Clinical manifestations of psychogenic non-epileptic seizures in children: Experiences from a single center

Chia-Yih Wang a,b,*, Ting-Rong Hsu b,c, Kai-Ping Chang b,d

a Department of Pediatrics, New Taipei City Hospital, New Taipei, Taiwan
b Division of Pediatric Neurology, Department of Pediatrics, Taipei Veterans General Hospital, Taipei, Taiwan
c Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan
d Department of Pediatrics, Wei-Gong Memorial Hospital, Miaoli, Taiwan

Received Jun 28, 2021; received in revised form Aug 31, 2021; accepted Sep 22, 2021
Available online

Key Words
clinical manifestations; epilepsy; pediatric; psychogenic non-epileptic seizures

Background: This study aimed to determine the clinical features of psychogenic non-epileptic seizures (PNES) and to enhance the accuracy of the differential diagnosis of epilepsy.

Methods: This retrospective case series included patients diagnosed with PNES between December 2003 and February 2019 at Taipei Veterans General Hospital. We used International Classification of Diseases (10th revision) codes for screening, and relevant medical records were reviewed. Experienced pediatric neurologists diagnosed PNES based on clinical manifestations, and occasionally on confirmatory video-electroencephalography (EEG) or simultaneous scalp-EEG during the paroxysmal attack. General information, clinical manifestations, psychological conditions, and relevant laboratory or imaging test results were collected and analyzed.

Results: Twenty-six patients (mean age, 13 years 8 months) were evaluated, 9 male and 17 female. Ten patients with PNES had a previously established diagnosis of epilepsy. The duration between symptom onset and diagnosis ranged from 1 to 120 (mean, 21; median, 12) days. Sixteen patients showed possible causative psychosocial stressors. Multiple characteristic features or specific clinical manifestations of PNES—that usually differ from epileptic seizures—were observed in all patients with PNES.

Conclusion: A detailed evaluation of clinical manifestations and medical history is important for the accurate diagnosis of PNES.

Copyright © 2022, Taiwan Pediatric Association. Published by Elsevier Taiwan LLC. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Abbreviations: PNES, psychogenic non-epileptic seizures; EEG, electroencephalography; DSM-5, Diagnostic and Statistical Manual of Mental Disorders; VGHTPE, Taipei Veterans General Hospital; SD, standard deviation; AEDs, antiepileptic drugs.

* Corresponding author. 4F., No.118-15, Jin-Hua St., Da-An Dist., Taipei City 106006, Taiwan.
E-mail address: wcywe@yahoo.com.tw (C.-Y. Wang).

https://doi.org/10.1016/j.pedneo.2021.09.008
1875-9572/Copyright © 2022, Taiwan Pediatric Association. Published by Elsevier Taiwan LLC. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Please cite this article as: C.-Y. Wang, T.-R. Hsu and K.-P. Chang, Clinical manifestations of psychogenic non-epileptic seizures in children: Experiences from a single center, Pediatrics and Neonatology, https://doi.org/10.1016/j.pedneo.2021.09.008
1. Introduction

The accurate and timely diagnosis of psychogenic nonepileptic seizures (PNES)—a type of conversion disorder—can be challenging, as the clinical manifestations are those of epilepsy and related medical and psychiatric comorbidities. Approximately 5%—25% of patients in outpatient epilepsy centers have been estimated to have PNES. An even higher rate of PNES (25%—40%) has been reported in patients with intractable seizures in inpatient epilepsy monitoring units.¹

Video-electroencephalography (EEG) recording is a diagnostic reference standard for differentiating PNES from epileptic seizures; however, this test is not readily available in most parts of the world. Based on the inclusion of clinical findings not in accordance with known anatomical, physiological, or pathological mechanisms of disease, the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) modified the diagnosis of PNES to be a “rule-in” conversion disorder. An accurate personal and family history (including social/psychological background, physical illness, family functioning, and educational status) and details concerning the seizure course and peri-ictal behaviors are important for making a diagnosis. Moreover, neurodiagnostic tests may help diagnose PNES by ruling out organic etiologies.

