Clinical Research

Clinical Features and Prognosis of Nonepileptic Seizures in a Developing Country

*,†W. Silva, *B. Giagante, *R. Saizar, *L. D′Alessio, *,†S. Oddo, *,†D. Consalvo, *P. Saidón, and *,†S. Kochen

*Municipal Epilepsy Center, Department of Neurology, Ramos Mejía Hospital, and †CONICET, Buenos Aires, Argentina

Summary: *Purpose:* To determine the predictive value of clinical features and medical history in patients with nonepileptic seizures (NESs).

Methods: One hundred sixty-one consecutive ictal video-EEGs were reviewed, and 17 patients with 41 NESs identified. NES diagnosis was defined as paroxysmal behavioral changes suggestive of epileptic seizures recorded during video-EEG without any electrographic ictal activity. Clinical features, age, sex, coexisting epilepsy, associated psychiatric disorder, social and economic factors, delay in reaching the diagnosis of NES, previous treatment, and correlation with outcome on follow-up were examined.

Results: The study population included 70% female patients with a mean age of 33 years. Mean duration of NESs before diagnosis was 9 years. Forty-one percent had coexisting epilepsy. The most frequent NES clinical features were tonic–clonic mimicking movements and fear/anxiety/hyperventilation. The most common psychiatric diagnosis was conversion disorder and dependent and borderline personality disorder. Seventy-three percent of patients with pure NESs received antiepileptic drugs (AEDs), and 63.5% of this group received new AEDs. Fifty-nine percent of the patients received psychological/psychiatric therapy. At follow-up, 23.5% were free of NESs.

Conclusions: All seizure-free patients had two good prognostic factors: having an independent lifestyle and the acceptance of the nonepileptic nature of the episodes. Video-EEG monitoring continues to be the diagnostic method to ensure accurate seizure classification. Establishing adequate health care programs to facilitate access to new technology in public hospitals as well as the implementation of continuous education programs for general practitioners and neurologists could eventually improve the diagnosis and treatment of patients with NESs. **Key Words:** Developing country—Nonepileptic seizures—Psychogenic seizures—Outcome—Epilepsy.

Psychogenic nonepileptic seizures (NESs), also known as pseudoseizures, constitute a clinical phenomenon resembling epileptic seizures (ESs) and are very frequently misdiagnosed as such (1–4). Furthermore, both ESs and NESs may coexist in the same patient (4). Diagnosis is based on the recognition of typical clinical symptoms and the recording of normal EEGs during the episodes. Long-term video-EEG monitoring (LVEM) has completely changed the diagnosis of NES and allowed several groups of researchers to describe the different clinical signs observed (1,2,5–8).

An early identification of the existence of NESs is essential to determine the appropriate therapy. Patients with NESs may be inadequately treated with antiepileptic drugs (AEDs) for decades or even with invasive treatments for a nonepileptic status. Because Argentina is a developing country, we have used LVEM only since 1990. However, the process of diagnosis is difficult because of economic problems preventing the implementation of adequate diagnostic techniques. Most reports on this topic were carried out in developed countries.

METHODS

Between October 1995 and July 1998, 161 consecutive ictal video-EEGs were reviewed in 68 patients studied at the Municipal Epilepsy Center. Forty-one (25.4%) NESs were identified in 17 (25%) patients. Thirteen (76.4%) patients came from our Center, and four (23.6%) had been referred from other centers. Follow-up was obtained for all patients, between 6 months and 3 years after the diagnostic telemetry recording, by diary review

and patient contact. Electroclinical features were examined, and the following parameters were determined: age, sex, coexisting epilepsy, associated psychiatric disorder (using the DSM-IV scale for diagnostic criteria), social and economic factors, delay in reaching the diagnosis of NES, treatment administered, and its correlation with outcome on follow-up. The International League Against Epilepsy (ILAE) diagnostic criteria were used for the diagnosis of ES (9).

