

A study of psychogenic non-epileptic seizures in an inpatient video-electroencephalography monitoring service in Tabriz, northwest of Iran

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Keywords

Neurological Manifestations; Comorbidity; Iran; Psychology; Seizures

Abstract

Background: Psychogenic non-epileptic seizures (PNES) are manifested as paroxysmal alterations in motor, sensory, autonomic, and/or cognitive and behavioral signs and symptoms, without associated ictal epileptiform discharges. A misdiagnosis of PNES as epilepsy results in a prolonged and unnecessary (antiepileptic) drug treatment and social and psychological stigma of epilepsy in these patients. This study aimed to determine the epidemiology, clinical manifestations, and associated factors of PNES in hospitalized patients in the video-electroencephalography (EEG) monitoring (VEM) service of Razi Hospital, Tabriz, Iran.

Methods: In this cross-sectional descriptive study, 55 patients with a final diagnosis of PNES were selected from the patients referred to the VEM unit of Razi

Hospital for the evaluation of epilepsy. The study was performed from May 2017 to June 2019. Patient information included demographic data and medical history (drug history, comorbidities, trauma, and family history). The clinical manifestations (semiology and duration of attacks) and EEG findings, as recorded by VEM during hospitalization, were collected.

Results: 55 patients with PNES were studied with VEM, 27 (49.1%) of which were men, and 28 (50.9%) were women. The mean and standard deviation (SD) of age of the patients was 34.16 ± 12.64 years. No significant differences were observed in the semiology of PNES between men and women. Depression was the most common psychiatric comorbidity.

Conclusion: The clinical manifestations of PNES in

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the present study were similar to those in most previous studies from other countries. The culture and sex of the patients did not seem to be a contributing factor in PNES semiology.

Introduction

Seizures as a symptom of a neurological disorder can originate from one of these three states: epileptic seizures, psychogenic non-epileptic seizures (PNES), or physiologic non-epileptic events. PNES are clinically defined as episodic events appearing like epileptic seizures but caused by psychological processes.¹ Very similar to epileptic seizures clinically, PNES manifest themselves as paroxysmal alterations in motor, sensory, autonomic, and/or cognitive and behavioral signs and symptoms; however, unlike epilepsy, PNES are not associated with ictal epileptiform discharges.² The International League Against Epilepsy (ILAE) has identified PNES as one of the ten key neuropsychiatric issues associated with epilepsy.³

Video-electroencephalography (EEG) monitoring (VEM) is recognized as the gold standard for the diagnosis of PNES despite its limitations.^{4,5} The patient's history, witness reports, clinician's observations, and ictal and interictal EEG all have supportive roles in the diagnosis of PNES.

In recent years, the epidemiology, clinical manifestations, and the associated factors of PNES have been the focus of many studies from all around the world.⁶⁻¹¹ Studies from Iran are mostly from the southern area,¹²⁻¹⁵ and there is one study from the central region of Iran.¹⁶

In this study, we report on these aspects of PNES in the northwest of Iran, especially in Razi Hospital, Tabriz, East Azerbaijan Province. We hope that this study will improve our understanding of PNES. A misdiagnosis of PNES, as true epilepsy, results in prolonged inappropriate antiepileptic treatment, the relevant drug side effects, adverse psychological and social outcomes, and high costs on both the patients and the health care system.

Materials and Methods

The patients admitted into the VEM unit of Razi Hospital with a definitive diagnosis of PNES were included in this retrospective, cross-sectional, descriptive study, from May 2017 to June 2019. This hospital is a major academic center for the referral of epileptic patients from the northwest of

Iran. Three neurologists interviewed all the patients, and informed consent was obtained by a medical student from each patient. All the data acquired, including the interpretation of VEM recordings, were reviewed by an epileptologist. Ethical approval for this study was obtained from the Research Ethics Committee of Tabriz University of Medical Sciences, Tabriz (ethics approval code: IR.TBZMED.REC.1397.362).

The study population included all the patients who were admitted into the VEM service of Razi Hospital during the above time interval for the diagnostic evaluation of epilepsy.

The inclusion criteria consisted of any motor, behavioral, autonomic, and sensory manifestations that indicated the probability of epileptic or non-epileptic seizures and the absence of any ictal epileptic EEG discharges. The exclusion criteria consisted of epilepsy confirmed by clinical findings, definite epileptic EEG, VEM findings, or inadequate study due to patient non-compliance, all confirmed by the epileptologist's final review in each case. The psychiatric evaluation of the patients was performed by psychiatry consultation.