Before receiving the correct diagnosis, PNES patients may receive invasive examinations and treatments, as well as powerful medication, due to long attack duration, poor response to drugs, and vigorous seizure manifestations; and so PNES patients may suffer unnecessary physical and mental injuries as well as an unsustainable financial expenses. Comorbid neurologic illnesses have been reported in approximately 55% of pediatric patients with PNES.²

For patients and their families, a PNES diagnosis is difficult to accept. Partial acceptance or rejection of the diagnosis is possible, thus delaying psychological treatment with some patients seeking more medication or further testing. Up to 30% of patients may fail to comply with an initial referral for psychological therapy.³

This study aimed to analyze the clinical manifestations of pediatric PNES. Specifically, we aimed to identify subtle signs manifesting in patients with PNES that differ from those presenting in patients with epilepsy, with the overarching objective of facilitating a rapid PNES diagnosis and improved management. We believe that this case series contributes significantly to the literature because, unlike previous studies, this work emphasizes the importance of clinical symptoms in diagnosing PNES.

2. Material and methods

2.1. Patient inclusion and clinical data

This retrospective observational case series was undertaken at Taipei Veterans General Hospital (VGHTE), a tertiary hospital that receives referrals from across Taiwan, between December 2003 and February 2019. This study was approved by the Ethics Committee of the Institutional Review Board at VGHTE (IRB approval number: 2019-01-037BC) and conformed to the World Medical Association Declaration of Helsinki. The requirement for informed consent was waived due to the retrospective nature of the study. The International Statistical Classification of Disease and Related Health Problems (10th Revision) (ICD-10) codes for conversion disorder, somatoform disorder, pseudoseizure, and psychogenic seizure were obtained from the VGHTE electronic medical database. Raw screened data from the VGHTE Big Data Centre identified 2742 potential candidates. After a search of electronic medical records completed during outpatient clinic visits, emergency department visits, and hospital admissions, we found 45 patients with an established diagnosis of conversion disorder and/or psychogenic seizures initially made by experienced pediatric neurologists and psychiatrists. Following a further search for patients with “suggested diagnostic criteria for PNES,”⁴ the medical records of 26 patients were included. All 26 patients with a confirmed diagnosis of PNES had a follow-up period of >12 months.

The patients’ individual clinical records were reviewed, and variables were analyzed as follows: gender; age; medical history; patterns of medication use for epilepsy (if applicable); medical comorbidities; possible psychological stressors; laboratory test results; diagnosis lag time (from first attack to diagnosis); clinical manifestations (including induction responses); duration of each attack; and witness status. We did not analyze patient socioeconomic status, PNES attack frequency, long-term outcomes, or the incidence or prevalence of PNES in the local population.

2.2. Diagnosis of PNES

Suggested diagnostic criteria for PNES (based on history, witnessed events, and investigations including video-EEG) include the following four categories: “possible” (based on a witness or self-reported description), “probable” (based on a review of a video recording by clinicians that reveals the typical semiology of PNES), “clinically established” (showing the typical semiology of PNES without corresponding epileptiform discharges on scalp-EEG, according to an experienced neurologist’s direct observation), and “documented” (no epileptiform activity immediately before, during, or after an event with typical PNES semiology captured on video-EEG or simultaneous scalp-EEG recording).⁵ Here, only patients with “probable”, “clinically established”, or “documented” certainty levels were included.

2.3. Scalp-EEG, video-EEG, blood biochemistry tests, and neuroimaging

Scalp-EEG, video-EEG, brain imaging, and general blood biochemistry tests were performed according to clinical indications. Scalp-EEG and video-EEG were conducted with a standard protocol using scalp electrodes, in accordance with the international 10—20 electrode system.⁶ Brain magnetic resonance imaging was performed using 1.5-T or 3-T scanners (Signa Excite 1.5T, GE Healthcare, Milwaukee, WI, USA; SignaHDxt 1.5T, GE Healthcare; Discovery MR750 3.0T, GE Healthcare), with a standard protocol. Scalp- and video-EEG were conducted to assist with the PNES
diagnosis. Organic lesions and systemic illnesses were ruled out with laboratory tests and neuroimaging investigations.

