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Psychological Problems and Clinical Outcomes of Children with Psychogenic Non-Epileptic Seizures

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Purpose: Our purpose was to investigate psychological problems and clinical outcomes in children with psychogenic non-epileptic seizures (PNES). **Materials and Methods:** We retrospectively reviewed the data of 25 patients who were diagnosed with PNES between 2006 and 2012. **Results:** Twenty-five children with PNES, aged 8 to 19 years (mean 13.82), were referred to psychiatrists for psychiatric assessment. On their initial visit, 72% of patients had comorbid psychological problems, including depression, anxiety, conduct disorder, adjustment disorder, Attention Deficit Hyperactivity Disorder, schizophrenia, and bipolar disorder. Among these, depression was the most frequent (36%). Predisposing and triggering factors included familial distress (40%), social distress (24%), and specific events (20%). The following treatment was advised based on the results of the initial psychological assessment: 3 patients regularly visited psychiatric clinic to assess their clinical status without treatment, nine underwent psychotherapy, and 13 received a combination of psychotherapy and psychopharmacological therapy. At the mean follow-up of 31.5 months after diagnosis, 20 patients (80%) were event-free at follow-up, three (12%) showed reduced frequency, and two (8%) experienced persistent symptoms. **Conclusion:** The outcomes of PNES in children are much better than those in adults, despite a high rate of psychological comorbidities.

Key Words: Seizure, children, psychological

INTRODUCTION

Psychogenic non-epileptic seizures (PNES) are defined as seizure-like movements without electrophysiological abnormalities. The prevalence of PNES in children with suspected epilepsy was reported as 4.8% in one study.[1] Because of the similarities between epilepsy and PNES, pediatric neurologists are usually the first to identify PNES in children, and they are often involved in developing treatment plans. After a child is diagnosed with PNES, urgent treatment is important for reducing unnecessary exposure to antiepileptic drugs (AEDs) and to address comorbid psychosocial problems. In many previous studies, clinical outcomes in adults

were associated with underlying psychological factors; however, data on PNES in children are limited. Accordingly, herein, we studied the characteristics and clinical outcomes of PNES in children and investigated the psychogenic aspects of PNES.

MATERIALS AND METHODS

We performed a retrospective chart review study of children diagnosed with PNES between 2006 and 2012 in the pediatric neurology department of a tertiary care hospital in Korea. PNES was defined as sudden paroxysmal behaviors without corresponding electroencephalography (EEG) abnormalities. The inclusion criteria for PNES included age under 20 years old and paroxysmal behavioral changes suggestive of epileptic seizures without electrographic ictal activity during video EEG monitoring. Patients with PNES and co-existing epilepsy were also included. Children with a diagnosis of other non-epileptic paroxysmal events, such as parasomnia, chorea, and stereotyped movements, were excluded.

The age of symptom onset, use of AEDs, semiology, past neurologic and psychiatric history, family history, and social background were assessed. Brain magnetic resonance imaging (MRI) was carried out in 19 patients. All patients underwent video EEG monitoring for an average of 2 days (range, 1 day to 3 days). Electrodes were placed according to the 10–20 International system, and EEG was recorded with a 16-channel Grass machine. If there were no suspicious events during recording, we performed a provocation test for symptom induction. We received written informed consent from parents of children with PNES before the test. The test was performed as follows: we told the patient that we will inject an intravenous drug that will induce seizure. Saline solution was intravenously injected a milliliter at a time to a maximum of 10 mL. We then asked the patient if they felt anything. After observation of the spell, we explained that the action of the solution was over, in order to stop the event. After the test, we presented the family with the video to ensure the similarity of the recorded event with typical ones.

After diagnosis, patients with PNES gradually discontinued AEDs related to PNES and were recommended to see a psychiatrist. All patients attended at least one psychiatric counseling session. We obtained psychiatric data including the number of psychiatric medications and diagnoses of depression, posttraumatic stress disorder, conversion disorder, anxiety, somatization disorder, or psychosis. We also considered any history of trigger or precipitating factors associated with PNES. The self-report Children's Depression Inventory and Revised Children's Manifest Anxiety Scale questionnaires were used to screen for depression and anxiety, respectively. Other psychological assessments including the Korean-Wechsler Intelligence Scale for Children-third edition, the Minnesota Multiphasic Personality Inventory, the Advanced Test of Attention, Conner's rating scale, the Korean-Attention Deficit Hyperactivity Disorder (ADHD) rating scale, and the Korean-Child Behavior Checklist were administered to 11 patients. Patients' final psychiatric diagnoses were made by the psychiatrist based on Diagnostic and Statistical Manual of Mental Disorders-4th edition (DSM-IV) diagnostic criteria. Clinical outcomes of PNES were investigated by reviewing the psychiatric charts and counseling after receiving written informed consent forms signed by the patients and their parents.