For inclusion, patients met the following criteria: (a) recording of at least one witnessed seizure episode; (b) compliance with the diagnostic criteria for NES: paroxysmal behavioral changes suggestive of epileptic seizure recorded during video-EEG monitoring without electrographic ictal activity; and (c) no other clinical evidence suggesting that the seizures were due to epilepsy or any other neurologic disorder.

Patients were excluded if the documented seizures differed from their usual episodes or whenever any doubts remained to confirm the diagnosis after video telemetry. Patients with purely subjective phenomena were excluded from the study, because ictal epileptiform activity may not always be apparent during simple partial seizures. In all cases, the video-EEGs were ordered by a neurologist. For economic reasons, the first video-EEG was always performed in ambulatory conditions for 2–6 h, without any reduction of the AEDs. Whenever necessary, this study was continued with patient hospitalization.

On the identification of nonepileptic events, psychiatric therapy was indicated in all cases. Therapeutic regimens were also reviewed to determine whether the adequate diagnosis might eventually lead to a simplification of treatment, by decreasing the number or dose of the different AEDs in patients with coexisting epilepsy, or to a discontinuation of medication in patients with pure NESs.

To determine the existence of risk factors related to the prognosis of these patients, the data were assessed by statistical analysis using logistic regression and Fisher's exact test. All quoted confidence intervals (CIs) are two-sided 95% CIs.

RESULTS

Among the 17 patients entered in the study, 12 (70%) were female and five (30%) were male patients; mean age, 33 years (range, 12–69 years). The mean age at onset of NESs was 25 years (range, 8–59 years), and the mean duration of the NESs before diagnosis was 9 years (range, 1–30 years).

The most frequent NES clinical features were tonic–clonic mimicking movements, nine (21.9%) patients; fear/anxiety/hyperventilation, nine (21.9%) patients; apparent decreased responsiveness and motionlessness,

eight (19.5%) patients; mimicking automatism movements, five (12.1%) patients; vocalization, two (4.8%) patients; and head dropping, two (4.8%) patients. Urinary incontinence was found in one subject. One NES event type in 13 (76.5%) patients and two event types in four (23.5%) patients were identified. The mean number of NESs recorded was 2.7 (range, 1–7). The mean NES duration was 8.8 min (range, 40 s to 40 min). The mean duration of the video-EEG recording time was 6 h per patient (range, 2–16 h). All except one of the LVEMs were performed in an ambulatory setting.

The psychiatric diagnoses based on DSM IV criteria were: in Axis I (Clinical Disorders): conversion, nine (52.9%); anxiety, four (22%); dissociative, two (11%); psychotic, one (5.8%); and malingering, one (5.8%) patient. In Axis II (Personality Disorders): dependent, three (25%); borderline, three (25%); histrionic, one (5%); and mental retardation, one (95.8%) patient.

In seven (41.1%) patients, clear clinical evidence of coexisting epilepsy was found, supported by interictal epileptiform EEG abnormalities and/or magnetic resonance imaging (MRI). Six patients had a partial syndrome, and one, a generalized syndrome, all misdiagnosed as having refractory epilepsy. The mean duration of the epilepsy was 4.5 years (range, 1–10 years). All patients with NESs and ESs were treated with AEDs, and none of them received psychiatric pharmacologic treatment.

The analysis of the social and economic features of the entire study population indicated that 14 (82.3%) patients had an independent lifestyle, eight (47%) patients were unemployed, and 10 (58.8%) patients had a conflicting affective/emotional relationship. A history of family violence was reported in three (17.6%) patients and of sexual abuse in one patient.

In the group of 11 (64.7%) patients with pure NESs, eight (72.7%) patients received AEDs, and 63.5% of this group received new AEDs. Six (54.5%) pure NES patients also received other pharmacologic treatment, including neuroleptics and antidepressants. Furthermore, four (36.3%) patients with pure NESs had been treated pharmacologically for status epilepticus. One patient had been intubated.