2.4. Data analysis and statistics

Descriptive statistics (mean, median, and standard deviation [SD]) were used to analyze the study data. No inferential statistics were used because of the limited number of patients and the uncontrolled nature of this study. SPSS Version 20 (IBM Corp., Armonk, NY) was used for descriptive statistics.

3. Results

Among the 26 patients, PNES occurred in 9 males and 17 females. The age of diagnosis ranged from 4 years 8 months–32 years, with a median of 12 years, a mean of 13.63 years, and a standard deviation 5.09 years. Among them, the only patient with the extreme age at onset was a woman who was 32 years old at the time of PNES onset. She had been diagnosed and treated at Taipei Veterans General Hospital since she had a seizure at the age of 7 and followed in the Division of Pediatric Neurology into adulthood. At the age of 32, she started to have psychogenic convulsions. The second oldest onset was 19 years old. The rest of the included patients were all under 19 at the time of PNES onset. The levels of diagnostic certainty in this case review included the category of probable, clinically established, and documented diagnosis, with 5 patients (19.23%), 15 patients (57.69%), and 6 patients (23.08%), respectively. The duration between symptom onset and diagnosis ranged from 1 to 120 days (mean [SD], 21 [26] days). Patients with PNES had medical comorbidities, such as illnesses other than epilepsy (n = 9), epilepsy (n = 10), and family history of illnesses that included lung cancer, epilepsy, or fragile X syndrome (n = 4). Sixteen patients were referred from primary care physicians and other medical facilities to our hospital for further diagnosis. Patient demographic characteristics are shown in Table 1.

Possible causative psychosocial stressors were identified in 16 patients, including 10 with existing epilepsy, which was the most common comorbidity. A history of medical illness was also included as a possible stressor for PNES induction. Relevant medical history included: congenital hearing impairment, intellectual disability, spastic paraplegia, left leg numbness, exotropia, Hirschsprung disease, epidural hemorrhage, Tourette’s syndrome, and nephritis. The patient’s family or friends also disclosed possible relevant stressors: interpersonal conflicts, bullying at school, teenage abortion, suicide attempts, drug abuse, poor school performance, domestic violence, parent’s illness, and family disharmony. A list of possible causative psychological stressors is shown in Table 2.

Besides physical and neurological examinations, 23 patients had undergone further targeted tests, and the results were either normal or unrelated to PNES. Most of the scalp- and/or video-EEGs, undertaken interictally or during events, showed either completely normal results or some epileptiform discharges unrelated to PNES symptoms. Regarding the phenomenological patterns of PNES, the first, second, and third patterns comprised 80.77% of the total involved excessive motor components; these included twitching, jerking, and shaking movements of the limbs (Table 3). Some patients exhibited head shaking, probable loss of consciousness, and tonic limb or whole-body posture. Regarding event duration, 92.31%, 7.69%, and 30% lasted >3 min, 3–10 min, 10–30 min, and >30 min, respectively. In total, 42.31% of patients (11 cases) with PNES were either inducible or responsive during the events (Table 3). All seizure-like PNES attacks were observed when the patients were awake, surrounded by familiar people; there were no serious concerns for patient safety during the attacks. While two patients experienced an acute loss of consciousness, both had closed eyes and exhibited verbal responsiveness; a simultaneous scalp-EEG recording was conducted for one patient during the attack, the results of which were normal. None of the patients experienced traumatic injuries, urinary incontinence, or post-ictal drowsiness from the PNES attacks. Various unique motor features of the clinical manifestations were observed, including prolongation of the seizure-like movements and unusual seizure patterns. Subtle features or specific clinical manifestations of PNES that usually differ from epileptic seizures are listed in Table 4.

In patients who have been diagnosed with epilepsy and secondary PNES, sometimes there are still epileptic seizures. These two different episodes can be distinguished. Epileptic seizures can generally be controlled well or to some extent with antiepileptic drugs (AEDs), and the duration, pattern, and the circumstances or predisposing factors of the seizures are relatively stable. PNES attacks occur some time after epilepsy is diagnosed, especially when epilepsy has been well controlled. PNES attacks are more frequent, especially at the beginning, and last longer. PNES attacks are correlated with recent mental and emotional states. The situation and companions at the time of PNES attacks are correlated with recent mental and emotional states.
of the attack onset are also relevant. The duration and pattern of each attack may be different, manifesting PNES clinical features. The attacks can be induced, changed with the environment, and have placebo reactions, inconsistent responses to regular AEDs, and no response to original AEDs.