RESULTS

Between 2006 and 2012, 25 patients were diagnosed with PNES in our pediatric epilepsy center. The median age of diagnosis was 13.71±2.69 years old (range, 8.77 to 19.93) and the male to female ratio was 1:1.27. The mean delay in correct diagnosis was 9.61±14.05 months (range, 1 day to 4.3 years). Thirteen patients were taking AEDs at the time of diagnosis.

Prior to PNES diagnosis, two patients had febrile convulsions and eight patients had histories of afebrile seizures. Two of eight patients had intractable epilepsy, one of the patients had undergone left temporal lobectomy, and another patient had been admitted for presurgical evaluation. Two patients were born premature. Other medical histories included Behcet's disease, encephalitis, and rhabdomyolysis due to assault. Patient clinical characteristics are shown in Table 1.

Brain MRIs were normal in 15 of 19 patients. Abnormal brain MRI findings included hippocampal sclerosis, venous angioma, mild cortical atrophy, and a slightly hypoplastic vertebral artery. Interictal EEG was normal in 19 of 25 patients. Abnormal findings on the interictal EEG included focal slowing, voltage attenuation, and occasional sharp wave discharges.

Events spontaneously occurred in 11 patients during vid-

Table 1. Clinical Characteristics of 25 Children with Psychogenic Non-Epileptic Seizure

Age (yrs), median±SD	13.71±2.69
Male:female	11:14 (1:1.27)
Delay in PNES diagnosis (months), mean±SD	9.61±14.05
AED therapy at the time of diagnosis (number)	13
Monotherapy	4
Polytherapy	9
Withdrawal of antiepileptic drugs after PNES diagnosis (number)	6
Total follow-up duration (months), mean±SD	31.5±22.4
Past history	
Febrile convulsions/epilepsy (left temporal lobectomy)	2/8 (1)
Prematurity	2
Intellectual disability	4
Asthma	2
Behcet's disease	1
Encephalitis	1
Rhabdomyolysis	1
Restless leg syndrome	1
Epilepsy diagnosis in 8 patients	
Generalized tonic and clonic epilepsy	2
Simple or complex partial epilepsy	4
Partial epilepsy with secondary generalization	2

SD, standard deviation; PNES, psychogenic non-epileptic seizure; AED, antiepileptic drug.

Table 2. Semiology of Psychogenic Non-Epileptic Seizure (n=25)

Semiology	Number of patients
Generalized tonic-clonic movement	8
Focal tremor	5
Focal clonic movement	3
Headache or abnormal sensation	4
Dissociative symptom	1
Dystonia after hyperventilation	1
Atonic feature with unresponsiveness	1
Vacant staring with tonic posture	2

eo EEG monitoring. Provocation involved saline injection in 13 patients and verbal suggestion in 1, and 11 patients showed positive results in response. One patient had no event during monitoring and a negative provocation test; however, she was diagnosed with hyperventilation syndrome due to positive results in the Nijmegen scale. The other patient who had 10 daily seizures during 1 month stopped having seizures after starting video EEG monitoring for 6 months until last follow-up. Both of these patients were considered as suspicious PNES. In one case, PNES was found incidentally during presurgical evaluation.

Episode semiology is shown in Table 2. Generalized tonic-clonic movement was observed in 8 patients, focal tremor in five, focal clonic movement in three, headache or abnormal sensation in four, dissociative symptoms in one, dystonia after hyperventilation in one, atonic feature with unresponsiveness in one, and vacant staring with tonic posture in two.