Patient information included demographics (age, sex), medical history (previous diagnosis of seizure, drug history, opiate or other drug addiction, comorbidities, trauma, and familial history), current illness (the type of seizure, duration of symptoms, ongoing medications, and therapeutic response), and information acquired during hospitalization (EEG reports, clinical manifestations, involuntary movements, disturbance of consciousness, behavioral and emotional changes, and frequency of attacks).

The data were recorded in a questionnaire, including all the above items, and analyzed with SPSS software (version 24, IBM Corporation, Armonk, NY, USA). All the data were kept confidential.

Results

A total of 246 patients were registered in our center from May 2017 to June 2019. In 55 patients included in the study, the diagnosis was compatible with PNES according to clinical and EEG findings. The frequency of PNES compared to total hospitalizations for epilepsy was 22.35%.

27 patients (49.1%) were men, and 28 (50.9%) were women. The female-to-male ratio was 1.03:1. The mean and standard deviation (SD) of age at the time of hospitalization was 34.16 ± 12.64 years.

The youngest patient was 11 and the oldest was 59 years old. In this study, the patients were divided into five age groups with a range of 10 years. The age groups included 10-20 years with 13 patients (23.54%), 20-30 years with 9 patients (16.36%), 30-40 years with 16 patients (29.09%), 40-50 years with 16 patients (29.09%), and 50-60 years with 16 patients (29.09%). The most prevalent range of PNES diagnosis was in the age range of 30-40 years, with 16 cases (29.09%).

The other demographic characteristics of the patients are summarized in table 1.

Table 1. Demographic characteristics of the patients with psychogenic non-epileptic seizures (PNES)

Demographic variable	Value
Age (year) (mean \pm SD)	34.16 \pm 12.64
Sex (male/female)	27/28
Duration of disease before diagnosis (year) (mean \pm SD)	4.59 \pm 3.83
Education (illiterate/some high school/high school graduate/university)	5/29/11/10
Marital status (married/unmarried/divorced)	18/33/4
Living place (urban/rural)	44/11

SD: Standard deviation

The clinical manifestations of PNES during the study and a comparison of these findings between men and women revealed no statistically significant differences (Table 2).

The mean and SD of duration of symptoms before the diagnosis was 4.59 \pm 3.83 years, with a mean of 4 years. The minimum duration of symptoms was 1 year, with a maximum duration of 20 years. The mean and SD of number of PNES attacks per hospitalization was 4.31 \pm 3.31. The lowest number of attacks was 1 and the highest was 18 times during the hospitalization at the

VEM unit. There was no statistically significant difference between the two genders ($P = 0.40$). The mean and SD of duration of hospitalization was 7.35 \pm 4.21 days. The minimum duration was 1 day, and the maximum was 11 days.

The comorbidities were divided into three groups: 1) the medical comorbidities with 25 patients (45.5%), 2) psychiatric comorbidities with 19 patients (34.5%), and 3) no history of comorbidities with 11 patients (20.0%). The medical comorbidities included common neurological problems (migraine, tension-type headache) and general medical disorders [hypertension (HTN), ischemic heart disease (IHD), and diabetes] with 24 patients (43.6%). Depression was the most common psychiatric comorbidity. The other associated factors are summarized in table 3.

Table 3. Factors associated with psychogenic non-epileptic seizures (PNES) attacks*

Associations	n (%)
A history of mild head trauma**	5 (9.1)
A history of febrile seizures	1 (1.8)
Family history of seizure or epilepsy	8 (14.5)
Medical comorbidity	25 (45.5)
Psychiatric comorbidity	19 (34.5)
Drug abuse (opiates)	5 (9.5)

*Some patients had more than one factor, **Mild head trauma is defined as head trauma without loss of consciousness

Only 21 patients (38.0%) were taking antiepileptic drugs (AEDs), of which 3 patients (5.5%) also had epileptic seizures. 6 patients (11.0%) exhibited partial treatment response, and 49 (89.1%) had no response. Drug addiction to opiates was reported in 5 patients (9.1%). The psychoactive medications, most commonly selective serotonin reuptake inhibitors (SSRIs), were used by 23.6% of the patients.