4. Discussion

It is important to identify specific historical and semiological characteristics when making a diagnosis of PNES in children. Direct observation of the clinical event by experienced clinicians (either in person or on video) can facilitate higher levels of diagnostic certainty, according to the International League Against Epilepsy staged approach to the diagnosis of PNES. Specific subtle clinical manifestations of PNES were determined in this study. These features can be used to facilitate a rapid and accurate diagnosis, especially in emergency situations, before assessments such as EEGs, brain imaging, or biochemical tests are available. Herein, psychological stress factors and events characteristic of PNES were analyzed in patients categorized into the “probable,” “clinically established,” and “documented” diagnostic certainty levels for PNES. All patients were followed up for over 12 months to confirm the diagnosis of PNES. The mean patient age was 13 years 8 months, with a female preponderance. The mean duration of lag in diagnosis was 21 days. The delay of PNES diagnosis in pediatric patients has been reported to be considerably shorter than in adult patients. However, diagnosis in pediatric patients may be delayed up to 3 years 6 months. Common factors for delay include misdiagnosis of epilepsy, lack of a video-EEG investigation, or denial of psychological origin by the patient and family. The delay of PNES diagnosis in our study was shorter than in a recent study (5 months, with a range of 15 days–48 months) due to the convenience and availability of medical care in Taiwan.

Two main types of psychological background for PNES, namely, post-traumatic and developmental, have been reported. Pediatric patients with PNES have increased anxiety, sensitivity, and somatization. PNES has been well described in patients with neurological developmental disabilities. Learning difficulties, bullying, social withdrawal, and school refusal have been identified as common risk factors for PNES in pediatric patients. Separation anxiety, school avoidance, and parental discord or divorce may also contribute. Compared with their siblings, children with PNES have more coexisting medical, neurological, and psychiatric illnesses over their lifetimes. They have been reported to require more medications and intensive

| Table 2 Possible causative psychological stressors in patients with PNES. |
| Possible causative psychological stressors | Number of patients |
| Total number | 17 (65.38%) |
| A. Traumatic |
| a. Violence and abuse |
| Domestic violence | 1 |
| Bullied in primary school | 1 |
| Traumatic epidural hemorrhage | 1 |
| b. Medical illness |
| Epilepsy | 10 |
| Other illness<sup>a</sup> | 9 |
| c. Procedures |
| Teenage abortion | 1 |
| B. Developmental |
| a. Daily task difficulty |
| Intellectual disability | 2 |
| b. Milestone delay |
| Poor school performance | 1 |
| Dropout from middle school | 1 |
| Detained in the same grade in school | 1 |
| c. Psychosocial difficulty |
| Poor peer relationship (Changed to: |
| Poor peer relationship) | 2 |
| Drug abuse history | 1 |
| Conflicts in class | 1 |
| Conflicts with parents | 1 |
| Social anxiety | 1 |

PNES, psychogenic non-epileptic seizure.

| Table 3 Phenomenological patterns in patients with PNES. |
| Phenomenological patterns | Number of patients |
| Five different PNES patterns | 26 (100%) |
| 1. Attacks of excessive, violent movements of the limbs, often associated with hyperventilation | 10 (38.46%) |
| 2. More bizarre attacks of motor activity manifesting with trunk extension | 9 (34.62%) |
| 3. Attacks associated with a rhythmic motor pattern, resembling tremor | 2 (7.69%) |
| 4. Attacks with unresponsiveness as the only clinical feature | 3 (11.54%) |
| 5. Subjective feeling of dizziness, anxiety, abdominal pain, or swelling in the throat | 2 (7.69%) |

Event duration |

| <3 min | 2 (7.69%) |
| 3 to <10 min | 2 (7.69%) |
| 10 to 30 min | 9 (34.62%) |
| >30 min | 13 (50%) |

Induction or responsiveness during events | 11 (42.31%) |

PNES, psychogenic non-epileptic seizures.