All patients were recommended to visit our psychiatrists after discussion about the diagnosis of PNES. Intelligence quotient tests were performed in 14 patients, and the average was 90.93±22.96. Four patients had mild intellectual disability with intelligence quotients between 60 and 69. Self-assessed anxiety by Revised Children's Manifest Anxiety Scale and depression by Children's Depression Inventory were reported for all patients at the first psychiatric visit. Scores greater than or equal to 15 were suggestive of anxiety and depression disorders. The formal neuropsychological tests could be performed in 11 patients. Based on the results of the initial psychiatric consultation and tests, major depressive disorder was noted in 3 patients, depressive disorder in six, anxiety disorder in three, conduct disorder in one, adjustment disorder in two, schizophrenia in one, and bipolar disorder in one. ADHD was diagnosed in 7 patients (28%) before and after the diagnosis of PNES. Eight of 25 patients had more than two of the diagnoses and 9 patients had no psychological diagnosis (Table 3).

PNES onset was frequently precipitated by stressful situations, including familial or interpersonal distress. Familial distress was reported for 10 patients and social distress in six. Social distress included academic failure, adjustment failure, assault, and bullying. Five patients experienced events of diverse severity, from vaccination or minor collision to kidnapping or epilepsy surgery (Table 4). These events were considered triggering factors of PNES. We were unable to identify precipitating factors in 4 patients.

Treatment plans varied depending on the results of the psychological consultation; psychotherapy in 9 patients, and a combination of psychotherapy and psychopharmacological therapy in 13 patients. The three remaining patients regularly visited our psychiatric clinic to assess their clinical status without treatment. After a mean follow-up of 31.5±22.4 months (range, 2 months to 6.6 years), 20 patients were event-free (80%) during mean 33.60±21.79 months (range,

2.1 months to 6.35 years), three exhibited reduced episode frequency (12%), and symptoms persisted in two (8%). Six patients had stopped taking AEDs, and 4 patients had their dosage decreased after diagnosis.

All patients under observation and those receiving psychotherapy were event free. Thirteen of 25 patients received psychopharmacological drugs concurrently with psychotherapy. Nine patients maintained the drug regimen, and 4 patients discontinued drug treatment after they recovered. Alprazolam, fluoxetine, escitalopram, sertraline, and lorazepam were used for depression or anxiety symptoms, and schizophrenic or bipolar symptoms were treated with aripiprazole, risperidone, and quetiapine. Among 13 patients, eight were event-free, three showed reduced frequency, and two exhibited persistent symptoms.

Eight patients with both PNES and epilepsy received psychotherapy and six of them had psychopharmacological therapy. After treatment, 4 patients were event-free, three had reduced frequency of events and one showed persistent symptom.

Our study group was too small to obtain meaningful statistical data. However, we made several observations based on the patients' clinical courses. Despite the high rate of comorbid psychological problems, the clinical outcome of children with PNES was favorable. The observation-only and psychotherapy groups had relatively benign underlying psychological problems that were easily improved. Upon follow-up children with persistent PNES, three out of five children still suffered from depression, and two children continued to experience familial distress.

Table 3. Psychological Diagnoses of 25 Children with Psychogenic Non-Epileptic Seizures

Diagnosis	Number of patients
Major depressive disorder	3
Depressive disorder	6
Anxiety disorder	3
Conduct disorder	1
Adjustment disorder	2
Schizophrenia	1
Bipolar disorder	1
Attention deficit hyperactivity disorder	7
Number of patients with more than two of the diagnoses	8
Number of patients with none of the diagnoses	9

Table 4. Precipitating Factors of Psychogenic Non-Epileptic Seizure (n=25)

Precipitating factors	Number of patients
Familial distress	
Parental divorce, separation, or discord	3
Stress from family	7
Social distress	
Academic failure	1
Adjustment failure	2
Assault	2
Bullying	1
Accident before onset or Posttraumatic stress disorder	5
None	4

DISCUSSION

PNES are defined as seizure-like movements without electrophysiological abnormalities. The prevalence of PNES has been estimated as 2 to 33 per 100000, and the percentage of epilepsy center patients with PNES is estimated to be 10–20%.[2,3] The majority of patients (83%) are 15–35 years of age.[4] In children who underwent video EEG monitoring, the prevalence of PNES was reported as 4.8% in one study, which is similar to that described in adults[1]; the mean age of symptom onset was 13.03 years in our study.

There were various efforts to differentiate between PNES and epilepsy by ictal semiology before the era of video EEG monitoring. However, the wide availability of video EEG monitoring has shortened the duration of diagnostic delay and increased the detection rate of PNES. In our study, the mean delay of diagnosis (9.61 months) was shorter than that reported in previous studies (22.3 months–3.5 years).[5,6] However, there are still cases where PNES is mistaken for epilepsy, and the incidence of epilepsy coexisting in patients with PNES is considerable.[7] Thus, early suspicion of PNES and video EEG monitoring are important.