Table 2. Clinical manifestations recorded during video-electroencephalography (EEG) monitoring (VEM) study and sex distribution and comparison in patients with psychogenic non-epileptic seizures (PNES)

Clinical manifestation	Total	Men [n (%)]	Women [n (%)]	P
Induced seizure attack	28	13 (28.9)	15 (33.3)	0.672
Crying during seizure	23	12 (25.5)	11 (23.4)	0.664
Whispering during seizure	19	8 (17.0)	11 (23.4)	0.440
Opisthotonus posturing	25	12 (28.6)	13 (31.0)	0.753
Fine shaking movements	19	9 (19.1)	10 (21.3)	0.859
Snoring after seizure	1	1 (2.3)	0 (0)	0.312
Eyes closed	27	14 (29.8)	13 (27.7)	0.642
Eye movements	26	13 (28.9)	13 (28.9)	0.882
Fencing posture	12	6 (14.0)	6 (14.0)	0.924
Side-to-side head movements	23	11 (23.4)	12 (25.5)	0.229
Pelvic thrusting during seizures	5	2 (4.3)	3 (6.4)	0.672

Discussion

PNES are frequently reported at epilepsy centers. Approximately, 20%-40% of inpatient epilepsy patients are reported to have PNES.¹⁷ It constituted 22% of all the patients referred to our center.

In most previous studies, women (75%-80%) made up most of the patients.^{6,17} However, the female-to-male ratio in this study was 1.03:1. A study from China also reported similar results.¹¹ The possible cause of this difference in this study might be a higher proportion of young male patients referred to our center for ruling out non-epileptic seizures. These referrals were made from the military authorities evaluating their eligibility for military service; these volunteers might feign epilepsy.

There is no age limit for the presentation of PNES; however, young adults are the most commonly affected subjects.^{18,19} The most common age group in our patients with PNES was 30-40 years with 16 cases (29.09%). The frequency of PNES in the age group > 50 years was 7.3%, which is similar to another study of late-onset PNES.²⁰

The semiological features of PNES have widely been reported in studies.^{21,22} We observed no cross-gender differences in the semiology of PNES (Table 2), consistent with the results of another study in Iran and a study in another country.^{12,22} Ictal eye closure is a reliable indicator for the diagnosis of PNES.²³ We observed this finding in almost one-half (49.0%) of our patients. The other symptoms observed more frequently in our study were crying during seizures, opisthotonus posturing, eye movements during the attack, and side-to-side head movements. In comparison to similar studies in Iran and other countries, the present study also showed a somewhat similar spectrum of semiological features of PNES in most cases.^{14,21,22} This finding also further emphasizes the shared cross-culture elements of the clinical manifestations of PNES.¹⁸

A significant delay usually occurs between the clinical presentation of PNES and its definitive diagnosis. This time interval has been reported with a wide range of mean time from 0.60 to 11.18 years in different studies.¹⁸ In our study, it was 4.59 ± 3.83 years, with a minimum of 1 and a maximum of 20 years. This rather long delay poses adverse effects of prolonged unnecessary drug treatment and the social and psychological consequences of an erroneous diagnosis of

epilepsy for these patients. This unwelcome fact is further substantiated by the finding that more than one-third (38.0%) of our patients were taking at least one AED before admission. Likewise, in another study, 59.7% of patients were taking AEDs at referral, and 23.3% of patients were on polytherapy with AEDs.¹³

Medical comorbidities have also (38.5%) been reported in patients with PNES.²⁴ In the present study, mainly chronic non-surgical disorders were detected in 43.6% of the patients. Psychiatric comorbidity is common among patients with PNES. A recent review reported it in various studies with a range of 53%-100%. Posttraumatic stress disorder (PTSD), depression, and personality and anxiety disorders were the most prevalent diagnoses.²⁵ The most common psychiatric comorbidity in the present study was depression. This association might suggest a role for psychiatric problems, especially depression, in non-epileptic seizures.⁶

The history of head injury is commonly reported in PNES (44.6%) and claimed to be a significant risk factor in these patients, affecting its prognosis.²⁶ In the present study, there was a history of mild head trauma in 9.1% of the cases.

A history of sexual abuse is commonly reported as an associated factor in PNES. Studies in western countries have reported a rate of 24%-67% for this experience.^{18,27} A recent large-scale study in Iran reported it in 8.3% of their cases.²⁸ None of the patients in the present study reported such a history despite direct questioning, which might be due to a very negative cultural and religious perspective of such experience in our country, contributing to the patients' reluctance to report the experience openly.

The limitations of the present study include its retrospective design, the limited sample size, the relatively large proportion of male patients, no use of a formal psychiatric interview for comorbid psychiatric problems, and the lack of information concerning sexual or physical abuse.

Conclusion

PNES are relatively common in epilepsy centers. The demographic and clinical characteristics of patients with PNES are similar in different cultures and between men and women. The associated factors might have a role in predisposing patients to PNES, but it seems that more studies are necessary for their better clarification.

Conflict of Interests

The authors declare no conflict of interest in this study.

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