study, the fever in PS was short and related to autonomic seizure, which was quite different from most encephalitis cases of "persistent fever." In addition, the relatively rapid recovery of consciousness distinguishes it from encephalitis, which typically

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Table 4. Common autonomic symptoms associated with different disorders that can be easily confused with Panayiotopoulos syndrome

	Epilepsy syndrome		Others disorder mimicking Panayiotopoulos syndrome				
	Panayiotopoulos syndrome	Temporal lobe epilepsy	Septic shock	Encephalitis	Gastroenteritis	Cyclic vomiting	Atypical migraine (i.g. basilar type)
Impairment of consciousness	++	++	++	++	-	-	++
Focal seizure duration	>5mins	30s to 120s	N/A	Variable	-	-	-
Status epilepticus	++	+	+	+	-	-	-
Fever	+/-	-	++	++	+	-	-
Persistent fever	-	-	++	++	+/-	-	-
Syncope	+	+/-	N/A	N/A	+/-	-	+/-
Nausea or vomiting	++	Epigastric aura	+	+	++	++	+
Loss of muscle tone	++	Few	++	+	-	-	-
Pallor	+	+	++	+	+/-	+/-	N/A
Miosis	+	Few	N/A	+	-	-	N/A
Cardiac disturbances	Tachycardia, few cardiopulmonary arrest	Tachycardia, few bradycardia	Tachycardia	Variable	-	-	-
Reference	This work	13	14	15	16	17	18

+, occasionally appeared; ++, frequently appeared; +/−, may or may not appear; −, did not appear; N/A, not available

involves prolonged consciousness disturbance (15). In Case 1 in this study, hyperthermia, loss of consciousness, and other autonomic symptoms such as vomiting, pallor change, and cyanosis at seizure onset was easily interpreted as encephalitis or a complex febrile seizure. According to Yoshinaga et al (21), the fever observed at the seizure onset and the history of febrile seizure in patients with PS should be very carefully interpreted. Thus, the absence of inflammation evidence and the rapid recovery of body temperature followed by seizure remission indicate an epileptic origin. Second, nausea and vomiting was observed in 16 patients (72%) in this study, and most of them sought a pediatric gastroenterologist or pediatric emergency physician rather than a pediatric neurologist during the first event. Parisiet al (22) also emphasized that a differential diagnosis must be made between gastroenteritis or gastroesophageal reflux disease (GERD) and PS in patients with "unusual" late-onset manifestations of GERD and acid therapy-resistant gastroesophageal reflux. However, based on our experience, the unexplained, sudden attack of vomiting, the absence of other gastrointestinal symptoms (such as epigastric pain and history of gastroesophageal reflux disease), and most importantly, different severities of consciousness impairment make the diagnosis of gastroenteritis less likely. Another event that is easily misconstrued as PS is migraine, particularly the atypical type, which

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includes cyclic vomiting and basilar type migraine. The pathogenesis of cyclic vomiting syndrome (CVS) remains unknown; it may represent a heterogeneous group of disorders, but dysautonomia is often the hallmark (17) Similar to PS, CVS affects young children, peaking at age 5, and is resolved during adolescence. One-third of the patients later develop migraine headaches (17) Basilar-type migraine is a rare type of migraine characterized by brainstem aura, with symptoms such as vertigo, dysarthria, diplopia, and a decreased level of consciousness (18). However, although migraine is considered as a differential diagnosis from PS, according to our review of relevant literature, PS has been misdiagnosed as basilar type migraine for the first time.

The EEGs in children with PS may be normal or reveal focal spike discharge. The spike discharge was more commonly located in the occipital region, followed by the frontal and central areas (1, 5, 23). In the present study, 80% of the patients exhibited occipital spikes, and 20% of the spikes were located on the extra-occipital region. This result is consistent with those of previous reports (23). In Case 2 in the present study the patient presented bilateral occipital spikes at the initial EEG recording and had nausea and vomiting; however, when the discharge spread to the right centrotemporal region, she manifested right eye deviation and left side clonus. This interesting case provided a clear evidence that rolandic epilepsy and PS can coexist in the same patient during the same EEG recording. This result was consistent with that reported by Yoshinaga et al (24) This finding was similar to a recent study conducted by Caraballo et al (25). During the course of PS, the evolution of the foci of epileptiform activity has been reported. The occipital spikes may disappear at a mean of 5.7 years (25). In this study, 19 of the 25 patients were followed up for 5 years, and 13 (68%) had normal EEGs at the end of follow-up.

There were some limitations with respect to the analysis and data that may have affected the accuracy of our results. The number of PS cases was small. A strict included criteria may exclude cases with probable PS. Further study is noteworthy.

In conclusion, this study demonstrated the misdiagnosis of PS cases as other emergent disorders on the basis of its typical and atypical presentations. A thorough understanding and correct interpretation of this syndrome is essential for its management. We hope to broaden the clinical spectrum of PS and raise awareness regarding this easily misleading epileptic syndrome.

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Contributors:

Lee IC designed the study. Hong SY analysed the data and wrote the paper.