If there are no events during video EEG monitoring, provocation methods of saline injection or verbal suggestion can be used. If patients still do not experience any events in the observed setting, ambulatory EEG may be useful. Without video monitoring, ambulatory EEG may have limitations and should be interpreted with caution. In patients with frequent events, recording an event or establishing that spells only occur when the patient is not being monitored should confirm the diagnosis of PNES. In our study, PNES was highly suspected in one patient who experienced daily seizures until video EEG monitoring was started.

PNES is classified as a somatoform disorder in the DSM-

IV and as a conversion disorder in the International Statistical Classification of Diseases and Related Health Problems, 10th revision. Bodde, et al.[8] suggested a theoretical model for PNES diagnosis. Five different aspects were proposed to explain underlying psychogenic factors, consisting of underlying psychological etiology (sexual abuse or traumatic experiences), vulnerability of patients (cognitive function, personality), shaping factors (epilepsy history, relatives with epileptic seizure), triggering factors (specific situations that provoke a seizure), and prolongation factors (secondary gain). Because triggering and prolongation factors may determine event frequency and resistance to therapy, all of these factors should be screened early in the differential diagnosis of PNES.

In our study, familial and social distress was reported in 10 and 5 patients, respectively. Familial distress included parental divorce, familial separation, and parent-child relationship problems. One patient reported psychological shock after his father's imprisonment for financial reasons. Social distress included adjustment failure, bullying, and assault by peers. One patient who underwent left anterior temporal lobectomy experienced recurrent seizures 1 month later that were determined by video EEG monitoring to be PNES. After we informed her of PNES, there were no more events. Epilepsy surgery had temporarily induced PNES symptoms by acting as a cause of severe stress. Less severe psychological stressors, such as school examination, vaccination, and minor collision, were reported in three patients.

Comorbid psychogenic disorders are reported in 60–70% of PNES patients.[9,10] In our study, 72% patients had comorbid psychological problems that included depression, anxiety, conduct disorder, adjustment disorder, schizophrenia, and bipolar disorder. Among them, depression was the most frequent (36%). Despite a high proportion of comorbid psychogenic disorders, patient outcomes were good (remission in 80%), which contrast those of previously published studies on adults (remission in 19–25%).[7,11,12] A few studies have described outcomes in children diagnosed with PNES. Wyllie, et al.[13] reported a 78% remission rate in children after a mean follow-up of 30 months, a result that was similar to ours. Children tend to have relatively more benign underlying psychological problems or experience temporary psychological impacts, compared to adults.

However, if children with PNES have serious psychological problems, their clinical outcomes can be poor. Psychological treatment should be applied to the patient depending on their underlying psychological pathophysiology. A pilot randomized control trial in adults reported that treating comorbid depression using sertraline achieved a 45% reduction in PNES rate, compared to an 8% increase in the placebo group.[14] The effect of psychopharmacological therapy in children might not be the same as in adults; some studies have reported on the usage of psychopharmacological drugs in children.[13,15,16] The patients described in the present study were treated with psychotherapy or combined psychotherapy and psychopharmacological therapy at the discretion of the psychiatrists. Patients with relatively benign underlying psychological problems showed complete symptom improvement after just observation or psychotherapy alone. Psychopharmacological drugs were prescribed to 52% (13/25) of patients in parallel with psychotherapy, and 9 patients continued the drug regimen at the last follow-up. Eight of thirteen (61.5%) patients were event free, three (23%) showed reduced frequency, and two (15.3%) exhibited persistent symptoms.

Recently, various studies have discussed the use of structured methods of psychotherapy in patients with PNES, such as cognitive behavior therapy, psychodynamic therapies, and group interventions. Among them, only cognitive behavior therapy was studied in randomized, controlled pilot studies. Cognitive behavior therapy reduced the frequency of events compared with standard medical care.[17] Although the trials involved adults and there is limited evidence in children, combined treatment with psychopharmacological medication and cognitive behavior therapy in children with PNES is expected to be advantageous and may be the optimal therapy. Further studies are needed to evaluate the effectiveness of different therapeutic approaches in a pediatric population.