<sup>a</sup> Other illnesses comprised congenital hearing loss (n = 1), exotropia (n = 1), Hirschsprung disease (n = 1), spastic paraplegia (n = 1), intellectual disability (n = 1), epidural hemorrhage (n = 1), left leg numbness (n = 1), Tourette’s syndrome (n = 1), and nephritis (n = 1).
The prevalence of PNES with comorbid epilepsy in this population has been reported to be up to 30%. A family history of chronic physical illness can be a stressor for PNES. Four patients (15.38%) had a family history of illnesses other than epilepsy in 9 (34.62%) patients, and 35% have a family history of neurologic illness. Most patients and their parents found to have a history of neurologic illness, and 35% have a family history of chronic physical illness can be a stressor particularly during a major convulsion, suggests PNES. "Occurrence of true sleep favored epileptic seizures. Patients with PNES may appear to be asleep immediately before seizure onset; however, EEG findings in these patients demonstrate wakefulness. "Occurrence from sleep" has 100% specificity for epileptic seizures and is only applicable for seizures in EEG-confirmed sleep. The success rate of induction may be higher among patients with certain clinical characteristics, including hypermotor ictal features, uncommon cognitive and affective self-reported symptoms, and an absence of prior induction exposure. Herein, 11 (42.31%) patients presented either major induction or responsiveness during attacks. An explosive attack burden from the moment of the first event onward can also characterize PNES. A sudden increase in attack frequency was observed in some of the enrolled patients. While the ictus of an epileptic seizure is typically brief (often <1 min), PNES events have been reported to be much longer. Convulsive seizures, which almost always last >2 min, should be examined for the possibility of PNES, and duration of >10 min strongly suggests PNES. A non-epileptic psychogenic status, also known as "pseudo-status" or "status pseudo-epilepticus," has been defined as a PNES lasting ≥30 min, or repetitive non-epileptic seizures without a return to baseline mental status. Non-epileptic psychogenic status was reported in 13.5% of children with PNES, who had been treated with intravenous AEDs and received invasive diagnostic investigations and/or prompt tracheal intubation. In this study, 92.31%, 84.62%, and 50% of the attacks lasted >3 min, >10 min, and >30 min, respectively. No patients received intensive care or tracheal intubation during PNES during the study. In patients diagnosed with PNES alone (without comorbid epilepsy), the prevalence of interictal EEG abnormalities has been reported to range from 10% to 18%. Only 15% to 33% of simple partial seizures or seizure auras are associated with scalp-EEG abnormalities. In one case series with video-EEG documentation of PNES and epileptic seizures (both present in each patient), most patients (18/20) had a notably different clinical semiology for PNES compared with their epileptic seizures. Herein, 23 patients had undergone pertinent tests and examinations (in addition to physical and neurological examinations) that indicated normal or minor results without meaningful or relevant pathological findings. Most EEG readings were normal or exhibited spikes or epileptogenic discharges that were not correlated with PNES symptoms. Except for video-EEG and scalp-EEG assessments performed during an attack, laboratory and imaging investigations can only be used to rule out related pathology and do not contribute to PNES diagnosis.