Competing interests:

None

Reference:

1. Ferrie CD, Grünewald RA. Panayiotopoulos syndrome: a common and benign childhood epilepsy. *Lancet* 2001; 357:821-3.
2. Covanis A. Panayiotopoulos syndrome: a benign childhood autonomic epilepsy frequently imitating encephalitis, syncope, migraine, sleep disorder, or gastroenteritis. *Pediatrics* 2006; 118:e1237-43.
3. Koutroumanidis M. Panayiotopoulos syndrome: an important electroclinical example of benign childhood system epilepsy. *Epilepsia*2007; 48:1044-53.
4. Specchio N, Trivisano M, Di Ciommo V, *et al.* Panayiotopoulos syndrome: a clinical, EEG, and neuropsychological study of 93 consecutive patients. *Epilepsia* 2010; 51:2098-107.
5. Panayiotopoulos CP. Benign childhood epilepsy with occipital paroxysms: a 15-year prospective study. *Ann Neurol* 1989; 26:51-6
6. Zaki SA, Verma DK, Tayde P. Panayiotopoulos syndrome in a child masquerading as septic shock. *Indian J Crit Care Med* 2016; 20:361-3.

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7. Mujawar QM, Sen S, Ali MD, *et al.* Panayiotopoulos syndrome presenting with status epilepticus and cardiorespiratory arrest: a case report. *PediatrEmerg Care* 2011; 27:754-7. doi: 10.1097/PEC.0b013e318226e0a9.
8. Dirani M, Yamak W, Beydoun A. Panayiotopoulos syndrome presenting with respiratory arrest: A case report and literature review. *Epilepsy Behav Case Rep* 2015 Feb 20;3:12-4.
9. Leal AJ, Nunes S, Martins A, *et al.* Brain mapping of epileptic activity in a case of idiopathic occipital lobe epilepsy (Panayiotopoulos syndrome). *Epilepsia* 2007; 48:1179-83.
10. Leal AJ, Nunes S, Dias AI, *et al.* Analysis of the generators of epileptic activity in early-onset childhood benign occipital lobe epilepsy. *Clin Neurophysiol* 2007; 118:1341-7
11. Leal AJ, Lopes R, Ferreira JC. Origin and dynamics of epileptic activity in a symptomatic case of Panayiotopoulos syndrome: correlation with clinical manifestations. *Clin Neurophysiol* 2013; 124:20-6.
12. Yalçin AD, Toydemir HE, Celebi LG, *et al.* Panayiotopoulos syndrome with coincidental brain lesions. *Epileptic Disord*2009; 11:270-6.
13. Whealy M, Wirrell E, Wong-Kisiel L, *et al.* Prevalence and Risk Factors of Peri-ictal Autonomic Changes in Children With Temporal Lobe Seizures. *Pediatr Neurol.* 2017;67:36-39.
14. Pavare J, Grope I, Gardovska D. Prevalence of systemic inflammatory response syndrome (SIRS) in hospitalized children: a point prevalence study. *BMC Pediatr*2009; 9:25.
15. Tunkel AR, Glaser CA, Bloch KC, *et al.* The management of encephalitis: clinical practice guidelines by the Infectious Diseases Society of America. *Clin Infect Dis* 2008; 47:303-27.
16. Osborne CM, Montano AC, Robinson CC, *et al.* Viral gastroenteritis in children in Colorado 2006-2009. *J Med Virol*2015; 87:931-9.
17. Pareek N, Fleisher DR, Abell T. Cyclic vomiting syndrome: what a gastroenterologist needs to know. *Am J Gastroenterol* 2007; 102:2832-40
18. Kirchmann M, Thomsen LL, Olesen J. Basilar-type migraine: clinical, epidemiologic, and genetic features. *Neurology* 2006; 66:880-6
19. Kato K, Jin K, Itabashi H, *et al.* Earlier tachycardia onset in right than left mesial temporal lobe seizures. *Neurology* 2014; 83:1332-6.
20. Bartlam R, Mohanraj R. Ictalbradyarrhythmias and asystole requiring pacemaker implantation: Combined EEG-ECG analysis of 5 cases. *Epilepsy Behav* 2016; 64(Pt A):212-15.
21. Yoshinaga H, Kobayashi K, Akiyama T, *et al.* Clinical implications of preceding positive spikes in patients with benign partial epilepsy and febrile seizures.*BrainDev* 2013;35:299-306.
22. Parisi P, Pacchiarotti C, Ferretti A, *et al.* Gastroesophageal reflux disease vs. Panayiotopoulos syndrome: an underestimated misdiagnosis in pediatric age? *Epilepsy Behav* 2014; 41:6-10.
23. Ohtsu M, Oguni H, Hayashi K, *et al.* EEG in children with early-onset benign occipital seizure susceptibility syndrome: Panayiotopoulos syndrome. *Epilepsia* 2003; 44:435-42
24. Yoshinaga H, Kobayashi K, Shibata T, *et al.* Manifestation of both emetic seizures and sylvian seizures in the same patients with benign partial epilepsy. *Brain Dev* 2015; 37:13-7.
25. Caraballo RH, Pasteris MC, Portuondo E, *et al.* Panayiotopoulos syndrome and diffuse paroxysms as the first EEG manifestation at clinical onset: a study of nine patients. *Epileptic Disord* 2015; 17:143-9.