Once the diagnosis was disclosed, six (35.2%) patients recognized a probable trigger cause. Seven (41%) patients accepted the nonepileptic nature of their seizures. Ten (59%) patients agreed to receive psychological/psychiatric therapy. During the follow-up period, four (23%) patients were free of NESs, and 13 (77%) patients continued having seizures.

We found that two factors had a predictive value for a good outcome: the acceptance of the nonepileptic nature of the seizures and an independent lifestyle (RR = 2.38; $p < 0.05$). However, a positive association was found between the outcome and other factors assessed (coex-

istence of any type of psychiatric disease, sex, social/economic and affective/emotional situation, and psychiatric or psychological treatment). Because of the small size of the sample, the confidence interval is too large to have an actual statistical value. Discontinuation of AEDs was recommended for all patients with pure NESs, yet only four (23.5%) patients accepted this suggestion.

DISCUSSION

This study included patients with pseudoseizures recorded on video-EEG monitoring and duly diagnosed on the basis of strictly defined criteria. Most patients were referred to the Center's laboratory for outpatient video-EEG monitoring. The mean time of video-EEG recording was 6 h, similar to reports by Luther et al. (10). Monitoring allowed confirming the efficacy of a single 3-h video-EEG recording for the diagnosis of NES.

In keeping with most other studies, the majority of these patients were female subjects (5), and the age ranged between 12 and 69 years (7,11,12). The recorded NESs generally lasted longer than the ESs (13), and tonic–clonic activity mimicking epileptic movements was the single most common "ictal" characteristic of NESs (7). Another feature frequently found in this study was responsiveness and motionlessness, mimicking complex partial seizures. General practitioners considering that psychogenic seizures are restricted to bizarre and neurologically incongruent behavior may be especially prone to a NES misdiagnosis in patients with only unresponsiveness. Such psychogenic seizures may be taken for complex partial seizures or absence seizures (3,14–16). Contrary to previous reports (8), it was found that fear, anxiety, and hyperventilation were the second most frequent clinical signs. It was considered that this difference in prevalence of these symptoms could be due to the different criteria used by the individual authors to classify clinical features of NESs, or due to a different approach and cultural background.

There have been considerable discrepancies regarding the incidence of true epilepsy coexisting in patients with pseudoseizures (ranging from 20 to 72%) (4,17–20). In these series, 41% of the patients had coexisting epilepsy. All these patients carried the diagnostic of refractory epilepsy. The clinical diagnosis of both disorders in the same patient is difficult. The condition may not respond to treatment because only NESs or ESs are identified. Furthermore, whenever both types of disorders are present, the relative frequency of ESs and NESs may be difficult to determine. Some or most of the events may be either ESs or NESs. NESs usually do not occur during apparent sleep and typically develop after the onset of ESs. In a patient with well-characterized seizure phenomena, the appearance of a different type of episode may suggest NESs.

The DSM IV (21) criteria were applied, and it was found that the most common psychiatric diagnoses were conversion disorder, posttraumatic stress disorder, and dissociative disorder, and the main personality disorders were dependent and borderline. A revision of the published literature (22–26) has shown that the criteria governing psychiatric diagnosis were based on different methods, thus complicating the comparison between different studies. Patients with pseudoseizures frequently report coming from chaotic families. In addition, a number of reports postulate that psychogenic seizures may arise in response to sexual or physical abuse. Coinciding with other studies (16,27), a history of family violence or sexual abuse was found in 23.5% of the cases. Because physical and sexual abuse may be more common in the general population than previously thought (16), one must be cautious about inferring that a specific association is present unless it is actually demonstrated.