Patients with recurrent PNES tend to experience diminished quality of life. Furthermore, one study showed the premature mortality in patients with a diagnosis of PNES, which was 0.58% per year, compared with 0.41% per year in the general Scottish population. Thus, it is important to understand the mechanisms underlying psychogenic seizures in each individual case to reduce morbidity and mortality. Etiological mechanisms could be found using the theoretical model of PNES diagnosis, and it may inform treatment choices and prevent future morbidity in children.

Because of the small number of patients and its retrospective nature, our study has some limitations. Even so, we found that children with PNES had a high proportion of comorbid psychological disorders but achieved better outcome than adults with PNES. Even children with severe

psychological problems could improve with proper psychotherapy or psychopharmacological therapy. Multicenter studies with greater numbers of patients are needed to confirm our findings.

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REFERENCES

1. Szabó L, Siegler Z, Zubek L, Liptai Z, Körhegyi I, Bánsági B, et al. A detailed semiologic analysis of childhood psychogenic nonepileptic seizures. Epilepsia 2012;53:565-70.
2. Szaflarski JP, Ficker DM, Cahill WT, Privitera MD. Four-year incidence of psychogenic nonepileptic seizures in adults in hamilton county, OH. Neurology 2000;55:1561-3.
3. Benbadis SR, Allen Hauser W. An estimate of the prevalence of psychogenic non-epileptic seizures. Seizure 2000;9:280-1.
4. Shen W, Bowman ES, Markand ON. Presenting the diagnosis of pseudoseizure. Neurology 1990;40:756-9.
5. Lancman ME, Asconapé JJ, Graves S, Gibson PA. Psychogenic seizures in children: long-term analysis of 43 cases. J Child Neurol 1994;9:404-7.
6. Finlayson RE, Lucas AR. Pseudoepileptic seizures in children and adolescents. Mayo Clin Proc 1979;54:83-7.
7. Silva W, Giagante B, Saizar R, D'Alessio L, Oddo S, Consalvo D, et al. Clinical features and prognosis of nonepileptic seizures in a developing country. Epilepsia 2001;42:398-401.
8. Bodde NM, Brooks JL, Baker GA, Boon PA, Hendriksen JG, Aldenkamp AP. Psychogenic non-epileptic seizures--diagnostic issues: a critical review. Clin Neurol Neurosurg 2009;111:1-9.
9. Lempert T, Schmidt D. Natural history and outcome of psychogenic seizures: a clinical study in 50 patients. J Neurol 1990;237:35-8.
10. Reuber M, Howlett S, Khan A, Grünewald RA. Non-epileptic seizures and other functional neurological symptoms: predisposing, precipitating, and perpetuating factors. Psychosomatics 2007;48:230-8.
11. Kanner AM, Parra J, Frey M, Stebbins G, Pierre-Louis S, Iriarte J. Psychiatric and neurologic predictors of psychogenic pseudoseizure outcome. Neurology 1999;53:933-8.
12. Ettinger AB, Devinsky O, Weisbrot DM, Ramakrishna RK, Goyal A. A comprehensive profile of clinical, psychiatric, and psychosocial characteristics of patients with psychogenic nonepileptic seizures. Epilepsia 1999;40:1292-8.
13. Wyllie E, Friedman D, Rothner AD, Luders H, Dinner D, Morris H 3rd, et al. Psychogenic seizures in children and adolescents: outcome after diagnosis by ictal video and electroencephalographic recording. Pediatrics 1990;85:480-4.
14. LaFrance WC Jr, Keitner GI, Papandonatos GD, Blum AS, Machan JT, Ryan CE, et al. Pilot pharmacologic randomized controlled trial for psychogenic nonepileptic seizures. Neurology 2010;75:1166-73.
15. Vincentiis S, Valente KD, Thomé-Souza S, Kuczinsky E, Fiore LA, Negrão N. Risk factors for psychogenic nonepileptic seizures in children and adolescents with epilepsy. Epilepsy Behav 2006;8:294-8.
16. Wyllie E, Glazer JP, Benbadis S, Kotagal P, Wolgamuth B. Psychiatric features of children and adolescents with pseudoseizures. Arch Pediatr Adolesc Med 1999;153:244-8.
17. Baslet G. Psychogenic nonepileptic seizures: a treatment review. What have we learned since the beginning of the millennium? Neuropsychiatr Dis Treat 2012;8:585-98.