We identified several subtle features to enable PNES diagnosis and to differentiate it from other conditions. In the pediatric population, 76.8% of PNES cases have an abrupt start, and 68% end abruptly. During the attacks, a long seizure duration, waxing and waning consciousness, forceful eye closure, ictal crying, side-to-side head shaking, tremor (especially in the upper extremities), asynchronous limb movements, pelvic thrusting, a fluctuating ictal course, pause patterns, memory recall issues, and absence of postictal confusion were the most reliable signs for distinguishing PNES from epileptic seizures. Autonomic manifestations during an ictus (e.g., tachycardia and cyanosis) suggest epileptic seizures, and their absence, particularly during a major convulsion, suggests PNES. In the DSM-5 diagnostic criteria, "la belle indifférence" refers to a relative lack of concern regarding the symptoms that are not listed in the DSM-5 diagnostic criteria. In one study, "la belle indifférence" was found to be over-emphasized in patients with PNES and may, in fact, have been absent. Occurrence of true sleep favored epileptic seizures. Patients with PNES may appear to be asleep immediately before seizure onset; however, EEG findings in these patients demonstrate wakefulness. "Occurrence from sleep" has 100% specificity for epileptic seizures and is only applicable for seizures in EEG-confirmed sleep. The success rate of induction may be higher among patients with certain clinical characteristics, including hypermotor ictal features, uncommon cognitive and affective self-reported symptoms, and an absence of prior induction exposure. Herein, 11 (42.31%) patients presented either major induction or responsiveness during attacks. An explosive attack burden from the moment of the first event onward can also characterize PNES. A sudden increase in attack frequency was observed in some of the enrolled patients. While the ictus of an epileptic seizure is typically brief (often <1 min), PNES events have been reported to be much longer. Convulsive seizures, which almost always last >2 min, should be examined for the possibility of PNES, and duration of >10 min strongly suggests PNES. A non-epileptic psychogenic status, also known as "pseudo-status" or "status pseudo-epilepticus," has been defined as a PNES lasting ≥30 min, or repetitive non-epileptic seizures without a return to baseline mental status. Non-epileptic psychogenic status was reported in 13.5% of children with PNES, who had been treated with intravenous AEDs and received invasive diagnostic investigations and/or prompt tracheal intubation. In this study, 92.31%, 84.62%, and 50% of the attacks lasted >3 min, >10 min, and >30 min, respectively. No patients received intensive care or tracheal intubation due to PNES during the study. In patients diagnosed with PNES alone (without comorbid epilepsy), the prevalence of interictal EEG abnormalities has been reported to range from 10% to 18%. Only 15% to 33% of simple partial seizures or seizure auras are associated with scalp-EEG abnormalities. In one case series with video-EEG documentation of PNES and epileptic seizures (both present in each patient), most patients (18/20) had a notably different clinical semiology for PNES compared with their epileptic seizures. Herein, 23 patients had undergone pertinent tests and examinations (in addition to physical and neurological examinations) that indicated normal or minor results without meaningful or relevant pathological findings. Most EEG readings were normal or exhibited spikes or epileptogenic discharges that were not correlated with PNES symptoms. Except for video-EEG and scalp-EEG assessments performed during an attack, laboratory and imaging investigations can only be used to rule out related pathology and do not contribute to PNES diagnosis.

One useful method for communicating PNES diagnosis to patients is to present it in a non-judgmental fashion, striving to maintain patient dignity. For a diagnosed patient, the term "functional" is considered the most neutral, while the term "psychogenic" is not helpful. When a video-EEG-confirmed diagnosis of PNES has been appropriately communicated, up to one-third of patients may experience improvement in their seizure burden with short-term follow-up. For most children with PNES, a clear,
persuasive, and empathetic expression of the diagnosis is essential in achieving the best long-term outcome. Some patients with PNES exhibit exacerbations of their episodes after diagnosis. Our experienced pediatric neurologists disclosed the PNES diagnosis to patients while exercising patience and sympathy. They also provided an explanation of the video-EEG recording results, aiming to obtain acceptance of the diagnosis from patients and their parents. For patients without known epileptiform EEG findings, we advise neurologic follow-up for at least 6 months after the discontinuation of AEDs. Some patients did not proceed with advised follow-up appointments. On average, patients with PNES receive a higher total dose burden of antiseizure therapies. This study had some limitations. First, the sample size was relatively small and lacked a control group. Second, psychosocial status was not quantified according to an established standard. Finally, the effects of AEDs on the behaviors of patients with epilepsy were not evaluated. In conclusion, detailed clinical manifestations, medical information, and skillful observation are important and necessary for PNES diagnosis. Many subtle characteristics of PNES should be carefully monitored. Future studies with more sensitive and detailed assessments of patient symptoms are required to facilitate a rapid and accurate PNES diagnosis.

Data statement

The data that support the findings of this study are available from the VGHTPE electronic medical database. Restrictions apply to the availability of these data, which were used under license for this study, and are not publicly available. Data are, however, available from the authors upon reasonable request, and with the permission of VGHTPE.

Declaration of competing interest

None.

Acknowledgments

This study is based in part on data from the Big Data Centre, VGHTPE. The authors appreciate the statistical assistance and support provided by the Maintenance Project of Big Data Centre, VGHTPE, for study design and monitoring, data analysis, and interpretation.

References