Seventy-three percent of the patients with pure NESs were wrongly treated with AEDs, and 63.5% of this group received new AEDs after a misdiagnosis of refractory epilepsy. In our environment, this percentage becomes even more relevant in view of the social and economic difficulties for the implementation of treatment. As reported by Saidon et al. (28), in Argentina only 9% of the patients with refractory epilepsy were treated with new AEDs, mainly for economic reasons, even more so, taking into account that new AEDs are more expensive in Argentina than in developed countries (29). Furthermore, in this study four patients with pure NESs were treated pharmacologically for status epilepticus. As described in other reports (2,30), this suggests that the mistaken diagnostic of status epilepticus occurred because of failures in the elementary steps to be followed to reach any medical diagnosis (differential diagnosis, examinations, review of medical records, etc.). These diagnostic pitfalls allowed the implementation of strong and potentially dangerous treatments based merely on observation.

Twenty-three percent of these patients were free of seizures at follow-up. This outcome is similar to that reported by other authors (31,32). In this study, all seizure-free patients had two good prognostic factors. In coincidence with Bowman (33), it was found that patients with an independent lifestyle are associated with a better prognosis. The second factor associated with better prospects was the acceptance of the nonepileptic nature of the spells. The therapeutic process we applied began by confronting the patient with the nonepileptic nature of the events; thus the first consideration should be the manner in which the diagnosis of psychogenic seizures is presented to the patient and family. It is important to be honest with the patient, showing a positive approach to the diagnosis.

Contrary to other authors' reports (7), it was not found that being female, the absence of coexisting epilepsy, or

the existence of psychiatric or psychological treatment were factors associated with a more favorable outcome. One reason for the poor results in these patients undergoing psychiatric/psychological treatment may be a poor knowledge of this disease by mental health professionals. It would be worthwhile for neurologists and mental health professionals to work together toward developing and assessing the efficacy of treatment strategies devised for specific groups of patients. In view of the potential morbidity of the disorder and its implications regarding the overall condition of the patient, diagnosis and treatment should occur as early and as quickly as possible. Further research is required to identify the optimal approach.

In spite of the difficulty of accurately defining the NES onset, we estimate it on the basis of history obtained through patients' contacts. The delay in reaching the diagnosis of NESs (1–30 years) may be attributable to two reasons. In the first place, mistakes may have been made when distinguishing NESs from ESs. The second probable factor includes the high costs and difficulties of implementing the video-EEG in this country, where only a small fraction of patients currently have access to this technology. A study (34) performed in a developed country has shown the overuse of health-care services for patients with NESs who do not benefit from AEDs and, due to misdiagnosis, typically experienced detrimental psychosocial and social/economic outcomes. Health resources are very limited, and this situation is worse in developing countries in view of the social and economic hardships.

Establishing adequate health care programs to facilitate access to new technology in public hospitals as well as the implementation of continuous education programs for general practitioners and neurologists could eventually improve the diagnosis and treatment of patients with NESs.

REFERENCES

1. Gates JR, Ramani V, Whalen S, et al. Ictal characteristics of pseudoseizures. *Arch Neurol* 1985;42:1183–7.
2. Leis AA, Ross MA, Summers AK. Psychogenic seizures: ictal characteristics and diagnostic pitfalls. *Neurology* 1992;42:95–9.
3. Gowers W. *Epilepsy and other chronic convulsive diseases: their causes, symptoms and treatment*. New York: Dover, 1964:115–49.
4. Ozkara C, Dreifuss FE. Differential diagnosis in pseudoepileptic seizures. *Epilepsia* 1993;34:294–8.
5. Leser RP. Psychogenic seizures. *Neurology* 1996;46:1499–507.
6. Boon PA, Williamson PD. The diagnosis of pseudoseizures. *Clin Neurol Neurosurg* 1993;95:1–8.
7. Meierkord H, Will B, Fish D, et al. The clinical features and prognosis of pseudoseizures diagnosed using video EEG telemetry. *Neurology* 1991;41:1643–6.
8. Devinsky O, Sanchez-Villasenor F, Vazquez, et al. Clinical profile of patients with epileptic and nonepileptic seizures. *Neurology* 1996;46:1530–3.
9. Commission on Classification and Terminology of the International League Against Epilepsy. Proposal for revised classification of epilepsy and epileptic syndromes. *Epilepsia* 1989;30:389–99.
10. Luther JS, McNamara JO, Carwile S, et al. Pseudoepileptic seizures: methods and video-analysis to aid diagnosis. *Ann Neurol* 1982;12:458–62.
11. Fakhoury T, Abou-Khalil B, Newman K. Psychogenic seizures in old age: a case report. *Epilepsia* 1993;34:1049–51.
12. Lancman ME, Asconapé JJ, Graves S, et al. Psychogenic seizures in children: long-term analysis of 43 cases. *J Child Neurol* 1994; 9:404–7.
13. Silva W, Polo G, Consalvo D, et al. Seizures involving the frontal lobe: a video-EEG analysis. *Epilepsia* 1997;38(suppl 7):s17.
14. Riley TL. Hysterical seizures [Letter]. *Arch Neurol* 1979;36:859–60.
15. Moore PM, Baker GA, McDade G, et al. Epilepsy, pseudoseizures and perceived family characteristics: a controlled study. *Epilepsy Res* 1994;18:75–83.
16. Alper K, Devinsky O, Perrine K, et al. Non-epileptic seizures in childhood sexual and physical abuse. *Neurology* 1993;43:1950–3.
17. Liske E, Forster FM. Pseudoseizures: a problem in the diagnosis and management of epileptic patients. *Neurology* 1964;14:41–9.
18. Willie E, Friedman D, Luders H, et al. Outcome of psychogenic seizures in children and adolescents compared with adults. *Neurology* 1991;41:742–4.
19. Krumholz A, Niedermeyer E. Psychogenic seizures: a clinical study with follow-up data. *Neurology* 1983;33:498–502.
20. Gulick TA, Spinks IP, King DW. Pseudoseizures: ictal phenomena. *Neurology* 1982;32:24–30.
21. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders*. 4th ed. DSM IV. Washington, DC: American Psychiatric Association, 1994.
22. Ljungberg L. Hysteria: a clinical, prognostic and genetic study. *Acta Psychiatr Neurol Scand* 1957;32(suppl 112):1–62.
23. Wilkus RJ, Dodrill CB, Thompson PM. Intensive EEG monitoring and psychological studies of patients with pseudoepileptic seizures. *Epilepsia* 1984;25:100–7.
24. Alper K, Devinsky O, Perrine K, et al. Psychiatric classification of non-conversion nonepileptic seizures. *Arch Neurol* 1995;52:199–201.
25. Henrichs TF, Tucker DM, Farha J, et al. MMPI indexes in the identification of patients evidencing pseudoseizures. *Epilepsia* 1988;29:184–7.
26. Vanderzant CW, Giordani B, Berent S, et al. Personality of patients with pseudoseizures. *Neurology* 1986;36:664–8.
27. Lesser RP. Psychogenic seizures. In: Pedley TA, Meldrum BS, eds. *Recent advances in epilepsy*. Edinburgh: Churchill Livingstone, 1985:273–96.
28. Saidon P, Giagante B, Gonzalez L, et al. Follow-up of 256 patients with epilepsy treated with new anticonvulsant drugs in a developing country. *Epilepsia* 1997;38(suppl 3):S74–5.
29. Kochen S. Costing of antiepileptic drugs. *Lancet* 1996;347:226.
30. Anonymous. Pseudostatus epilepticus. *Lancet* 1989;1:485.
31. Carter AB. The prognosis of certain hysterical symptoms. *BMJ* 1949;1:1076–9.
32. Lempert T, Schmidt D. Natural history and outcome of psychogenic seizures: a clinical study in 50 patients. *J Neurol* 1990;237:35–8.
33. Bowman ES. Nonepileptic seizures: psychiatric framework, treatment, and outcome. *Neurology* 1999;53(suppl 2):S84–8.
34. Roy CM, Guilliam FG, Faught E, et al. Nonepileptic psychogenic seizures. *Seizure* 1998;6:1.